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Case reports

Pyoderma gangrenosum of the vulva

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INTRODUCTION

Pyoderma gangrenosum is a rare disease that can effect skin on any part of the body. It was first described by Brunsting et al in 1930.[1] Ulcerated lesions can be single or multiple and are frequently acutely painful. A case of pyoderma gangrenosum occurring on the vulva is presented.

CASE REPORT

A 19-year-old university student was referred to the Vulva Clinic with a two-month history of vulvar pain. This had increased slowly and finally the patient noticed an ulcer on the vulva. There had been no gynaecological symptoms. She had had occasional mouth ulcers but none recently. The patient had never been sexually active, was a non-smoker and generally in good health with no history of inflammatory bowel disease. She had had atopic eczema in the past. She was allergic only to sulphonamides.

On examination there was a 2.5 cm ulcer on the right lower labia (Figure 1). This was acutely painful. The edge was raised with some surrounding tissue oedema. Blood vessels in the base of the ulcer were prominent. A number of investigations were instituted including biopsy of the lesion. These are presented in Table 1.

Regular analgesia, salt baths and metronidazole gel to control symptoms was commenced and she was

Figure 1 Lower right vulvar ulcer

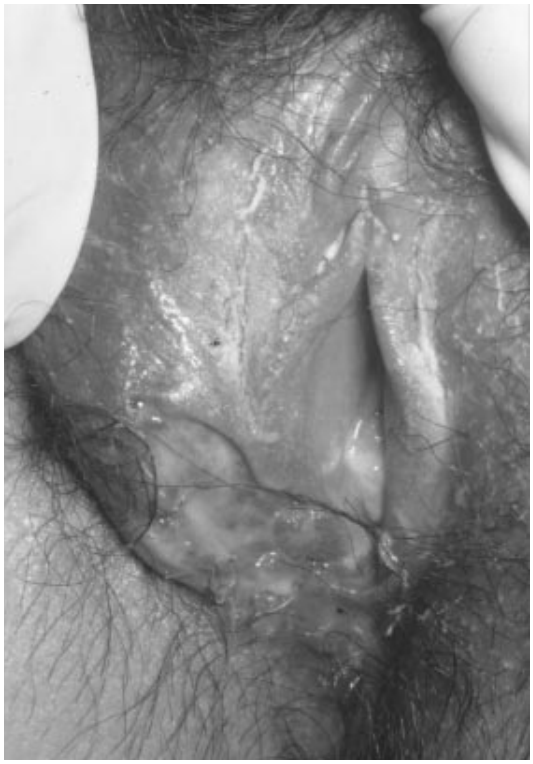

Table 1

Syphilis serology	negative
Vaginal swab	negative
Bacterial culture/stain	negative
Fungal culture/stain	negative
Herpes simplex viral culture	negative
Acid-fast bacilli culture/stain	negative
Chest X-ray	normal
Full blood count	normal
Liver/renal function	normal
ANA/Rh factor	normal
Tissue culture/stain bacteria Acid-fast bacilli fungi mycobacteria viruses	negative
Tissue biopsy	non-specific acute ulceration with mixed inflammatory infiltrate including plasma cells present in the stroma. Special stains for cytomegalovirus, herpes simplex, fungi and spirochaetes negative.

seen 10 days after the biopsy for review. The biopsy showed non-specific ulceration only but not all the cultures were complete. Pain control had been good and general measures were continued with the patient to return in a further two weeks. However, she returned early because of increasing pain and with bleeding from the ulcer base. She was admitted for pain control and for further investigation as the ulcer was showing no decrease in size. The Dermatology Department was consulted. They requested further cultures, all of which returned negative results. Their opinion was either Behcet's syndrome or pyoderma gangrenosum.

The patient was then reviewed by the Ophthalmology Department who found no evidence of ocular lesions consistent with Behcet's syndrome. In the absence of concurrent ocular or oral lesions, the diagnosis of pyoderma gangrenosum was made. She was commenced on prednisolone 30 mg daily reducing weekly by 5 mg. There was rapid improvement in her symptoms with this medication and she was discharged. Within four weeks with continuing dose reduction there had been almost complete resolution of the ulcer. Treatment was ceased after five weeks. There has been no recurrence of the ulcer since that time and the patient has been discharged from follow-up.

DISCUSSION

Pyoderma gangrenosum can occur at any age and has been reported in children as young as seven years. The most common age is 25–60.[2,3] The pathogenesis of pyoderma gangrenosum is unknown. Of patients, 27–38% will give a history of some form of trauma[2,3] and there is an association with inflammatory disease at other sites, more so in women than men,[3] in up to half of reported cases. No history of trauma or other association was found in this case. As is not infrequently the case, all investigations to identify an infective agent were negative as were markers of systemic inflammatory problems. The lower limbs are the most common sites for the ulceration followed by the trunk and upper limbs.

There has been one case reported in a caesarean section incision.[4] No other cases of vulvar disease could be found in the literature. Powell et al[2] refer to one patient with a perineal ulcer but it is not clear if this was a male or female patient.

As is common, there was a rapid response to steroids with symptomatic improvement within two to three days of commencement. Subsequent scarring at the ulcer site was minimal. While some patients will develop recurrent disease after cessation of treatment, this was not the case with our patient.

Histopathological changes in pyoderma gangrenosum vary as to where the biopsy is taken from relative to the lesion. There seem to be three commonly seen patterns.[2] A biopsy taken from the peripheral erythematous area demonstrates changes typical of a lymphocytic vasculitis: lymphocyte infiltration, endothelial swelling and fibrinoid necrosis of vessel walls. If the biopsy is taken more centrally a denser infiltrate of mixed lymphocytes and polymorphonuclear leucocytes is commonly seen. Changes indicative of early abscess formation can also be present. Finally, the specimens taken from the edge of the ulcer or from the ulcer floor typically demonstrate changes associated with abscess formation. The biopsies from our patient did not demonstrate any of the typical histological features associated with pyoderma gangrenosum.

While a rare disease, in any patient with ulceration and no identifiable causative agent, pyoderma gangrenosum should be considered.

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Lymphangioma vulva

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INTRODUCTION

Lymphangioma circumscriptum is a rare non-malignant skin tumour that presents as a local eruption of thin walled translucent vesicles on the skin, in groups or in patches. Lymphangioma circumscriptum can occur anywhere on the body surface but axillary folds, neck, proximal limbs and buccal mucosa are the most common sites.

Lymphangioma circumscriptum is an unusual entity in the anogenital region and may be clinically indistinguishable from genital warts. Biopsy of such a lesion is necessary to both confirm the diagnosis and to formulate appropriate treatment. To our knowledge, there have been only five cases of lymphangioma circumscriptum of the vulva reported in the literature.

We present a case of an extensive growth over the vulva that was treated successfully with wide and deep local excision of skin and subcutaneous tissue.

CASE REPORT

A 48-year-old parous woman attended the gynaecological clinic with a history of recurrent vesicular lesions over the vulva. Her main complaints were perineal pain, troublesome discharge and dyspareunia. Clinical examination revealed an 8 x 8 cm, wet bosselated condylomatous growth involving the labia majora and minora, and a large pedunculated polyp measuring 3 x 5 cm arising from the labia majora. There were well circumscribed multiple small vesicles over the mons pubis. These lesions looked like 'rice crisps' stuck on the skin.

There was no evidence of similar lesions elsewhere on the body.

Multiple vulval biopsy was consistent with lymphangioma circumscriptum. The patient was treated with oral antibiotics and underwent a wide local excision of the growth with all its subcutaneous tissue excised down to the deep fascia. The defect was closed primarily. She recovered without any postoperative complications. Two years after surgery there is no sign of recurrence or sexual problem.

Histopathology showed a lesion involving the papillary and superficial dermis composed of thin walled dilated intercommunicating vascular channels containing proteinaceous eosinophilic material and few lymphocytes. The polypoid growth was reported as a benign fibroepithelial polyp of the vulva.

DISCUSSION

Lymphangioma circumscriptum is a rare benign disorder of the lymphatics characterised by subcutaneous lymphatic cisterns communicating through dilated channels with superficial thin walled vesicles.[1] It affects the skin and subcutaneous tissue. It is characterised by the appearance of persistent clusters of thin walled vesicles, usually filled with clear colourless fluid, and occasionally discoloured by the presence of altered blood.

The most common symptom of lymphangioma circumscriptum of the vulva is troublesome oozing of clear fluid (lymph discharge), perineal swelling, dyspareunia or recurrent infection. Lymphangioma circumscriptum was initially described by Fox and Fox in 1978 under the name of lymphangiectodes.[2] Malcolm Morris first used the term lymphangioma circumscriptum in 1889.[3] Different classifications of lymphangioma circumscriptum have been proposed. The most commonly accepted one was put forward by Peachey et al in 1970.[4] Accordingly, lymphangioma circumscriptum is divided into two main groups: classic and localised. The classic forms are often extensive, usually present at birth or soon afterwards, involving areas where a limb joins the trunk and commonly recurring after surgical excision. The localised form

Figure 1 Bosselated condylomatous growth involving the labia majora and minora, with a large pedunculated polyp arising from labia majora

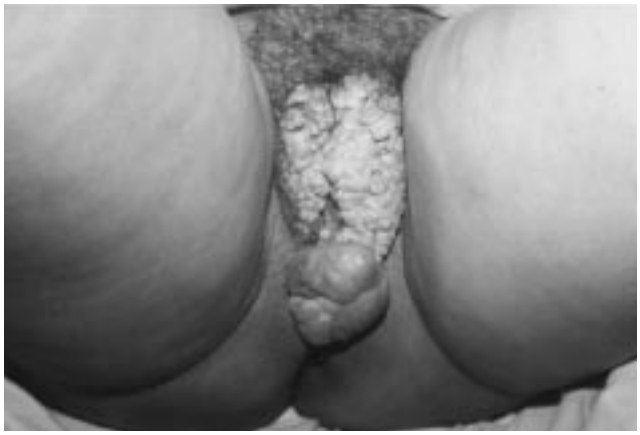
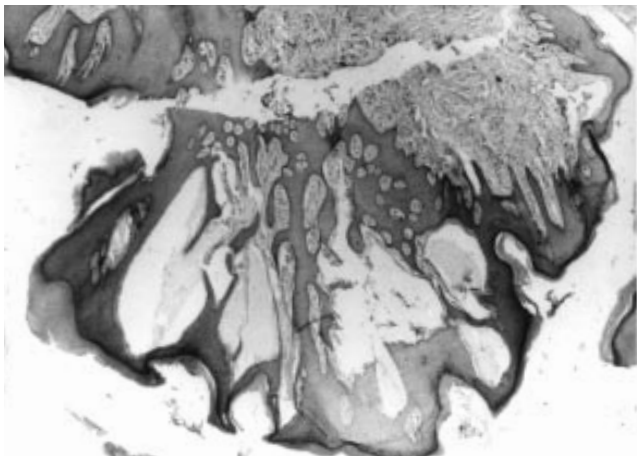


Figure 2 Histopathology of the vulval lesion, showing thin walled dilated intercommunicating vascular channels containing proteinaceous eosinophilic material and few lymphocytes within the papillary and superficial dermis



may appear at any age, usually involves areas of 1 cm^2 or less and has no definite area of predilection.

The pathological characteristics of this condition have been described by Whimster[5] in 1976 as collections of subcutaneous large lymphatic cisterns with thick muscular walls. These cisterns are connected through dilated lymphatics to the dermal lymphatics. The rhythmic contraction of the muscles in the cisterns raises the lymphatic pressure resulting in formation of skin vesicles. The importance of Whimster's work is that unless the deep cisterns are totally extirpated at the time of excision, recurrence is almost certain.

The clinical diagnosis of lymphangioma circumscriptum is, in most cases, easy but the differential diagnosis includes herpes simplex, herpes zoster and dermatitis herpetiformis. If the lesions are discoloured they may be confused with haemangioma and malignant melanoma.

Magnetic resonance imaging and lymphangiography are useful diagnostic tools that can help in accurate delineation of the lesion to assure its entire excision. Secondary infection and development of squamous cell carcinoma arising from the lesion are known.

The recent literature is optimistic about treatment and outcome. Lymphangioma circumscriptum has been treated in the past with multiple agents like liquid nitrogen, excisional surgery, electrocautery and radiotherapy. The current literature suggests that laser vaporisation with carbon dioxide or argon laser and excisional surgery have remarkable results. On the basis of the Whimster hypothesis,[5] we thought that treatment would be more successful and the cosmetic result better if the principal part of the operation was wide and deep excision of subcutaneous cisterns, leaving sufficient skin for primary suture. The cornerstone of therapy is total excision of the subcutaneous cisterns, failure to do so results in a 15–25% chance of recurrence.

