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Case report

Melioidosis complicating an ovarian teratoma with gliomatosis peritonei; a rare case with review of the literature on melioidosis affecting the gynaecological tract.

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Abstract

Introduction: Melioidosis is an endemic infection in Southeast Asia, caused by a soil associated saprophyte bacterium *Burkholderia pseudomallei*. Melioidosis can affect any organ systems in the body. This is a very rare case of an ovarian teratoma complicated by melioidosis.

Case report: A 38-year-old woman, who had a recent travel history to India and the North Central Province presented with low-grade fever, abdominal pain and weight loss for one month. Initial investigations revealed high C-reactive protein (CRP) levels and neutrophil leucocytosis. Blood and urine cultures were negative. Melioidosis antibodies were positive at a titre of 1:1280. Except for a solid and cystic lesion in the left adnexa suggestive of an ovarian teratoma, extensive radiological evaluation did not reveal any infective focus. She was treated with intravenous meropenem for four weeks, with which a transient improvement was observed. However, she was readmitted with high fever spikes and rising CRP two weeks after being discharged. The teratoma was suspected to harbour melioidosis infection and an oophorectomy was performed. Macroscopically, the ovarian mass showed a solid, firm, gritty cut surface with cystic areas. Microscopy revealed an immature teratoma (grade-II) with evidence of gliomatosis peritonei. There were areas of suppurative inflammation within the teratoma and within the glial elements in the peritoneum. Tissue Gram stain for bacteria and stains for fungi and mycobacteria were negative. The patient's condition improved following oophorectomy and melioidosis serology became negative.

Discussion and conclusion: The possibility of melioidosis infection within an ovarian teratoma was confirmed by the histological findings of suppurative inflammation, marked post-operative clinical improvement and melioidosis serology becoming negative post-operatively. Melioidosis is known to cause suppurative inflammation in deep organs, but gynaecological manifestations have been limited to a few case reports, including tubo-ovarian abscesses, pelvic inflammatory disease and cervicitis. This is the first case reported as involvement of an ovarian teratoma.

Keywords: ovary, teratoma, melioidosis, abscess, suppurative inflammation

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Introduction

Melioidosis is an occupationally and recreationally acquired bacterial infection endemic in topical counties including Southeast Asia, South Asia and Northern Australia (1,2). The causative organism, *Burkholderia pseudomallei* is a facultative, intracellular, aerobic, Gram-negative bacterium mostly found in moist soil and surface water (2,3).

The clinical spectrum of melioidosis ranges from subclinical localized lesions to disseminated fulminant disease. It can affect almost any organ in human body and can mimic many diseases (1,2). Clinicians should have a high degree of suspicion for melioidosis in a patient with unexplained febrile illness with a history of travel to an endemic area and significant exposure to contaminated soil or water (4). Diabetes mellitus, alcoholism, chronic lung disease, renal insufficiency, thalassemia, and immune suppression are well recognized predisposing factors for melioidosis (1,2). This infection can commonly present clinically as pneumonia, skin infection, hepatic, splenic or prostatic abscesses, soft tissue infection, septic arthritis and osteomyelitis (5). Bacterial culture represents the diagnostic gold standard for melioidosis. However, partially treated cases require serological testing for the diagnosis (4).

Sri Lanka, being a tropical country, is endemic for melioidosis. Indigenous cases are mostly concentrated in lowland areas. Adult males with diabetes mellitus are reported to be at a greater risk (6). Gynaecologic involvement is rare even in endemic areas, with only a few reported cases in the literature (2). This is the first case of an ovarian teratoma harboring melioidosis infection.

Case report

A 38-year-old previously healthy woman from the Gampaha district presented to the National Hospital of Sri Lanka with low-grade fever, productive cough and abdominal pain for one month. This episode was preceded by abdominal distension for few months accompanied by a dull aching discomfort towards the lower abdomen. She had also experienced an unintentional weight loss of 10 kilograms.

She gave a history of recent travel to India and the North Central Province of Sri Lanka where she was involved in aquatic recreational activities. On examination, she was pale and febrile, and there was no lymphadenopathy. Her abdomen was asymmetrically distended with a tender pelvic mass of the size of a 20-week gravid uterus, which was confirmed to be a left adnexal mass on vaginal examination.

Her initial laboratory investigations revealed a neutrophil leucocytosis, with white blood cell count of 15 800 /mm^3 and 78% of neutrophils, and mild anaemia with a haemoglobin value of 9.1 g/dL. The blood picture revealed normocytic normochromic red cells and showed evidence of an acute bacterial infection. Acute inflammatory markers were elevated [C-reactive protein (CRP) 152 mg/L, erythrocyte sedimentation rate (ESR) 128 mm/1 hour]. The chest x-ray was normal. Bacterial cultures of blood, urine and sputum did not yield significant growths. Serum antibodies to melioidosis antigen using indirect haemagglutination assay (IHA) was positive with a high titre of 1:1280. The abdominopelvic ultrasonography revealed a heterogenous lesion in the left adnexa measuring 11x17 cm, with cystic and solid components. The computerised tomography (CT) confirmed this mass to be an ovarian teratoma. There were no mass lesions elsewhere.

Empirical treatment for melioidosis was commenced with intravenous meropenem, pending the confirmation of a possible infective focus. A satisfactory clinical and biochemical response was achieved after four weeks of antibiotic treatment, and she was discharged on oral cotrimoxazole. Since the ovarian mass was radiologically benign,

surgical management was planned following resolution of her ~~a~~cute condition. Two weeks later she was readmitted to hospital with recurring high fever spikes and rising CRP levels. Repeated extensive radiological evaluation failed to identify any infective focus and the ovarian teratoma was suspected as the focus harbouring melioidosis infection.

Left salpingo-oophorectomy and omentectomy was performed. Macroscopic examination revealed an intact ovarian mass measuring 170x160x100 mm with a solid, firm, gritty cut surface and areas of cystic degeneration. The histology confirmed this to be a grade II immature teratoma with primitive neuroectodermal tissue (Figure 1). The separately received omentum revealed extensive gliomatosis peritonei which was confirmed by positive GFAP immunohistochemistry (Figure 2).

There were prominent areas of suppurative inflammation involving both the teratoma and

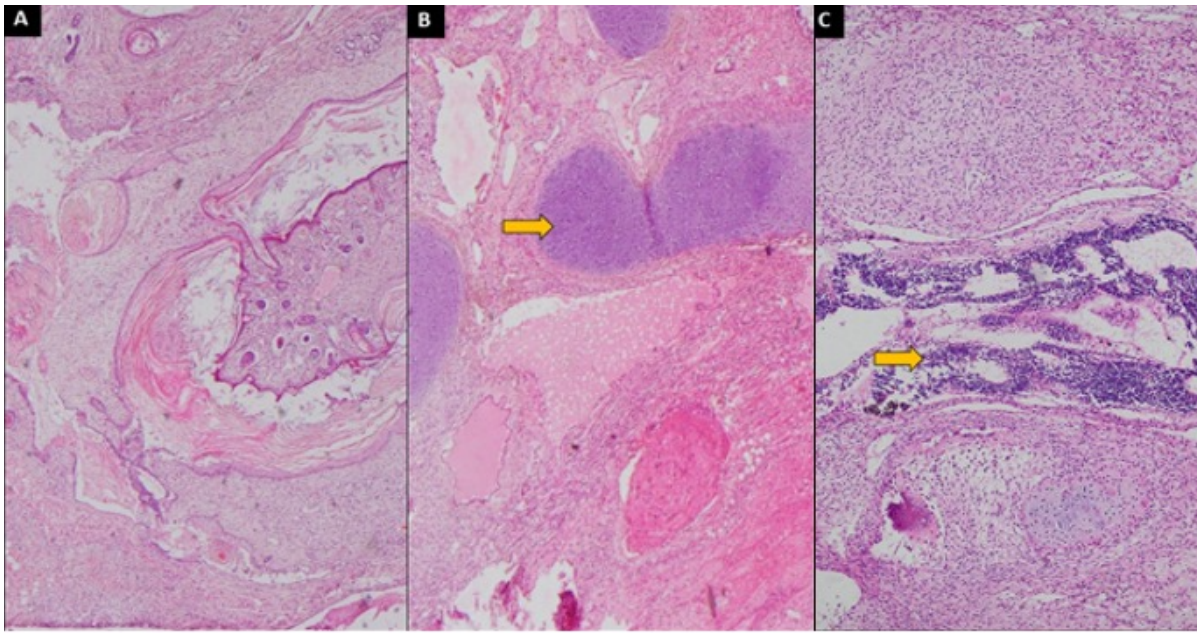

Figure 1. Immature teratoma grade II showing **A.** areas of mature skin, **B**, immature cartilage (arrow) and **C**. primitive neuroepithelium (arrow) (H&Ex200)