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Tuberous sclerosis in pregnancy: a case report and review of the literature

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INTRODUCTION

Tuberous sclerosis is a rare autosomal dominant condition. This multi-system disease is characterised by a combination of clinical and pathological lesions. The classical clinical triad was alluded to by von Recklinghausen and later described by Bourneville[1] and includes mental retardation, seizures and facial angiofibroma (adenoma sebaceum). Common pathological lesions occur in the central nervous system (cortical tuber, subependymal nodule and calcification), skin and appendages (adenoma sebaceum commonly occurring on the forehead and naso-labial folds, subungual fibroma and hypopigmented macules called ash-leaf spots), kidneys (angiomyolipoma and cysts), heart (rhabdomyoma), lungs (lymphangiomyomatosis) and eyes (retinal phacoma). The association with pregnancy is probably under-reported due to good outcomes. A Medline search has revealed six cases of tuberous sclerosis in pregnancy.[2–5]

CASE REPORT

The patient was a 21-year-old gravida 4 para 0. She had suffered one miscarriage and undergone two terminations. She booked at the antenatal clinic at 30 weeks gestation when she volunteered a history of tuberous sclerosis which had been diagnosed at 18 months of age. She was of normal intelligence, displayed the characteristic adenoma sebaceum on the left cheek and had ash-leaf spots, mainly on the upper limbs.

In addition, she had epilepsy, which was well controlled with carbamazepine and valproate. Routine antenatal serological and haematological surveillance were within normal limits. An ultrasound assessment performed late in the pregnancy revealed no abnormalities. The pregnancy continued normally and labour was induced with prostaglandins at 41+ weeks. She had a normal delivery of a female infant. The baby was assessed as normal by the hospital's paediatricians and

there was no evidence of tuberous sclerosis. Follow-up review is planned.

DISCUSSION

Tuberous sclerosis is reported to have an incidence of 1 in 150,000 births.[6] Given the rarity of the condition, most obstetricians are unlikely to encounter this problem. Of the six reported cases, the diagnosis was made prior to the pregnancy in four cases. In the remaining two cases, the patients presented with a retroperitoneal mass, one of which required laparotomy during the antenatal period and the other postpartum. Both masses turned out to be angiolipomas of the kidney. The former case represents one of the three acute presentations; the other two presented with acute pneumothorax and acute haematuria respectively.

Patients encountered for the first time require careful clinical examination to look for cutaneous stigmata. Examination under a Wood's lamp is sometimes helpful in diagnosing ash-leaf lesions. A full cardiac, abdominal and funduscopic examination is mandatory to look for murmurs, kidney enlargement and hamartomas respectively.

Biochemical investigation should include electrolytes, urea and creatinine. Imaging modalities should include a computerised tomography scan of the brain and an ultrasound of the kidneys. Intravenous pyelogram and arteriogram can be used depending upon clinical indications, noting that their use in pregnancy might be restricted due to radiation exposure. Intelligence quotient testing might also be of use as mental retardation is reported to occur in 62% of patients.[7] Of the six case reports, three had normal intelligence, mental function was not mentioned in two, and one had mild mental retardation.

Seizures are noted to occur in over 90% of subjects. The seizures are difficult to control, often requiring high doses of anti-convulsants that place the fetus at risk of malformations.

Antenatal complications included two cases of preeclampsia (one of which was complicated by intrauterine fetal growth restriction) and one case of preterm premature rupture of membranes. Petrikovsky et al[5] concluded that renal involvement appeared to be the most important prognostic factor in pregnancies with tuberous sclerosis and suggested renal evaluation as part of pre-conceptual counselling and for prognostic purposes. Four of the women had abdominal deliveries, all occurring before 37 completed weeks of pregnancy. Three of the infants (50%) had tuberous sclerosis.

Prenatal diagnosis is not available at present. Anomaly ultrasound scans should aim at detecting intracranial lesions, cardiac abnormalities (rhabdomyoma) and renal size.

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Benign cystic mesothelioma: a diagnostic dilemma

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INTRODUCTION

Multicystic benign mesothelioma is a primary proliferative lesion of the mesothelium occurring commonly in the pelvic parietal and visceral peritoneum and rarely in pleura, pericardium and tunica vaginalis of the testis. Plaut in 1928 described these tumours as benign cystic mesothelioma,[1] and their mesothelial origin was confirmed by electron microscopy by Mennemeyer and Smith in 1979.[2] Over 140 cases have been published in the literature to date. Due to its rarity and ill-defined clinical signs and symptoms, investigation and management of this condition lacks uniformity. We present a case report with an ultrasound appearance very similar to that of an hydatidiform mole, and a review of the literature with a view to obtaining a definitive plan for investigating and treating this entity.

CASE REPORT

A 53-year-old woman presented to the gynaecology department with a five-year history of recurring episodes of pain and heaviness in the perineum and discomfort during defecation. Her complaints had worsened in the two months prior and increased on assuming erect posture. She did not have any

associated bladder or bowel disturbances. She was not on hormone replacement therapy, and did not give a history of previous pelvic surgery, endometriosis or asbestos exposure. She was nulliparous and had reached menopause ten months prior to presentation. There was no history of previous menstrual problems, anorexia or weight loss.

On examination, the abdomen was soft, non-tender and there was no palpable mass. Cervix and vagina were healthy. The uterus was of normal size with no adenexal enlargement, but the pouch of Douglas was tender. Per-rectal examination revealed a mass protruding from underneath the anterior rectal wall and the rectal mucosa was free.

Transvaginal ultrasound examination revealed a large vesicular mass posterior to the uterus with varying echogenicity and fluid filled vesicles, which closely resembled the snowstorm appearance of a hydatidiform mole (Figure 2). The size of the mass was 10.9 x 7.1 x 8.4 cm with ill-defined margins. Both uterus and ovaries were normal. The origin of the mass could not be ascertained. An impression of post-infective collection or hydropic degeneration of an extra-ectopic gestation was made. Tumour markers for ovarian neoplasm were not raised and beta-HCG was negative. Sigmoidoscopy was normal.

On diagnostic laparoscopy, a lobulated mass with multiple, clear fluid filled vesicles was seen arising from the pouch of Douglas. This again was similar to the grape like vesicles seen in a hydatidiform mole. The mass was not attached to the fallopian tube, ovary or the uterus, which were essentially normal.

Laparotomy was performed to excise the mass. At laparotomy, this vesicular mass (Figure 2) was arising from the posterior surface of the right broad ligament and was adherent to the bowel at several places, but was easily separated. The omentum and parietal peritoneum were studded with similar clear fluid filled vesicles. The uterus, ovaries, fallopian tubes and other abdominal organs were normal. The bulk of the mass was excised and a partial omentectomy performed. Postoperative recovery was uneventful.

Histological examination showed the mass to be a benign multicystic mesothelioma and the vesicles were lined with flattened mesothelial cells with no atypia or mitotic figures (Figure 3).

The patient presented with chronic persisting pelvic pain postoperatively, and minimal residual disease was confirmed on subsequent MRI scan. However, no evidence of disease progression has been noted with repeat MRI scan one year later.

DISCUSSION

There are suggestions in the literature[3] that this tumour shows female preponderance. The median age in males was 44.5 years. (range: 29–70) which was higher than that for females (median age: 36 years, range 13–79). These cases presented to different specialities, such as general surgery, gastroenterology, urology, obstetrics and gynaecology, etc which is why various investigations were carried out to diagnose the condition.

From the available information, we found that this entity seemed to be more common in the Caucasian

Figure 1 Clear fluid filled vesicles of mesothelioma

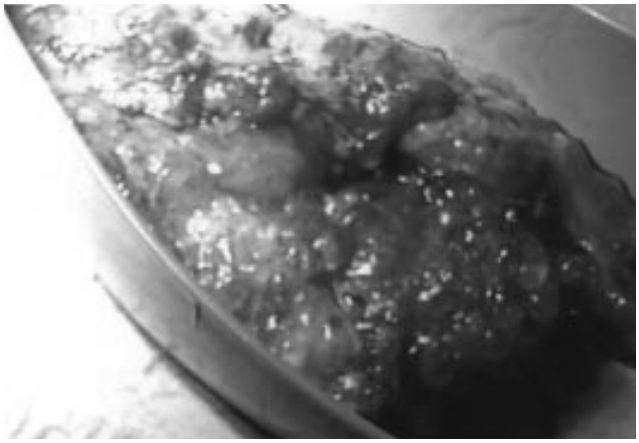


Figure 2 Snow storm appearance of multicystic mesothelioma similar to hydatidiform mole

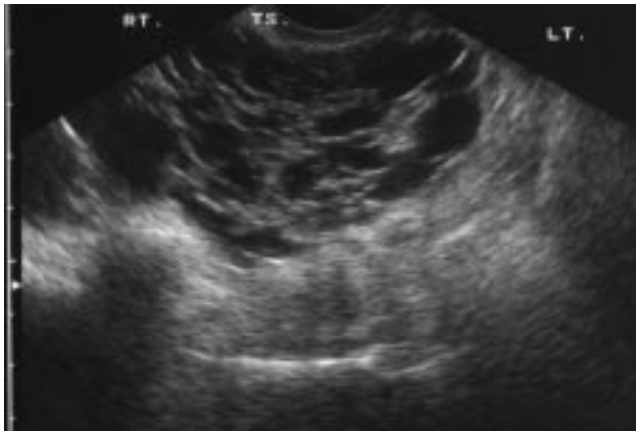
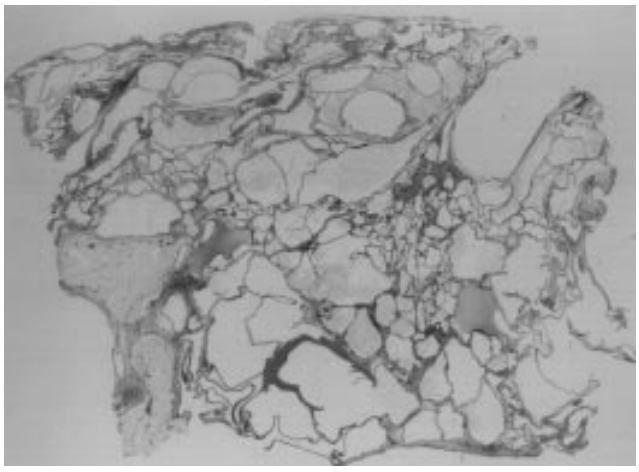


Figure 3 Microscopic appearance of cystic mesothelioma: thin walled cysts lined with flattened mesothelial cells



race, but information on race, parity and endometriosis was not available in all the cases. It is repeatedly stated that previous scarring due to surgery is one of the factors implicated in the aetiopathogenesis[3] of cystic mesothelioma and a history of prior surgery was documented in 28% (22/79) of the cases.

A common mode of presentation was pain with or without mass per abdomen. No distinguishing clinical signs were noted. In the majority of cases, symptoms lasted for several months before the patient came to hospital, but there were a few cases with relatively acute presentations. This indicates the slow growing nature of this tumour.

Rare associations with mucinous cystadenoma, pseudomyxoma peritonii, leiomyaomatosis peritonalis disseminata, and serous adenomatoid tumour of the uterus have been reported, and in our literature review we noted a recurrence rate of 33%. Although recurrences can either be single or multiple, one of the cases had 35 recurrences. All these were local recurrences and with no distant metastases. Single recurrences seemed to be more common, probably indicating residual tumour at the first operation.

There was no uniformity in the use of investigations to diagnose this condition. Final diagnosis was obtained in all cases after electronmicroscopy and immunohistochemistry. Presence of long slender apical microvilli, abundant intracytoplasmic organelles and filaments with hobnailed appearance of the cells are some of the distinguishing features of mesothelial cells.[3] Positive staining with keratins, EMA and Vimentin and inability to stain with endothelial markers like factor 8 and Ulex europaeus distinguishes these cells from endothelial cells of lymphangioma[3,5] origin. Recognition of these distinguishing features confirms the diagnosis.

Treatment was mainly in the form of open surgical resection. Catheter drainage has been successfully tried in three cases. One of them developed infection, which in fact helped in obliterating the cavity, and hence cure of the condition. Laparoscopic KTP laser ablation was successfully performed in one of the cases. GnRH analogues, Tamoxifen and sclerosants like tetracycline treatment have been tried; chemotherapy and radiotherapy have no value, as these tumour cells do not show mitoses.

CONCLUSION

In cases presenting with a chronic history of vague symptoms of discomfort, pain or mass per-abdomen, without loss of weight or appetite, multicystic mesothelioma should be suspected, especially if the subject is a Caucasian female in the reproductive age group. Ultrasound and laparoscopy combined with fine needle aspiration biopsy can be useful in obtaining definitive diagnosis prior to treatment. This would assist in planning a conservative surgical mode of treatment as opposed to laparotomy, which is preferable as this tumour has a high rate of recurrence and the patients are at risk of multiple laparotomies. Laparoscopic laser ablation should be considered as the first line of management in tumours limited to the pelvis and not involving vital structures like the bowel. However, such treatment will be unsuitable in cases with extensive tumour spread and adhesions. Complete clearance of the tumour should be the aim of a primary operation to avoid recurrences.

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Staphylococcus septicaemia and massive vulvar oedema in pregnancy

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INTRODUCTION

Oedema is the presence of abnormally large amounts of interstitial fluid, which can be generalised or restricted to a single area. Increased vascular permeability, vascular proliferation and venous congestion in the vagina and vulva are common signs of early pregnancy. Hence, mild labial swelling during pregnancy is a common occurrence. However, massive vulvar oedema is a rare condition and only five previously reported cases have been found.[1–4]

CASE REPORT

A 32-year-old woman, gravida 1, para 0, at 35 weeks gestation presented to the hospital with a one-day

history of feeling unwell, fever and one-week history of lower abdominal pain over the pubic symphysis which was constant and gradually progressed to produce near immobility. There was no history of pelvic trauma or fracture. She complained of mild dysuria but had no bowel symptoms or vaginal discharge.

She had been bitten on her right thumb by a dog three weeks prior to admission with features of sheath infection and cellulitis; the wound was cleansed with antiseptics and she did not receive any antibiotics.

Her antenatal screen was unremarkable except for her low rubella immunity. Morphology ultrasound scan showed no fetal anomaly.

On admission, her temperature was 39°C and physical examination was unremarkable except for the abdomen being tender over the pubic symphysis area. The admission diagnosis was possible urinary tract infection, broad ligament strain and viral illness.

The empiric treatment was bed rest, ampicillin and regular paracetamol. Her haemoglobin was 112 g/L, platelet count 209 x 10^9, white cell count 15.2 x 10^9 with differentials of 94% neutrophils and 3% lymphocytes. Her electrolytes and liver function tests were within normal range with albumin level of 31 g/L. Urinalysis revealed no abnormality. On Day 2 of her admission, her blood culture grew *Staphylococcus aureus*, which was sensitive to flucloxacillin.

She was treated with high dose intravenous flucloxacillin 2 g four times daily. There were no peripheral stigmata of endocarditis, no murmurs were heard and her jugular venous pressure was not elevated. Vulvar oedema was noted, more on the right than left. The vulval skin was red but not fluctuant and per rectum examination showed no ischio-rectal tenderness.

On day 3, massive labial oedema developed on the right side and rapidly progressed to involve both sides with sacral oedema over the following few days (Figure 1). The patient complained of localised vulvar pain that restricted her mobility but had no difficulty with urination or defecation.

Repeat blood tests showed Hb 90 g/L, plt 200 x 10^9, WCC 10.2 x 10^9 with 79% neutrophils, 9% lymphocytes, 10% monocytes; electrolytes and liver function tests were normal with albumin 23 g/L.

Magnetic resonance imaging showed diastasis of the symphysis pubis, associated with perineal soft tissue abnormality around the vagina and posterior to the pubic symphysis together with mild right inguinal lymphadenopathy. There was no pelvic collection or osteomyelitis demonstrated and both the pubic bones and hip joints were normal.

Ultrasound of the pelvis showed no obvious pelvic collection and a translabial scan showed gross swelling of labia but no collection. An echocardiogram was also performed which showed no vegetation with left ventricular ejection fraction of 65% with trivial pericardial effusion noted. On day 7 of admission, her Hb was 89 g/L, plt 258 x 10^9, albumin 24 g/L, erythrocyte sedimentation rate > 140, C-reactive protein (CRP) 138 mg/L and her thrombophilia screen was essentially normal.

The differential diagnosis included inferior vena cava obstruction causing the swelling (either extensively or partially); lymphatic obstruction possibly due to a reaction to localised infection; focal infection in the symphysis or elsewhere in the pelvis.

A caesarean section was performed on Day 9 under general anaesthesia instead of a regional block due to the risk of infection, and resulted in the delivery of a live male infant of 3300 g with good Apgar scores. No ascites or pelvic congestion was noted intraoperatively.

Routine perineal care was maintained postoperatively. The labial swelling had greatly resolved by the third day following delivery. However, her suprapubic pain persisted and subsequent bone scan showed an increased uptake at the pubic bones with widening of the pubic symphysis as well as an increased vascularity over the region of involuting uterus giving a differential diagnosis of osteomyelitis and reactive change from pregnancy-related sprain.

Computerised tomography scan of the pelvis was arranged and confirmed osteomyelitis. She was discharged home on day 13 after delivery with a Cad pump for continuous IV flucloxacillin for six weeks, followed by another six weeks orally. Follow-up examination after the course of antibiotics completed was unremarkable.

Figure 1 Massive lateral oedema at 35 weeks gestation

DISCUSSION

Pregnancy has profound effects on the vascular system and the skin but most changes will revert to normal after delivery. Fluid retention resulting from renin-angiotensin activation predisposes to oedema formation due to an increase in hydrostatic pressure and a drop in oncotic pressure. The compression of the inferior vena cava by the enlarging uterus results in congestive-type oedema in the lower part of the body, particularly the lower extremities.

The vulva has thin epithelium and loose connective tissue, which render it an area of high compliance, particularly susceptible to mild disturbances in the pressure-volume relationship and leading to a large accumulation of fluid.

The possible cause leading to the massive vulvar oedema in our case was localised infection in the pubic symphysis together with hypoalbuminaemia and low oncotic pressure superimposed on lymphatic and venous obstruction caused by the gravid uterus. The dog bite was the likely source of *Staphylococcus aureus* bacteraemia, which led to osteomyelitis.

Massive vulvar oedema in pregnancy is a rare occurrence and some of the potential causes in the differential diagnosis include infectious disease, neoplasms, congenital anomalies, trauma, iatrogenic inflammatory conditions and metabolic disorders.[1]

Some of these causes may coincide with pregnancy while others are aggravated by it. Known pregnancy-associated causes are multiple gestation, preeclampsia, obstructed labour[1] and tocolytic therapy.[2,3]

In the five cases found in the literature, delivery was the single factor leading to the disappearance of vulvar oedema and the mode of delivery was caesarean section due to the vulvar pathology.

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Teratoma of the placenta

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ABSTRACT

Primary non-trophoblastic tumours of the placenta reported to date are chorioangioma and teratoma, both of which are extremely rare. A case of teratoma in a term placenta is reported.

CASE REPORT

A 25-year-old gravida 2 with Class III NYHA rheumatic heart disease and chronic renal failure complicating pregnancy underwent a normal delivery of a female infant weighing 2500 g with Apgar scores of 8 and 10. The placenta weighed 400 g and the cord length was 44 cm. A smooth thick-walled cyst containing clear yellowish fluid about 5 cm x 3.5 cm was found within the membranes.

Microscopic examination of the placental tissue showed vascularised chorionic villi and decidual plate with normal maternal blood vessels. The chorioamniotic membrane showed no specific lesion. The wall of the cyst was lined by mature pigmented keratinising squamous epithelium with attached pilosebaceous units, and focally by mucin-producing columnar epithelium, with underlying lobules of mature adipose tissue with smooth muscle fibres, nerve bundles, skeletal muscle, blood vessels, ganglion cells and a nodule of mature cartilage. The appearances were those of mature cystic teratoma. Further fresh portions showed mature bone and neuroglial tissue in one margin with neuroepithelial tubules. There was no evidence of malignancy.

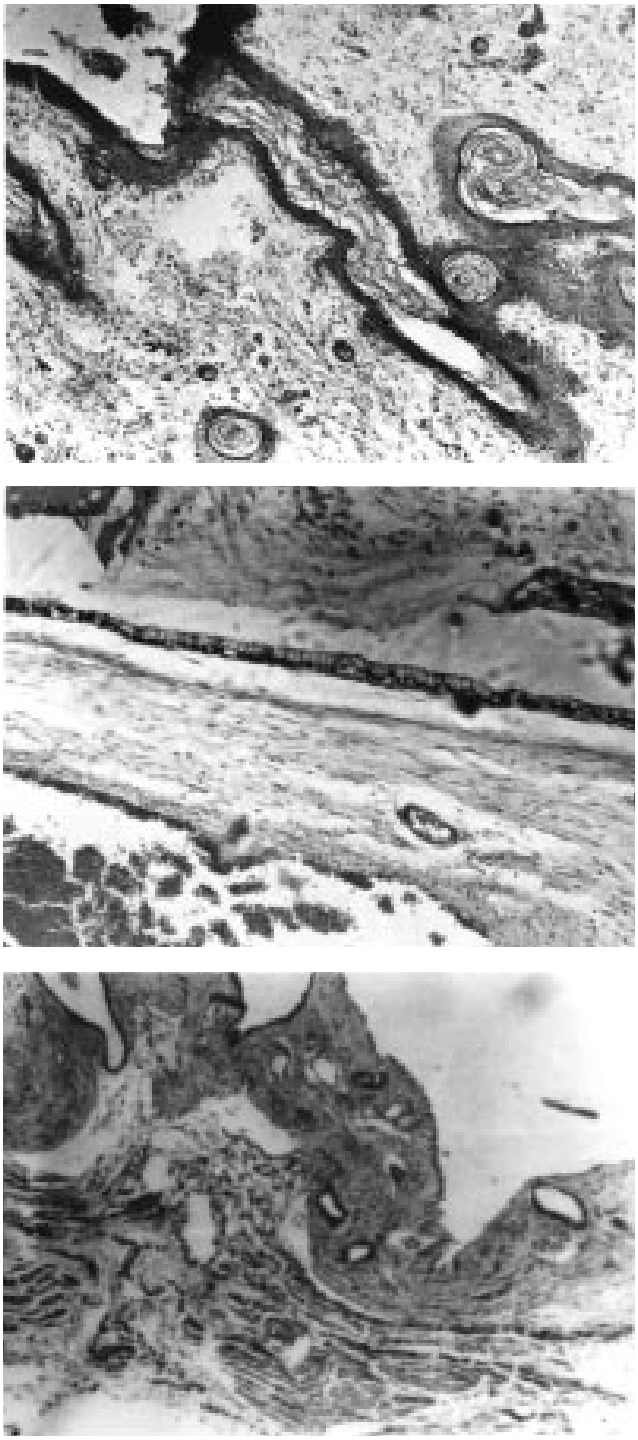
DISCUSSION

The first case of teratoma was described by Morville[1] in 1925 and since then only eight cases have been reported. Teratomas are neoplasms which produce a variety of tissues foreign to the part of the body in which they occur. It is generally accepted that they arise from totipotent embryonic germ cells and are thus capable of giving rise to virtually any type of tissue. The sites of occurrence of teratoma are ovary,

testis, anterior mediastinum, retroperitoneum and the presacral and coccygeal regions.

It is assumed that placental teratomas result from abnormal migration of germ cells from the dorsal wall of the yolk sac. These germ cells migrate into primitive gut wall and continue through the mesothelial coat into the rest of the mesentery to the dorsal body wall and genital fold during the first three months of gestation. There is evagination of primitive gut into the umbilical cord and the primordial germ cells migrate into the connective tissue between amnion and fetus into the extraplacental membrane between amnion and chorion.[2]

Figure 1 Photomicrographs show sections of placental cystic teratoma comprising cysts lined by keratinising squamous epithelium, columnar epithielium and neuroectodermal tissue (top to bottom)



A second hypothesis is that these lesions are actually extreme examples of fetus acardius amorphus,[3] an explanation favoured by Benirshke and Driscoll.[4] Fox,[2] however believes these entities can be differentiated by the following criteria; (i) Fetus acardius amorphus has a separate umbilical cord; and (ii) Fetus acardius amorphus usually displays some axial development so that cranial and caudal ends can be identified.

All of the placental teratomas reported so for have been instances of mature teratoma. The content of calcified tissue might at times be apparent on abdominal radiography. They are probably of no clinical significance, although Fujikura and Wellings[5] report a teratoma with a severely malformed infant. Whether they are separate tumours or extreme forms of fetus amorphus is not definitely known.

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Parasitic ovarian dermoid tumour

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INTRODUCTION

Mature teratoma is one of the most common ovarian tumours, but parasitic ovarian dermoid tumours are extremely rare.[1] Less than 25 cases have been reported[2] and the aetiology of these teratomas is obscure. However, they are found more frequently in women, suggesting an association with female reproductive organs.[1] In this report we describe a case of parasitic ovarian dermoid of the greater omentum and a dermoid cyst of the left ovary.