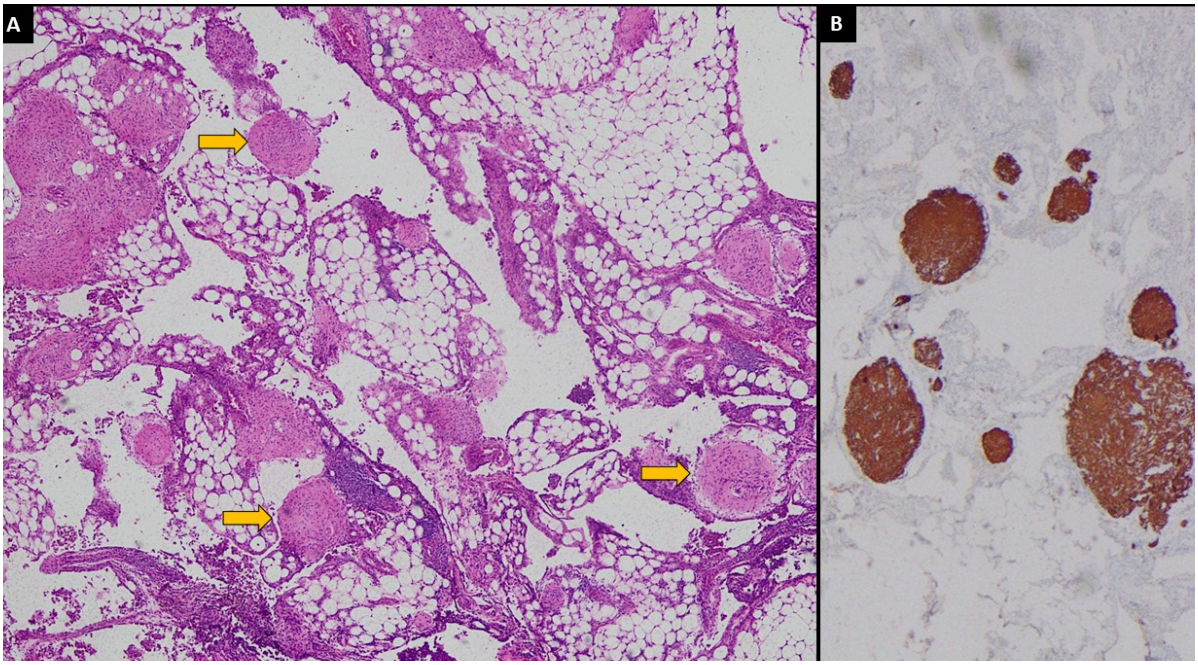

Figure 2. A. Gliomatosis peritonei in the omental tissue (arrows) (H&E x200) and **B**. glial tissue showing strong and diffuse cytoplasmic GFAP positivity (IHC x400)