CASE REPORT

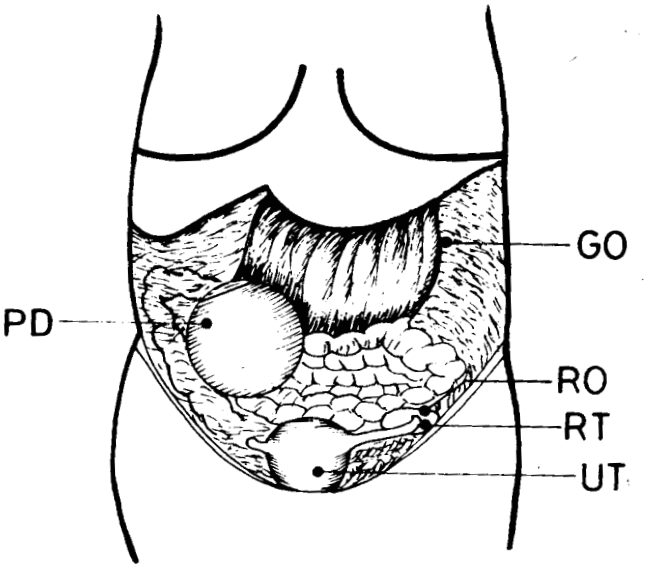
A 50-year-old multiparous woman was admitted with complaints of an abdominal lump and pain off and on for the past 20 years. There was no significant recent increase in the size of the tumour. There was no history of acute pain, or bladder or bowel complaint. Her past medical history was insignificant. The patient was menstruating normally and all her deliveries were full term, normal births conducted at home. Her last child had been born 13 years previously.

General physical examination was normal. Abdominal examination revealed a well defined, non-tender, 10 cm × 10 cm smooth, firm mass with restricted mobility in the right iliac fossa. There was no free fluid or hepatosplenomegaly.

Bimanual pelvic examination revealed first-degree cervical descent with minimal enterocoele and rectocoele. The uterus was parous size and mobile. The abdominal mass could be tipped high up in the right fornix and the other fornices were free and non-tender. A provisional diagnosis of ovarian tumour was made.

Routine haemotological and biochemical investigations, chest X-ray and ECG were normal. Ultrasound examination showed an 11 × 9 × 8.5 cm mass in the right pelvis with heterogeneous echotexture, irregular walls, and dense echogenic areas were seen within the mass. The right ovary was not seen separately and the left ovary was normal.

Figure 1 Diagrammatic representatation of explorative laparotomy findings



GO = greater omentum; PD = parasitic dermoid; RO = right ovary; RT = right fallopian tube; UT = uterus

On exploratory laparotomy, a normal uterus with only the round ligament attached to the right cornua was found, however, the right fallopian tube and ovary could not be traced. The left tube was normal but the left ovary was firm, irregular and slightly larger than normal. A large, firm to hard mass, approximately 10 × 10 cm, was found to be adherent to the right pelvic wall, omentum and bowel (Figure 1).

The rest of the abdomen was normal. There was no free fluid, and peritoneal washings were taken. The tumour was carefully dissected from the surrounding omentum, bowel and right pelvic wall ensuring complete haemostasis. Surprisingly, there was no major pedicle that needed to be clamped.

Considering her age and the appearance of the left ovary, a total hysterectomy with left salpingooophorectomy was performed.

The cut section of the right mass showed a dermoid consisting of sebaceous material and hair, and histopathology confirmed a benign cystic teratoma with remenants of ovarian stroma. The left ovarian cyst was a small benign dermoid tumour.

DISCUSSION

A review of the literature found 22 cases of teratoma of the greater omentum and three cases of teratoma of the lesser omentum. Their real incidence is unknown. They are more frequently found in women of reproductive age.[1] The aetiology of omental teratoma is poorly understood. The three main theories which have been proposed to explain the omental localisation of these tumours are: (i) primary teratoma of the

omentum originating from displaced germ cells; (ii) teratoma developing in a supernumerary ovary in the omentum: and (iii) autoamputation of an ovarian dermoid with secondary implantation into the greater omentum. The latter is most common and appears likely in the present case.[3,4]

The clinical presentation is usually abdominal pain, but unusual presentations such as abdominal distension, and lumbosacral neuropathy due to compression of the lumbosacral plexus may occur. One-third of cases reported were asymptomatic.[5–8]

On physical examination, omental teratomas are palpated as a mobile round abdominal mass. Localisation may vary from a pelvic tumour simulating an adnexal mass to periumbilical or upper abdominal mass. The mass can change its location on subsequent re-examination. Abdominal X-ray may visualise a teratoma as a radio-opaque mass, sometimes with calcification, but it may also be radiolucent. Abdominal or pelvic ultrasound with colour Doppler and computerised tomography may give additional information.

The treatment of choice is exploratory laparotomy. Tumour dissection and resection with partial omentectomy usually suffices.[9]

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Hymen re-formation after hymenotomy associated with pregnancy

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CASE REPORT

A healthy, 32-year-old pregnant woman came to our delivery room at 37 weeks gestation in her second pregnancy. A healthy, live-born male baby was delivered via caesarean section due to a breech presentation.

The operation went smoothly; however, a thick fibrotic membrane existed at the vaginal introitus, blocking the passage of lochia (Figure 1). An electrosurgical incision was performed on the membrane to create an opening (Figure 2). The postpartum course was uneventful, and the patient was discharged home without any specific complication.

When she was 13 years old she had experienced low abdominal distension, pain, urinary retention, and amenorrhea, and an imperforate hymen combined with haematocolpometra was diagnosed. A successful hymenotomy relieved all of her symptoms and her menstruation was normal for the next five years.

At age 18, she underwent significant intentional weight loss. Six months later, normal menstruation ceased and this situation persisted for about one year, however, there were no significant symptoms similar to her previous amenorrhea. When she sought medical help, a thin hymen membrane was discovered and another excision was undertaken. Surprisingly, neither haematocolpos nor haematometra existed.

She later returned to normal eating habits and her regular menstrual cycle resumed. She was married, and became pregnant when she was 31 years old. The first baby was born by caesarean section delivery due to cephalo-pelvic disproportion. According to her medical records, a narrow vaginal tract combined with a small hymen orifice was noted at that time; however, the lochia could still be passed. Further surgical treatment was suggested to ensure a better vaginal outlet, but the patient refused this procedure.

On further questioning, the patient stated that dyspareunia and profuse mucous discharge were common. She indicated that her husband had the problem of premature ejaculation and she seldom, if ever, felt penetration. Sexual activity had continued

Figure 1 A thick, obstructive hymen sheet noted at the vaginal introitus, inhibiting any leakage of lochia

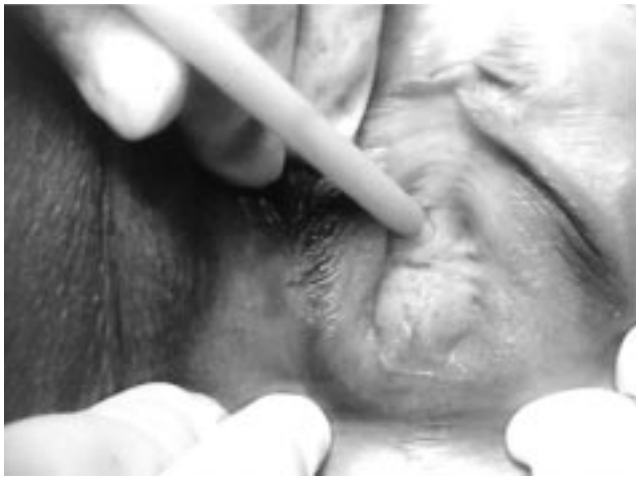
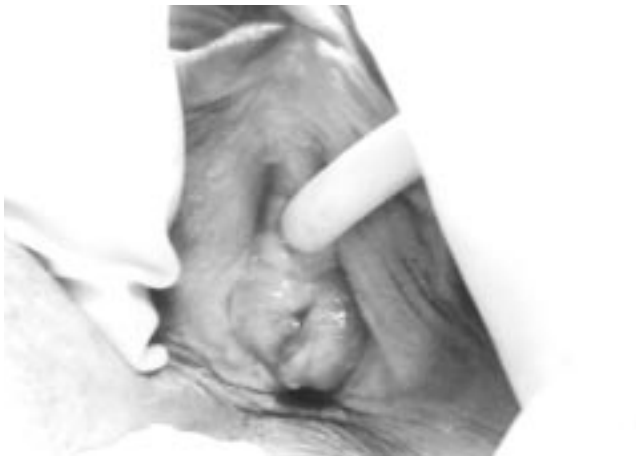


Figure 2 An electrosurgical incision was performed to ensure the passage of lochia



until the fifth month of her first pregnancy, but ceased after the first two months of the second pregnancy. She rejected further treatment and tissue biopsy.

DISCUSSION

To the best of our knowledge, this is the first case report in which an imperforate hymen was seen in pregnancy. Berkowitz suggested that an acquired imperforate hymen could be a result of adhesive, healing-like process after trauma[1] and it is possible that this may have been the mechanism in this patient during her pregnancy. However, it is impossible to pinpoint a single aetiology to fully explain such a phenomenon.

Although our patient claimed to have regular sexual activity, the quality of her sexual life was doubtful. Whether persistent sexual intercourse should maintain a hymenal opening is controversial, and the possible effect of ceasing intercourse to this case cannot be neglected. Without any sexual activity for six months during her second pregnancy, a concentric membrane was formed from the hymen.

Reports have stated that vaginal adenosis associated with imperforate hymen is not uncommon, with failure of upward migrating squamous epithelial cells of the urogenital sinus leaving remnants of Müllerian endometrium-like epithelium within the vaginal wall and hymen rim surface.[2] This patient had constant profuse mucous discharge and a narrow vaginal tract, which are specific characteristics for vaginal adenosis.

Two similar incidents of hymenal occlusion occurred secondarily after the absence of menstruation, one at the age of 19 after amenorrhea for one year and another at the end of her second pregnancy. We suspect that a strong correlation existed between menstruation and this acquired membrane. Koks et al[3] noted that in the menstrual phase, expression of matrix metalloproteinase (MMP) and tissue inhibitor of metalloproteinase (TIMP) is significant. Both enzymes are present in the endometrium and counteract each other.

Each month, menstrual shedding is evoked by activation of MMP, which is responsible for tissue lyses and breakdown. During the follicular phase, MMP return to an inactivate state and TIMP promotes the stability of endometrium tissue until the next menstruation. In pregnancy or any secondary amenorrhea, MMP is constantly in an inactive state, allowing TIMP to stabilise endometrium tissue through an unopposed healing, adhesive mechanism. If extrauterine endometrial tissue exists, as in vaginal adenosis, such tissue responds equally to the effect of TIMP.

In conclusion, we believe that, in the absence of menstruation, and without the impact of sexual intercourse, a concentric fibrotic process can form from the hymen rim. Eventually, an acquired pseudo-membrane was formed.

This case is important for several reasons. An imperforate hymen does not exclude possible antecedent vaginal penetration, and evaluation of an imperforate hymen needs not only full acknowledgement of its clinical symptoms but also its pathogenesis and embryogenesis. Further, single hymenotomy does not fully assure vaginal introital patency or prevent possible fibrotic process on the hymen rim. In this case, in the absence of additional treatments such as z-plasty or other pelvic reconstructive surgery, we expect that it is highly likely that another acquired, obstructive hymenal membrane would be seen in another episode of secondary amenorrhea.

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Borderline mucinous tumour with mural nodule of signet ring adenocarcinoma

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INTRODUCTION

The finding of one or more solid nodules in the wall of an otherwise unremarkable ovarian mucinous tumour is rare. According to the literature,[1–4] the prognosis depends on the solid nodule component. We describe a high-grade borderline mucinous tumour of the intestinal type with an intramural nodule of signet ring cell adenocarcinoma. To the best of our knowledge, no such case has been documented before.

CASE REPORT

Clinical features

A 60-year-old, gravida 3, para 3, Caucasian woman presented in March 1998, with a nine-month history of constant, low grade right iliac fossa pain associated with frequency, nocturia and incomplete voiding. She was otherwise asymptomatic. She had no significant past medical or family history of cancer.

Physical examination revealed an abdominopelvic mass extending to the umbilicus. A pelvic ultrasound revealed an 11 cm solid cystic mass occupying virtually the entire pelvis. There were no obvious metastases but calculi were noted in the gall bladder. Preoperative investigations included full blood examination, urea, electrolytes, creatinine and liver function tests, all of which were normal. Her serum CA125 was elevated at 149 u/mL (normal < 35). The chest X-ray showed a normal-sized heart, hyperinflated lungs and a right pleural effusion.

Findings at laparotomy included a large right ovarian tumour, diagnosed as a carcinoma on frozen section. There was no evidence of spread or ascites. Peritoneal washings were taken and a total abdominal hysterectomy, bilateral salpingooophorectomy, subcolic omentectomy, appendicectomy, and resection of the right pelvic and paraaortic lymph nodes were performed. No further treatment was given.

At six months postoperatively, the patient only experienced a little wound discomfort with movement, which prevented her from playing golf. Investigations including a barium enema, CEA, CA125 and inhibin were all normal. Her Ca 19.9 started to rise gradually from January 1999. In March she underwent a right mastectomy for ductal carcinoma in situ. In May 2000 she developed increasing constipation and abdominal pain. A CT scan revealed soft masses in the omentum and thickening on the left side. The Ca 19.9 was 363 (normal < 37).

At laparotomy, a hard nodule of tumour involved the gastrocolic ligament and transverse colon; miliary disease overlying the diaphragm and a small deposit in the pelvis were noted. There were no enlarged lymph nodes. Subtotal transverse colectomy, gastrocolic omentectomy and optimal debulking to < 0.5 cm^3 were carried out. Subsequently she received nine cycles of carboplatin and paclitaxel (Taxol) and her Ca 19.9 had fallen to 66 by January 2001.

Pathological features

Gross examination of the initial surgical specimen revealed a large, smooth and shiny-surfaced ovarian tumour that measured 150 x 100 x 80 mm. On sectioning it was polycystic and filled with thick mucinous tenacious material. A single creamy and homogeneous solid 50 x 20 mm mural nodule was seen at the periphery (Figure 1). The capsule was smooth but contained a further 5 mm nodule.

Microscopically there were numerous cysts, packed closely together, separated by thin fibrous septae containing occasional inflammatory cells. The cysts were lined by stratified mucin-secreting epithelium, up to three layers thick. There was moderate nuclear atypia and mitotic figures were easily seen. Goblet cells were prominent. Occasional argentaffine and argyrophil granules were observed in the cytoplasm. There was no

Figure 1 Multiloculated mucinous ovarian tumour with a prominent solid nodule in its wall

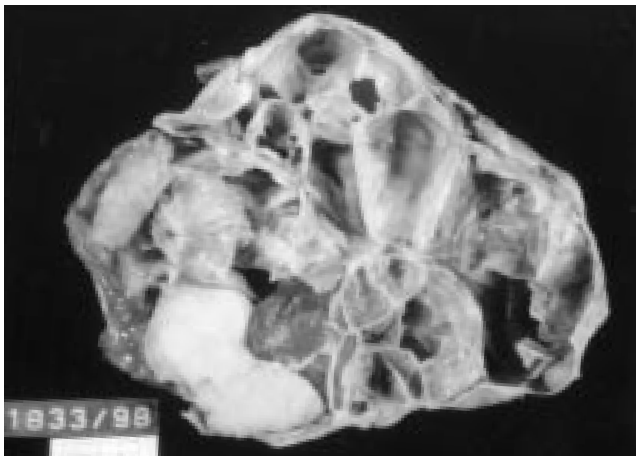

Figure 2 High power examination reveals the nodule to be composed of signet ring cells, this appearance being due to the presence of intracytoplasmic mucin, which displaces the nucleus to the periphery

evidence of stromal and/or vascular invasion. The solid nodule was well demarcated from the mucinous epithelium on low power examination. On high power the nodule consisted exclusively of round or oval cells distended by vacuoles, which displaced the nuclei, giving a signet ring appearance (Figure 2). Alcian blue and periodic acid schiff (PAS) stains showed the presence of intracellular mucin. The nuclei were small and pleomorphic, with coarse chromatin and prominent nucleoli. There was no transition between the mucinous cells of the cystic component and the signet ring cells in the nodule. Although the nodule was well circumscribed, there was invasion of the surrounding stroma, including lymphovascular involvement.

The histopathology of the recurrence confirmed poorly differentiated mucinous cystadenocarcinoma.

DISCUSSION

Benign, borderline and malignant mucinous tumour of the ovary may be associated with solid intramural nodules on rare occasions. This is a puzzling, heterogeneous group of lesions, which differ markedly in their histological features from the mucinous tumours themselves. The nodules have been classified as (i) anaplastic carcinomas; (ii) sarcomas of varying types; (iii) carcinosarcoma; (iv) sarcoma-like nodules; (v) mixed nodules; and (vi) leiomyoma.[5,6] Approximately 16 cases of anaplastic-carcinomatous nodules have been reported to date.[6]

To our knowledge, no case of mural nodules composed purely of signet ring cells has been reported to date. The presence of such endodermal-derived component in a mucinous neoplasm may lend credence to the theory of monodermal differentiation of a teratoma, in at least some cases.

The significance of mural nodules is that the prognosis depends on the type of nodules which, if malignant, overrides that of the main epithelial neoplasm. Thus most patients died rapidly from their tumour if the nodules were sarcomatous or anaplastic-carcinomatous.

From a practical point of view, the pathologist should search carefully for mural nodules associated with mucinous tumours, as their presence may alter the prognosis and treatment.

It remains to be seen whether the chemotherapy which our patient was given will maintain her remission.

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A case of splenic abscess in the postpartum period

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CASE REPORT

A 28-year-old nurse (gravida 2, para 1) was admitted at term plus 13 days to a community hospital for an artificial rupture of her membranes. Upon rupture, a note was made of the offensive odour of the liquor. Two hours later, the patient was noted to be tachycardic (120 bpm) and febrile (37.6°C). A high vaginal swab was obtained and a single dose of benzyl penicillin 600 mg (IM) was administered.

Twelve hours later, a non-elective lower uterine segment caesarean section was performed due to failure to progress. During the procedure, the patient was tachycardic (140–150 bpm) and febrile (37.9°C). A 4060 g boy was delivered. While in recovery, the patient

complained of a severe pain in the left shoulder tip. Over the next two days, the patient remained tachycardic (120 bpm), and complained of persisting shoulder tip pain. Results from the high vaginal swab were non-diagnostic. She was commenced on oral antibiotics (cephalexin and metronidazole) and discharged on day four.

On day six, the patient re-presented to hospital complaining of tachycardia and tachypnoea, persistence of the shoulder tip pain, and the development of a left pleuritic chest pain. A chest x-ray showed collapse/consolidation of the left lower zone. A ventilation-perfusion (V/Q) scan revealed a moderate-sized subsegmental perfusion abnormality involving the basal segments of the left lower zone. A diagnosis of pulmonary embolism was suggested and she was commenced on heparin (5000 units, subcutaneous, qid). By day nine, the patient had developed a fever (39ºC), chills and rigors. An abdominal ultrasound showed a left perinephric and perisplenic collection of 250 mL of fluid.

She was commenced on intravenous antibiotics (cephalexin, metronidazole) and transferred to a tertiary hospital. On admission, she was febrile (38.3ºC), tachycardic (130 bpm) and her blood pressure was normal. Her respirations were 24 per minute, and oxygen saturation was 95% on room air. Examination revealed reduced breath sounds in the left chest and marked tenderness in the left upper abdominal quadrant. Investigations showed the patient was hypoxic (pO_2 74 mmHg), with a high white cell count (25 × 10^9/L). The urine contained moderate blood and leucocytes, but microscopy and culture were unremarkable. Blood cultures were negative. The patient was treated for a suspected pulmonary embolism with an infusion of heparin and oral warfarin. In addition, she was commenced on intravenous antibiotics (ceftriaxone and gentamicin).

Over the next two days, the dyspnoea improved but she remained febrile (38.9ºC) and tachycardic. Hence, intravenous timentin was added to the antibiotic regimen and an abdominal CT scan was ordered. The scan showed a 12 cm × 4 cm × 4 cm subcapsular splenic collection (Figure 1). A diagnosis of a splenic abscess was suspected. The initial diagnosis of pulmonary embolism was now questioned because it was recognised that splenic pathology can cause diaphragmatic irritation, with resultant pulmonary effusion and basal atelectasis. A repeat V/Q scan excluded pulmonary embolism on the basis of a V/Q abnormality that corresponded with the pleural fluid seen on the chest X-ray.

The anticoagulants were stopped and their effect corrected with an infusion of fresh frozen plasma and intravenous vitamin K. A transfusion of two units of packed cells was also given to correct a low haemoglobin (78 g/L). An ultrasound-guided drainage of the splenic collection was then performed using a Gibson catheter. Approximately 75 mL of malodorous pink fluid was drained from the collection. Cultures showed profuse growth of *Enterococcus* and *Prevotella bivia*. Intravenous amoxycillin was commenced. A sinogram performed three days later showed an elliptical cavity within the spleen. The contents were leaking into the peritoneal cavity and subphrenic space. There was no bowel fistula identified. The patient made an uneventful recovery, and the drain was removed at 14 days. She remains well at three months post delivery.

DISCUSSION

The development of a splenic abscess is a rare event, and is typically characterised by non-specific symptoms and signs of sepsis.[1–3] Because of this, the diagnosis is often overlooked. The majority of splenic abscesses appear to result from metastatic haematogenous infection (especially intravenous drug use), and appear to be more common in immunosuppressed patients (eg human immunodeficiency virus). Alternatively, they can result as a secondary event from infection of a traumatic or spontaneous splenic haematoma. Typical symptoms include fever, chills, and left upper quadrant tenderness. On investigation, the patients will usually have a leucocytosis, left pleural effusion on chest x-ray, and an abdominal computerised tomography scan is the most accurate investigation to confirm the diagnosis. The infections may be either polymicrobial or monomicrobial, and isolates have included gram-positive organisms (*Streptococcus viridans*), gram-negative organisms (*Escherichia coli*), fungi (*Candida albicans*), and mycobacteria.[1–3]

The splenic abscess identified in this case report may have occurred as a result of metastatic haematogenous infection. Bacteraemia is common among women after labour, and risk factors include artificial rupture of membranes,[4] prolonged labour, and frequent vaginal examinations.[5] There are also historical reports linking splenic abscess formation with puerperal sepsis.[1,6] A variety of aerobic (*Enterococcus*, Group A, B and D *Streptcocci*) and anaerobic (eg *Peptococcus* species, *Clostridium*) bacteria have been implicated in the development of puerperal infections.[7–9] In particular, *Enterococcus*, as identified in this case report, is implicated. *Prevotella*, an anaerobe, has not previously been identified in such infections, but it is recognised as a commensal in the gastrointestinal tract and has been noted in intra-abdominal abscesses.[10] There has been only one other case report since 1966 detailing the development of a splenic abscess in the postpartum period, and in that report it was concluded that the abscess resulted from a puerperal infection.[11]

The splenic abscess may also have developed as a result of an infected haematoma.[1] Splenic injury and haematoma formation has been documented as occurring rarely either during or after delivery.[12,13] The aetiology of this may be either a spontaneous rupture, blunt trauma to the spleen (eg via a retractor), or tension on the omentum. Such an injury may explain the sudden and persistent left shoulder tip pain which developed in this patient immediately following the caesarean section, and also the low haemoglobin.

Although subphrenic, suprahepatic, and intra-abdominal abscesses have been reported as occurring in the postpartum period,[14] there have been no previous case reports of a splenic abscess resulting from a splenic injury either during or after delivery.

Traditional management of a splenic abscess involved splenectomy and antibiotics.[1–3] However, more recently there has been a trend towards percutaneous drainage under image control. One series of 21 patients reported a 100% success rate with percutaneous drainage for splenic abscesses.[15] The procedure had to be repeated on more than one occasion in several patients, and patients with multiple abscesses had multiple drainages performed. There were no significant complications. It would appear that this should be the first line of treatment in all patients, with splenectomy being reserved for patients who fail to respond.

In conclusion, this case report details how a 28-year-old woman developed a splenic abscess in the postpartum period. It illustrates how such a condition can present with obscure signs and symptoms, yet can be readily diagnosed on an abdominal CT scan. The initial treatment of choice is through antibiotics and percutaneous drainage under image guidance. Splenectomy should be reserved for those patients that fail to respond to these measures.

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Pregnancy ameliorates symptoms of insulinoma – a case report

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INTRODUCTION

Insulinoma occurring in pregnancy is a rare event. Most reported cases occurred in the first or second trimester. There have only been four cases of symptomatic insulinoma occurring in the latter half of pregnancy[1–4] and one case presenting immediately post partum.[5] We report a woman with insulinoma who presented post partum and whose symptoms had abated during pregnancy.

CASE REPORT

A 35-year-old hairdresser presented three weeks post partum, having suffered neuroglycopaenic symptoms on two consecutive mornings (confusion, abnormal behaviour and dysphasia) which responded to intramuscular glucagon administered by paramedics after capillary blood glucose measurements of 2.1 mM and 1.8 mM were recorded. Upon arrival at hospital her symptoms had resolved and her clinical examination was normal. The pregnancy was uncomplicated and she had delivered a 3660 g male in good condition at term. There was no testing for gestational diabetes mellitus during the pregnancy.

The patient reported intermittent symptoms of lethargy and feeling unwell for two years prior to pregnancy. These symptoms were relieved with food or drink. Her workmates had learnt to give her a sweet drink whenever she became vague or behaved unusually. She promptly returned to her usual self. She sought no medical advice. All symptoms abated completely during pregnancy. There was no family history of endocrine tumours.

While in hospital, hypoglycaemia and inappropriate endogenous hyperinsulinaemia were easily demonstrated (serum glucose 2.1 mM, insulin 15 mU/l, C-peptide 1.99 nM).

Dual phase CT scanning of the pancreas was unhelpful. Transabdominal ultrasonography only identified a hepatic haemangioma. Radio labelled octreotide scanning was unhelpful. At laparotomy, no tumour was demonstrated, despite mobilisation, bimanual palpation of the pancreas and intra-operative ultrasound. No pancreatic tissue was removed.

The patient was referred for selective intra-arterial calcium stimulation with hepatic venous sampling. The calcium stimulation caused insulin release in the territories of both the proximal splenic and inferior pancreaticoduodenal arteries. Arteriography demonstrated the latter artery perfusing the same territory as the proximal splenic artery. This localised the insulinoma to the body or tail of the pancreas.

At repeat laparotomy the tumour was identified in the tail of the pancreas and removed. The tumour was difficult to palpate, measuring 12 mm x 10 mm x 10 mm. The patient recovered uneventfully and remains asymptomatic thirty months post-operatively. Histology confirmed removal of an insulin-secreting tumour.

DISCUSSION

This case describes a rare event that has only twice previously been reported. In one case a diagnosis of insulinoma was made prior to pregnancy and the patient was managed with frequent feeding during pregnancy. While no symptomatic hypoglycaemia was reported, blood glucose levels as low as 1.9 mM were recorded. Symptomatic hypoglycaemia returned with the commencement of breastfeeding.[6]

In the second case, the woman suffered symptoms of insulinoma for four years. These symptoms had abated during pregnancy. Recurrence of hypoglycaemic symptoms occurred twelve hours post partum.[7] In the only other case in which the woman presented post partum there had been no symptoms prior to delivery.[5]

Hypoglycaemia occurring in the post partum period is rare in otherwise well women. Sheehan's syndrome needs to be considered but the often dramatic clinical picture and associated hormone deficiencies will usually assist in making the correct diagnosis. Lymphocytic hypophysitis, which classically occurs in the peripartum period,[8] may be more insidious in onset and can cause adrenocorticotrophic hormone alcohol dehydrogenase anodal duration (ACTH) deficiency alone.[9]

Pituitary apoplexy will usually be associated with fever, headache, hypotension, obtundation and visual disturbance. Factitious hypoglycaemia always needs to be considered, especially in those subjects with access to insulin or oral hypoglycaemic medications. Hepatic failure can cause hypoglycaemia but will usually be readily evident.

In this case, symptoms of insulinoma become evident in the post partum period. The patient had suffered symptoms prior to the pregnancy and those symptoms had abated completely during pregnancy. It is possible the insulin resistance that accompanies pregnancy may have provided this woman with protection from hypoglycaemia during her pregnancy. The post partum period may be a specific time at which an otherwise unrecognised insulinoma may present.

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Perineal endometriosis after vaginal delivery – clinical experience with 10 patients

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INTRODUCTION

Pelvic endometriosis is one of the most common diseases in women of reproductive age, generally occurring in the pelvis. It also occurs in ectopic sites such as bowel, omentum, vagina, caesarean section scars, episiotomy sites and so on, but the incidence in such sites is uncommon. Perineal endometriosis is a rare disease.

Although episiotomy is commonly performed at the time of vaginal delivery, it is surprising the incidence of perineal endometriosis at the episiotomy site is so low. So far, perineal endometriosis published in

the literature[1–3] is case reports of only a small number of cases. This paper reports our experience with 10 patients treated at Peking Union Medical College (PUMC) Hospital, China from 1983 to 2000.

MATERIALS AND METHODS

A computer search of pathology records between January 1983 and December 2000 revealed 10 patients out of 2993 patients with endometriosis treated surgically at PUMC Hospital in China. In this study, all patients received surgical treatment and some received hormonal treatment before and/or after operation. Postoperative follow-up ranged from three months to seven years. Data from the hospital records including age, parity, clinical presentation, operative findings, pathology, management and follow-up were analysed.

RESULTS

Of these 10 patients, four had one or multiple perineal tumours occurring at episiotomy sites and six had tumours occurring at perineal tear sites many months to many years after vaginal delivery.

The latent period ranged from four to 96 months, with an average of 45.4 months. The latent period was significantly shorter (6.25 months versus 70.67 months) in four younger patients (< 30 years old) than the remaining six older patients over 30 years old (p value < 0.05) when they presented with the tumours.

All patients suffered cyclical pain in the perineal mass(es), which were getting bigger and tender. Skin colour over the perineal lesions was normal in seven patients, but in three the perineal lesions were brownish. None reported any bleeding or ulceration from the perineal mass.

Diameters of these perineal lesions were from 0.5 cm to 3 cm, the average being 1.45 cm. Six patients had one endometriotic nodule and four had two to six nodules. Of the four patients with multiple perineal nodules, three had anal sphincter muscle involvement by the tumour.

Pathology result in all cases showed endometrial glands and stroma in hyperplastic connective tissue.

All ten patients had surgical excision of the perineal lesions. Four patients did not have any hormonal treatment before or after surgery and none had recurrence on follow-up from four months to four years. Two had used pseudo-menopausal therapy (GnRHa) for three to six months before operation. Three patients also used GnRHa for three to six months postoperatively.

Two reported no recurrence on follow-up at one year and four months. The three patients with anal sphincter muscle involvement were given progestogen or GnRHa therapy for six months before operation. Two of them had complete surgical excision of their lesions, and then continuing GnRHa treatment for three months and four months postoperatively. None had recurrence on follow-up at six years and seven years respectively.

In one patient, with deep anal sphincter muscle involvement, the surgical excision was reported incomplete. Although given GnRHa therapy for six months postoperatively, perineal lesions recurred at follow-up visit six years later.

At the time of recurrence, surgical excision was considered too extensive and invasive because it might require bowel resection. Instead she had a total abdominal hysterectomy and bilateral salpingo-oophorectomy for her painful adenomyosis. Following surgery, the perineal lesion began to reduce in size, with the cessation of cyclical perineal pain, although the mass remains small but intact.

DISCUSSION

Perineal endometriosis had been reported in a patient with prior delivery with uterine inversion,[4] which might spill viable endometrial cells into the wound. During normal vaginal delivery, possibly some viable decidual endometrial cells are transplanted into the episiotomy wounds or perineal tears and subsequent growth might theoretically occur.

However, the incidence of perineal endometriosis remains rare. Of our ten patients, only one was delivered to our hospital during this 18-year period. There were 11,538 vaginal deliveries in our hospital during this time; thus, a hospital-based incidence of perineal endometriosis was estimated to be around 0.008%.

The reason for this very low prevalence rate is unknown, though it can be theorised that: (i) bacteria often exist in the perineal wound, and together with tissue damage and low grade infection, might inhabit the growth of any transplanted endometrial cells; (ii) oestrogen level is reduced to a low level after delivery so transplanted endometrial cells are not stimulated to grow and establish in the wound.

Diagnosis of perineal endometriosis appears to be straightforward. All our patients had cyclical pain experienced at the mass during menstruation. Physical examination easily demonstrates a mass or masses at the episiotomy scar or perineal tear sites. In some cases, there is brownish discolouration of perineal skin over the lesions, though the majority show normal skin colour. Pathological examination easily confirms the clinical diagnosis.

Use of imaging investigations remains controversial.[3,5–8] Vincent[3] found that the ultrasound appearance of cutaneous endometrioma was a mixed predominantly anechoic pattern with irregular outline. However, it can exhibit a wide spectrum of sonographic findings. Goldberg[6] believes that ultrasound is useful in evaluating superficial masses, to determine their sizes and relationship to other surrounding structures. Other authors used Computer tomography (CT) to diagnose perineal endometriosis.[7] However, CT is not commonly used because of its expense and it adds no valuable information towards management.

Fine needle aspiration cytology can obtain important cytology from the lesion, to confirm the histologi-

cal presence of endometriosis before operation.[8] From our data, we made all diagnoses based on the typical history and examination.

The average latent period of perineal scar endometriosis was 45.5 months. The reason for a shorter latent period in young women (< 30 years old) remains unknown and the number of patients is too small to draw conclusions from.

Treatment of perineal endometriosis includes hormonal treatment and surgical excision. Whether pre-operative or post-operative hormonal treatment will reduce recurrence rate remains controversial. Wang[9] treated five patients with caesarean scar endometriosis with two to four months hormonal therapy preoperatively and reported no hormonal effect in the endometriotic lesion at histological examination of removed specimens.

Dense and relatively avascular fibro-connective tissue around the endometriosis might reduce the observable effect of hormonal treatment to a minimum. In this series, there appeared no obvious difference in recurrence whether using pre-operative or postoperative hormonal treatment or both. However, due to the small number of patients, no conclusion regarding the role of hormonal treatment in the management can be drawn.

Surgical excision aims at complete removal of the endometriotic lesion. All patients had surgical excision to remove the perineal lesion. Three patients had tumour infiltration of the anal sphincter muscle, yet complete excisions were achieved in two who have not had later recurrence of the lesion.

Complete surgical excision appears to offer a cure irrespective of whether or not preoperative and/or postoperative hormonal treatment is given. Surgical excision remains a mainstay of treatment. In one patient, surgical excision was believed incomplete, and she suffered a local recurrence six years later. Although radical local excision could not be offered, following total abdominal hysterectomy and bilateral salpingo-oophorectomy, the recurrent lesions regressed in size and became asymptomatic.

Probably due to the absence of ovarian hormonal stimulation, the recurrent lesions regressed spontaneously without treatment. Based on this limited experience, bilateral oophorectomy appears to be a last resort in the treatment of inoperable patients with recurrent lesions.

Although perineal endometriosis is a rare disease, its easy clinical diagnosis and appropriate treatment can make this disease a curable lesion.

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Spontaneous antenatal expulsion of fetal foot per vaginam – atypical presentation of congenital constriction band syndrome

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INTRODUCTION

Congenital constriction rings or bands are circular soft tissue depressions, usually of the digits or limbs, although they may rarely involve neck, trunk or abdomen and are associated with intrauterine amputations. The latter are abrupt terminations of limbs or digits without any bony defect or growth retardation of proximal parts.

We report an interesting case of intrauterine auto-amputation of fetal limb, in which right foot of the baby was expelled per vaginam and brought to us by

the patient. Such a presentation has not been mentioned previously.

CASE REPORT

A 20-year-old unbooked primigravida at 32 weeks gestation presented in a terrified state with complaints of blood stained discharge per vaginam for three days and expulsion of a fleshy mass resembling a fetal foot (Figure 1) two hours previously.

Figure 1 Expelled amputated right foot

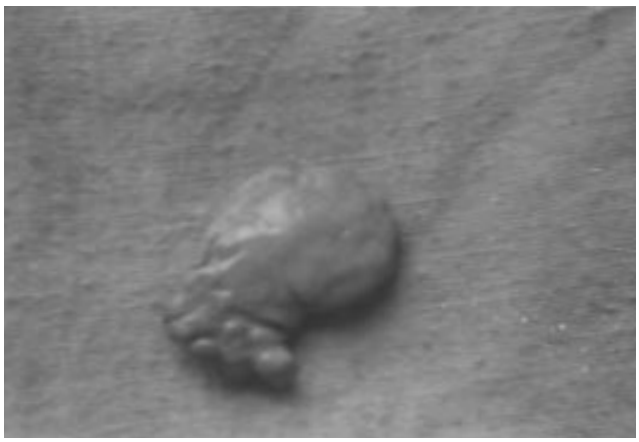
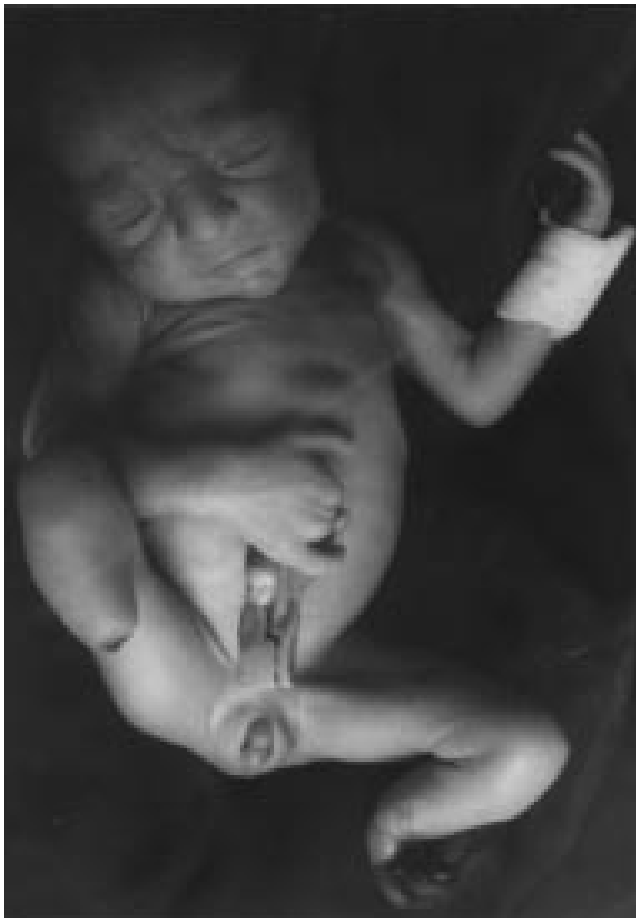


Figure 2 Baby with multiple amputations



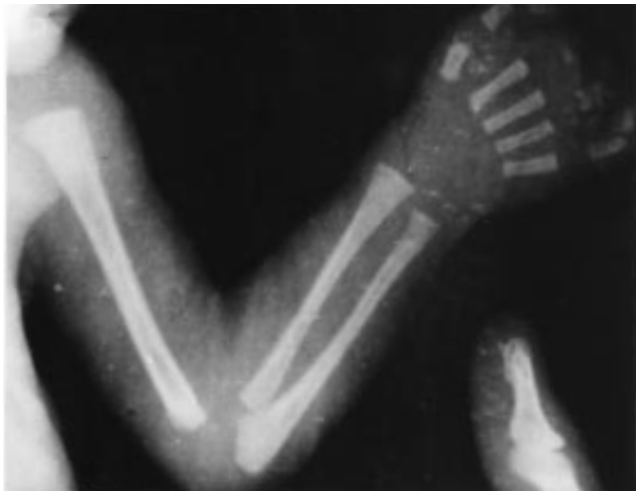
Her general condition was fair but she was intensely anxious. On abdominal examination, the uterine fundal height corresponded to 28 weeks with a single fetus in a cephalic presentation with a regular fetal heart. On speculum examination, the os was patulous and a bloody mucoid discharge was present in the vagina.

Ultrasound examination revealed a single fetus corresponding to 28 weeks maturity with an absent right foot and overall decreased liquor volume. No other congenital malformations were seen. Her antenatal course had been uneventful with no history of any drug ingestion or leaking per vaginam.

She went into labour 12 hours after admission and delivered a live pre-term female baby of 1200 g with mild birth asphyxia. The baby's right foot was absent below the ankle, while the left foot displayed a constriction band just above the ankle. The middle three fingers of right hand were partially amputated (Figure 2). Ultrasound of the baby did not reveal any other congenital anomaly. Radiological examinations of the affected limbs are shown in Figures 3 and 4. The

Figure 3 Radiophotograph of left foot

Figure 4 Radiophotograph of right hand



patient left the hospital with her baby next day and did not come back for follow-up.

DISCUSSION

Amniotic deformity, adhesion and mutilation (ADAM sequence) has been described previously.[1] The reported incidence of constriction ring deformities is one in 1500 to one in 15,000 live births.[2,3]

The theory of origin of constriction bands is debatable. According to Streeter, the primary defect lies in the germinal disc.[4] Torpin, however, postulated that inflammation, trauma or intrinsic weakness could lead to early amnion rupture, leading to fluid leakage and introduction of the fetus into the chorionic cavity. The chorion would reabsorb the fluid, stimulating proliferation of mesenchymal bands which entangle the fetal limb with subsequent mechanical deformity.[5] The occurrence of these deformities in women undergoing second trimester amniocentesis with subsequent fluid leakage supports the above hypothesis.[6]

The diagnostic criteria for this syndrome have been elucidated by Patterson, where two or more of the following characteristics must be present: simple constriction ring; constriction ring with distal deformity, with or without lymphoedema; constriction ring with distal part fusion; and intrauterine amputation – the most severe.[7] The present case met two of these criteria.

Routine ultrasonography helps in early prenatal diagnosis, allowing careful prenatal supervision of this mutilating intrauterine fetal pathology.[8,9] As our patient was unbooked and came to us with three days of leaking late in gestation, when liquor was already low, we were not able to see the rest of the fetal limb amputations on ultrasound. Had the patient presented to us earlier, the option of medical termination might have been offered to her after careful counselling.

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Using naltrexone implants in the management of the pregnant heroin user

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ABSTRACT

Objectives

To describe the case history and associated obstetric and neonatal outcomes of eight women who had their heroin dependency managed over pregnancy by naltrexone implant (two x 1.8 g of naltrexone embedded in poly-DL-lactide acid) treatment.

Method

Case data on maternal management associated with naltrexone implant were collected at the Australian Medical Procedures Research Foundation, Perth, Australia and three Perth hospitals.

Results

Despite earlier instability on oral naltrexone and repeated relapses back to dependent heroin use these women, following treatment with naltrexone implant, remained heroin free throughout their pregnancies. Neonatal and obstetric outcomes were unremarkable.

Conclusions

This case series provides preliminary evidence that the pregnant heroin user can be managed by naltrexone implant without obvious risk to the mother or developing foetus.

Importantly, the current case series suggests that the pregnant woman who finds it difficult to stabilise on oral naltrexone maintenance and returns to dependent heroin use may be managed using implantable naltrexone, thereby removing from her the onus for daily naltrexone medication compliance.

The authors conclude that naltrexone implant may represent an important procedure for managing the pregnant heroin dependent patient who finds it difficult to shift away from her heroin use patterns.

These preliminary findings require confirmation using a much larger controlled study.

INTRODUCTION

Naltrexone is a long acting opiate antagonist that can be taken orally as a single daily dose of 50 mg in persons who have detoxified completely from heroin,[1] and is effective in completely blocking the effects of heroin.[2] However, the major factor limiting the widespread adoption of oral naltrexone therapy for the treatment of opiate dependence is non-compliance. Trials have shown that while having some clinical value, oral naltrexone is often associated with non-compliance, which may result in a patient's withdrawal from treatment and return to heroin use.[3–7]

An alternative method of naltrexone maintenance delivery involves the injection or surgical insertion of a sustained release preparation of naltrexone. In Australia, a formulation of sustained release naltrexone, suitable for subcutaneous depot administration, has been used under Commonwealth Therapeutic Goods Administration Compassionate Guidelines in Western Australia since August 2000. In these implants naltrexone is encapsulated in poly-DL-lactide (a polymer similar to that used in surgical sutures and screws) microspheres compressed into pellets. Each implant consists of 10 pellets.

In vitro the implant has a release rate of about 0.4% of its residual mass per day. Patients presenting for implant treatment currently receive either a single (10 pellets) or double (2 x 10 pellets) implant, which is surgically inserted in the subcutaneous tissue on the right or left side of the lower abdomen. To date approximately 480 patients have been treated via this method.

Following naltrexone implant treatment a number of conceptions have been identified. A single case study describing the obstetric and neonatal outcomes in the first heroin dependent pregnant woman treated with implantable naltrexone has been reported previously.[8] The current paper describes eight further sequential cases and associated obstetric and neonatal outcomes in pregnant heroin dependent women managed with implantable naltrexone since this initial case report. To the best of the authors' knowledge this is the first published case series report on the use of implantable naltrexone during pregnancy.

MATERIALS AND METHODS

Maternal and neonatal data collection

Case data on maternal and neonatal outcomes associated with naltrexone implant were collected at the Australian Medical Procedures Research Foundation, Perth, Australia. Obstetric and neonatal birth outcome data were collected at King Edward Memorial Hospital for Women, St John of God Hospital and Peel Hospital Campus, Perth, Australia. Ethics approval for this study was provided by the Human Research Ethics Committee, University of Western Australia (Project no. 0469).

CASE STUDIES

Case 1

A 24-year-old dependent heroin user presented with her heroin dependent male partner for treatment. Her partner elected to have three x 1.8 g of naltrexone implanted subcutaneously in his lower abdomen. The young woman believed she would be able to control her heroin use if provided with heroin withdrawal and oral naltrexone, and was therefore treated with naloxone induced rapid opiate detoxification (ROD) followed by induction onto oral naltrexone maintenance as previously described.[9]

Over the next six weeks her compliance with oral naltrexone was poor and she continued to use heroin periodically.

Conception occurred approximately three weeks post-naloxone. Due to her vacillation between heroin abstinence and use and her partner's successful abstinence following implant treatment, she elected for naltrexone implant. At two weeks gestation she underwent ROD precipitated by naltrexone implant (two x 1.8 g of naltrexone subcutaneously). This young woman did not return to dependent heroin use throughout the remainder of her pregnancy and spontaneously delivered a live female at 41 weeks.

Case 2

A 29-year-old woman of three years dependent heroin use had previously received two treatments involving naloxone induced ROD and induction onto naltrexone maintenance over the previous year, with her returning to dependent heroin use following each treatment. At her third presentation she was, along with her heroin dependent brother, treated with a 1.8 g subcutaneous naltrexone implant. Following a period of heroin abstinence and stability she received a further two x 1.8 g naltrexone implants. She was subsequently found to have conceived approximately four weeks prior to the second implant treatment. Her pregnancy was devoid of heroin use and otherwise unremarkable.

Case 3

A 24-year-old woman with a two and a half year history of dependent heroin use, and treatment 21 months previously by naloxone induced ROD and induction onto oral naltrexone maintenance, presented to the clinic requesting treatment by naltrexone implant.

She stated that she had returned to heroin use four days following her previous treatment and had since been engaged in dependent heroin use. Her heroin dependent boyfriend had been treated with naltrexone implants three days prior. Withdrawal and maintenance was via the surgical insertion of two x 1.8 g subcutaneous naltrexone implants. She conceived approximately six days following implant. Pregnancy was uneventful and she delivered a live male at 39 weeks by elective caesarean section.

Case 4

A 26-year-old woman of two years dependent heroin use had been treated twice previously with naloxone induced ROD and induction onto oral naltrexone, returning each time to dependent heroin use. These treatments were approximately eight months apart. On further presentation and given her inability to stabilise on oral naltrexone, she was treated with a single 1.8 g naltrexone implant. She presented again seven weeks later following a period of stability and nil heroin use and was further treated with an additional two x 1.8 g implants.

She conceived approximately eight weeks after her second implant treatment and did not return to dependent heroin use throughout pregnancy. During her pregnancy three other family members (husband, husband's brother and sister) were all treated using naltrexone implants. A healthy live female was born at 37.5 weeks gestation. Given the previously high level of heroin use among close family, she elected to have a further two x 1.8 g implants surgically implanted 16 days after delivery.

Case 5

A 27-year-old woman with a two-year history of dependent heroin use presented to the clinic requesting naltrexone maintenance treatment via implant naltrexone. Her presentation followed ten days of regular intravenous amphetamine use which she had self initiated to assist her withdrawal from heroin dependence. She was treated with two 1.8 g naltrexone implants, and conceived approximately five days later. Pregnancy was uneventful with no heroin use. She gave birth to a live female at 40 weeks gestation.

Case 6

A young woman, 21 years of age, presented to the clinic requesting naltrexone implant treatment four weeks after her heroin dependent husband had been similarly treated. She had a nine-year history of heavy dependent heroin use and had been introduced to heroin at age 12 by her mother, a long term methadone and heroin consumer and major heroin dealer. Two 1.8 g naltrexone implants were subcutaneously implanted, with conception occurring 14 days later. Her pregnancy was uneventful and devoid of heroin use. Two months into her pregnancy her mother was treated with two x 1.8 g implants. This young woman delivered a live male at 38 weeks by elective caesarean section.

Case 7

A 26-year-old woman with four years of dependent heroin use and a history of repeated treatments involving six naloxone induced RODs and inductions onto oral naltrexone maintenance at approximately 14-week intervals presented for treatment with naltrexone implant. Her boyfriend had been treated by this method four days prior. She was treated with two x 1.8 g naltrexone implants. She conceived approximately 10 weeks following treatment. Pregnancy was uneventful with an absence of heroin use. She delivered a live female at 38 weeks by elective caesarean section.

Case 8

This 28-year-old woman with a history of five years of dependent heroin use had previously received three treatments involving naloxone induced ROD and induction onto naltrexone maintenance over the previous two years. Intervals between treatments ranged from 4–10 months, with her returning to dependent heroin use on each occasion following a short period of stability on oral naltrexone. At her fourth presentation she was treated with two x 1.8 g subcutaneous naltrexone implants. She conceived approximately eight weeks following this treatment. Her pregnancy was

Table 1 Neonatal and obstetric outcomes associated with naltrexone implant management in the pregnant heroin user

Case number	Age	Length of heroin use [years]	Gestational age at naltrexone implant	Gender	Weeks at delivery	Mode of delivery	APGAR 1/5 min	Birth-weight g	Head circum-ference	Length
Case 1	24	4	2 weeks	female	41	SVD	9:10	3240 g	33 cm	52 cm
Case 2	29	3	4 weeks	male	40	SVD	9:9	3505 g	35.5 cm	53 cm
Case 3	24	2.5	Conception 6 days following Implant	male	39	elective caesarean	9:9	3845 g	35 cm	50 cm
Case 4	26	2	Conception 8 weeks following Implant	female	37.5	induced	9:9	2800 g	31.5 cm	47 cm
Case 5	27	2	Conception 5 days following Implant	female	40	SVD	9:9	3000 g	32.5 cm	48 cm
Case 6	21	9	Conception 14 days following Implant	male	38	elective caesarean	9:9	3680 g	31 cm	52 cm
Case 7	26	4	Conception 10 weeks following Implant	female	38	elective caesarean	9:9	2720 g	34 cm	48 cm
Case 8	28	5	Conception 8 weeks following Implant	male	40	SVD	9:9	2855 g	35.5 cm	50 cm

devoid of heroin use and otherwise unremarkable. She had an unassisted birth of a live male at term.

General findings

Overall obstetric and neonatal data were reasonably unremarkable. Maternal, obstetric and neonatal outcomes for these eight cases are summarised in Table 1.

DISCUSSION

Obstetric and neonatal outcomes associated with naltrexone implant

Neonatal outcomes (weeks at delivery, birth weights, head circumference, length and Apgar at 1 and 5 minutes) associated with maternal naltrexone implant management were unremarkable. As such this case series provides preliminary evidence that the pregnant heroin user can be managed by naltrexone implant and the neonate can have exposure to naltrexone over gestation, without apparent major risk. This result is similar to those previously reported for pregnant heroin dependent women managed by oral naltrexone,[9] and for the previously reported single case study of a heroin dependent pregnant woman treated with implantable naltrexone.[2, 8]

Overall obstetric outcomes were also largely unremarkable, although three elective caesareans were observed amongst the eight cases. Two of these cases (3 and 6) were, however, by maternal choice and only one (case 7) was clinically indicated.

Maternal management

Importantly, the current case series suggests that the pregnant woman who finds it difficult to stabilise on oral naltrexone maintenance and returns to dependent heroin use may be managed using implantable naltrexone, thereby taking the onus for daily naltrexone medication compliance away from the prospective mother. Despite earlier instability on oral naltrexone and repeated relapses back to dependent heroin use, all women following implant management remained heroin free throughout their pregnancies.

In these cases the use of implantable naltrexone was clearly associated with lifestyle stabilisation. Associated improvements in maternal health, nutrition and antenatal care, and movement away from intermittent involvement with the narcotic network are likely to be important factors contributing to positive neonatal and maternal outcomes observed.

Of interest was that in six of the eight cases heroin using partners or significant others were also treated, in all but one instance, prior to the pregnant women. This no doubt encouraged these women to seek this treatment and likely led to a more stable home environment during pregnancy. This contrasts to the situation where the prospective mother and father are both maintained on methadone and the potential for heroin use to continue during pregnancy remains high.

Naltrexone Implant as an alternative to methadone

Maternal heroin use during pregnancy is associated with significant risks to both mother and neonate. These include increased antepartum haemorrhage, decreased neonatal birth weight and increased neonatal mortality.[10–15]

To date methadone maintenance treatment (MMT) has been the treatment of choice for the pregnant heroin user, with stabilisation on methadone prior to or near time of conception associated with considerable improvement in birth weight and decreased risk of neonatal mortality. For those women who do not stabilise on MMT and continue to use illicit heroin regularly during pregnancy, MMT is however associated with poor obstetric and neonatal outcomes.[10,11,14–17]

Comparison of neonatal outcomes observed in this case series with those associated with MMT needs to be approached with great caution due to the lack of a consistent methodology. Nevertheless, and given this qualification, obstetrics and neonatal outcomes associated with implant naltrexone management do appear to be better than those observed with MMT.[11, 12, 18] For example, Lam and colleagues[18] reported a mean birth weight of 2622 g (SD 463) among women treated with methadone compared to match control 3252 g (SD 347). Although small in numbers, birth weight outcomes associated with implant naltrexone are closer to those of controls noted in the above study, than those treated with MMT.

Neonatal and maternal outcomes of the current case series therefore suggests that naltrexone implant may be a viable alternative to MMT in the pregnant heroin user. In fact, given that a proportion of pregnant women maintained on MMT will continue heroin use throughout pregnancy with likely poorer obstetric and neonatal outcomes, and that this scenario of continued heroin use is virtually absent in the naltrexone implant patient, implant treatment may be desirable as the preferred treatment option over MMT for the pregnant heroin user who finds it difficult to move away from dependent heroin use.

Importantly, there is no neonatal withdrawal syndrome associated with management by naltrexone implant. This situation contrasts to that reported for MMT where a neonatal withdrawal syndrome is commonly associated with this treatment. This neonatal withdrawal syndrome is more significant in the patient who continues heroin use while receiving MMT.[11,2,18]

A larger controlled study is now required to confirm these preliminary findings and conclusions about the safety of implantable naltrexone, and to allow direct comparison to MMT.

CONCLUSIONS

The current case series provide a preliminary basis for believing that naltrexone implant treatment may offer significant benefits over existing procedures in

managing the pregnant heroin dependent patient who finds it difficult to shift away from her dependent use patterns. These preliminary findings however require confirmation using a larger controlled study.

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Competing interests

One author (G O'Neil) is involved in the production of implantable naltrexone.

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Delays in diagnosing breast cancer – the impact of concurrent pregnancy and lactation

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INTRODUCTION

Delays in diagnosing breast cancer are relatively common – up to 5% of patients will not be diagnosed until three months after the symptoms first become apparent.[1] There is good evidence that unusual symptoms,[2] young age[3] and presentation to a non-specialist,[4] are associated with a delay in recognising the symptoms of cancer or inadequate investigation.

Does this delay matter in terms of treatment or survival? This is a controversial area, which has been explored in a number of retrospective studies. Sainsbury first suggested that the treatment of breast cancer in the United Kingdom varied according to where you lived and thus to whom the patient was referred – this was taken up in the media as the 'post-code lottery' of breast cancer treatment.[5]

By implication some patients were being 'under-treated' by surgeons with a low breast cancer workload, with potential impact on patient survival.[6] In 1999, two large studies were published,[7,8] which examined the influence of delay in diagnosis on survival. The first, a meta-analysis of over 20 studies, suggested that a delay in diagnosis of 3–6 months was associated with lower survival, which could not be accounted for by lead-time bias. In contrast the second, a retrospective analysis of over 36,000 patients, found no evidence that delay by the health provider adversely affected survival.

These conflicting reports can, to some extent, be resolved if the reasons for delay are examined. In the first study, women who experienced delay in treatment may have received sub-optimal treatment by 'non-specialists'. In the second study those who received prompt treatment had worse outlook tumours – that is large tumours in younger women. There is evidence that prompt adjuvant therapy by a specialist team may benefit survival in early breast cancer.[9]

Delays due to pregnancy

Few studies have looked at the association of concurrent pregnancy or lactation with delay in diagnosis of

breast cancer.[10–13] These studies have suggested that a delay in diagnosis anywhere from two to 15 months is a common feature in gestational breast cancer, defined as breast cancer during pregnancy or up to one year post-partum. This delay is thought to lead to a more advanced stage of disease at diagnosis, compared to age-matched controls, and consequently a poorer survival outcome.

In one series[14] the average delay in diagnosis in pregnant women was 8.2 months compared to 1.9 months in women who were not pregnant. In fact, half of the patients in the study were not diagnosed until after pregnancy despite symptoms being present during it.

From a population based study that we are undertaking in Western Australia, called the Gestational Breast Cancer Project, it seems apparent that there are two categories of delay: those due to the patient and those due to the doctor. We illustrate these delays with three case histories from this study.

Delay due to patient

Case 1

A 37-year-old woman with four children first noted a mass in her right breast while weaning her last child at one year post-partum. She assumed that the change was due to physiological breast changes and delayed seeking medical advice for one year. Contributing to her reasons for delay was a congenital disability in her youngest child and marital difficulties. During this time the lump gradually increased in size and was 1.5 cm in diameter at presentation to a breast surgeon. Investigations included mammogram, ultrasound and a core biopsy confirmed carcinoma. Breast conserving surgery revealed a 16 mm grade 3 oestrogen receptor (ER) positive and lymph node negative tumour; she was given adjuvant chemotherapy consisting of cyclophosphamide, methotrexate and 5-fluorouracil (CMF), and tamoxifen. She remains alive and disease free at two years.

Case 2

A 32-year-old woman first noted a 'small' left breast lump at six months gestation in her second pregnancy. She was fit and well with no family history of significance. She was seen by her general practitioner who advised fine-needle aspiration cytology which she declined.

Post-partum the lump had increased in size and five months after first noting the mass, she underwent investigations. At this time the mass was 10 x 8 cm with peau d'orange and there was a mobile 3 cm lymph node. She had been unable to breastfeed on this side.

Staging was normal, so she underwent a mastectomy, followed by chemotherapy using 5-fluorouracil, epirubicin and cyclophosphamide (FEC), and radiotherapy. However, she developed bone metastases during radiotherapy and liver metastases nine months after surgery. Despite further systemic treatment she died two months later.

Delay due to doctor

Case 3

A 38-year-old woman with six children presented to a general surgeon with a two-month history of a lump in the left breast. She was three months post-partum and lactating. Clinical examination suggested a 1 cm x 2 cm cyst, but ultrasound demonstrated a solid lesion. Fine needle aspiration cytology was reported as atypical. Nonetheless, the surgeon, on the grounds of a low index of clinical suspicion, opted to re-examine and repeat an ultrasound in six months. The lesion had enlarged to 3 cm x 4 cm and an excision biopsy was performed (without further tests) which showed an invasive carcinoma on frozen section.

Mastectomy was performed and revealed a 35 mm grade 3 ER positive tumour with one of 18 nodes involved. The patient had adjuvant chemotherapy using cyclophosphamide, methotrexate and 5-fluorouracil (CMF), and remains alive and well seven years later.

DISCUSSION

Did these delays alter either the treatment or survival outcomes? In case 3, and possibly case 2, the delay may have resulted in the need for a mastectomy due to increase tumour size, thus denying the patient the option of breast-conserving surgery. It is unlikely that the delays resulted in more or less adjuvant systemic therapy being offered.

Consequences of a delayed diagnosis

In terms of survival these cases illustrate the uncertainty that the effect of delay on the outcome of the breast cancer may have. In case 1, despite a delay of over a year and the high nuclear grade of the tumour, it was clearly slow growing, had not spread to lymph nodes and was small at presentation. It is unlikely that earlier systemic intervention would have changed the patient's fairly good prognosis.

In case 2, the tumour was clearly a rapidly growing, poor prognosis tumour, which did not respond to medical intervention – earlier diagnosis would probably have only added lead time to the patient's overall survival. In case 3, the earlier misdiagnosis and consequent delay had no effect on the long-term survival of the patient.

Assessment of the breast during pregnancy

While the effect of delay in diagnosis is unclear in terms of outcome or treatment, it is clear that prompt and correct diagnosis is preferable. The recommended path to a diagnosis of breast cancer in women with a breast symptom is clinical examination, imaging and pathological testing.[15] If the patient is pregnant or lactating this pathway can be complicated, but should still be followed.

Clinical breast examination can be difficult due to the masking of lumps by the physiological changes of pregnancy. Nevertheless, any new, persisting change should be investigated – in particular a lump, bloody nipple discharge or skin changes.

Imaging by mammography is notoriously difficult during pregnancy and lactation. In one small series 80% of cancers did not show up on mammogram,[16] although modern techniques will perform better. Ultrasound by an experienced breast ultrasonographer may prove better at diagnosing malignancy, but mammography to look at both breasts, for calcification in particular, should also be performed.

The use of magnetic resonance imaging (MRI) in diagnosing breast cancer is still under scrutiny but may prove very valuable, although the increased general vascularity of the pregnant breast may limit its specificity in this situation. Safety issues regarding ionising radiation must obviously be taken into account, with fetal shielding. There are theoretical dangers to the fetus from ultrasound and MRI (heating and cavitation with the former and heating effects of a high static magnetic field with the latter) but these have not been demonstrated in practice.[17]

Fine needle aspiration cytology of the pregnant breast may be difficult as the cytological features of normal breast epithelial cells in pregnancy may mimic those of malignancy,[18] thus an experienced cytopathologist, who is aware that the sample is from a pregnant or lactating patient is needed to interpret the cytology correctly. Core biopsy will give a more accurate picture than cytology, but can prove a difficult procedure in lactating breasts, as can open surgical biopsy, resulting in excessive bleeding, milk fistula or infection.[19,20]

Following this pathway should lead to prompt referral of women to specialist breast cancer services when appropriate. This is not only important for the women but for all clinicians involved in the diagnosis of breast cancer in young women.

Role of the primary health physician, obstetrician and midwife

Most non-breast cancer specialists will rarely see a patient with gestational breast cancer: breast cancer only complicates between one and three of every 10,000 pregnancies[21] and benign breast conditions such as an enlarging fibroadenoma, lactational abscess or galactocele are much more common. It is important that health professionals consider breast cancer as a differential diagnosis and investigate any breast abnormality with triple assessment. Appropriate investigation could reduce the social and legal consequences that misdiagnosis, or delay in breast cancer diagnosis, can cause.

Figure 1 Advice

- Maintain index of suspicion of cancer with any new breast symptoms presenting during pregnancy
- Perform triple assessment
- Cytology can be confusing due to cellular changes of pregnancy
- Mammography should be performed although sensitivity is low. Ultrasound is a useful adjunct

More importantly health professionals involved in obstetric and primary care have an important role to play in encouraging young women who are pregnant or could become so, to be 'breast aware'. If women are 'breast aware', and their physician investigates breast symptoms with triple assessment and appropriate referral, all without delay, it is likely that the outcome of this rare but devastating disease may be improved.

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