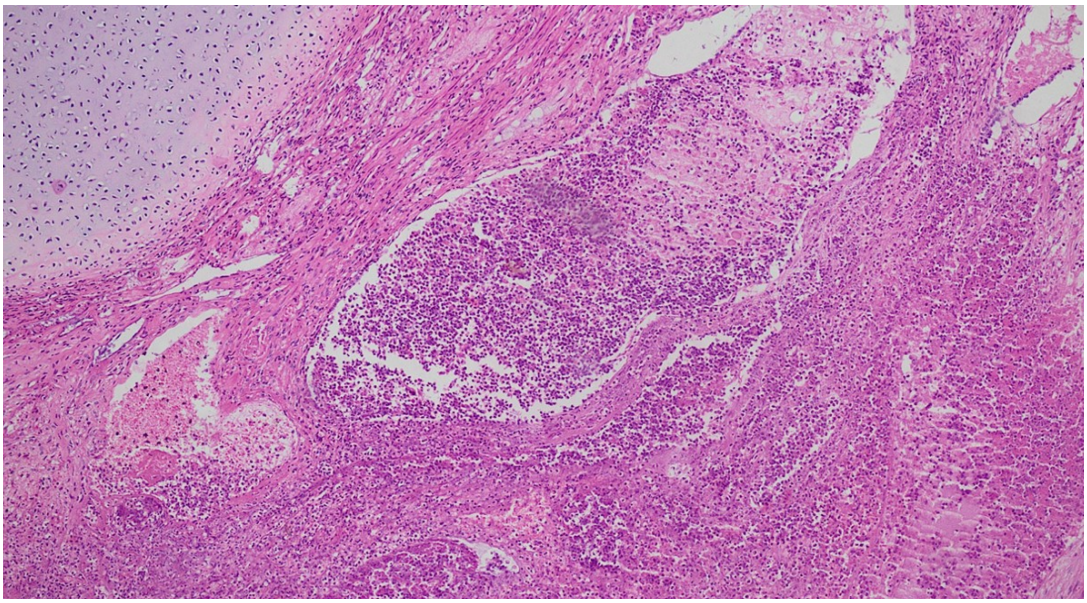

Figure 3. Foci of suppurative inflammation within the immature teratoma (H&E x400)

the glial tissue in the peritoneum, which was an unusual finding (Figure 3). The possibility of fungal and tuberculous infections was excluded by negative fungal and Ziehl-Neelsen/Wade-Fite stains, respectively. Tissue Gram stain was negative. Cyst fluid was negative for bacterial culture, tuberculosis culture and tuberculous gene expert.

After surgery her condition improved dramatically, and the melioidosis antibody assay titre declined rapidly.

Discussion

The first human case of melioidosis was detected in 1912 in a Burmese man with a history of drug abuse (1). A decade later, in 1927, it was reported from Sri Lanka (6). Despite being located within the melioidosis-endemic belt, no cases had been reported during the seven decades following the detection of its first case. However, the infection began to re-emerge during the last two decades (7), and 250 culture-positive cases were reported between January 2006 and March 2017. In addition, more than 100 patients were treated as for melioidosis based on serological testing (7). Farmers, manual labourers and workers involved in the fisheries sector and gardening are at risk of acquiring the infection mainly due to occupational exposure (6). An increase in the case load has also been observed during the two monsoon periods in Sri Lanka (7).

The organism enters the human body mainly via direct cutaneous inoculation through wounds, oral ingestion and inhalation (1,2). Infections can be localized or systemic and result in acute disease which may even lead to fatal septicaemia, subclinical disease or chronic disease (6), that can . It can remain asymptomatic and recur many years later (1,3).

Melioidosis can affect many organs and predominantly involves the lungs, liver, spleen, musculoskeletal system, soft tissue, skin and genitourinary organs (6). Encephalomyelitis, pancreatitis, mediastinal lymphadenitis and suppurative pericarditis have rarely been reported (5). Despite antibiotic therapy, bacteraemic melioidosis with severe sepsis carries a poor prognosis and a high mortality rate due to multi-organ failure (1, 8). The mortality rate can be as high as 90% without effective treatment and even with antibiotic therapy it can reach up to 50%. (6). A mortality rate over 20% was reported in cases detected in Sri Lanka (6).

Table 1. Cases of Melioidosis involving the gynaecological tract, reported in the literature

Study	Age (years)	Endemic area	Clinical presentation	Focus of infection	Histological findings	Microbiological findings	Management and outcome
Nernsai et al. (2)	31	Thailand	Fever and left lower abdominal pain for one month	A left tubo-ovarian abscess measuring 9.4 × 4.8 cm and multiple hepatosplenic abscesses	Chronic and acute suppurative inflammation with necrotic tissue	Pus culture yielded *B. pseudomallei*.	Treated with intravenous ceftazidime for one month, and clinical symptoms improved.
Chang et al. (8)	25	Malaysia	Fever, dysuria, urinary frequency and vaginal discharge for one week	Multiple splenic abscesses and vagina	Histopathological examination of the products of conception did not reveal any significant pathology or evidence of foetal infection with *B. pseudomallei*	Blood and high vaginal swab cultures yielded *B. pseudomallei* grown on modified Francis culture medium	Had uneventful complete spontaneous abortion. Treated with intravenous ceftazidime for a total of four weeks, and repeat abdominal ultrasonography showed resolution of the splenic abscesses.
Subramanium et al. (9)	55	India	A history of total abdominal hysterectomy with bilateral salpingo-oophorectomy for ovarian mucinous cystadenocarcinoma five years prior. presented with abdominal distension for one week	Pseudomyxoma peritonei	Cytologic analysis of the aspirate was negative for malignant cells	Bacterial culture of thick gelatinous material from the peritoneum was positive for *B. pseudomallei*	Treated with Ceftazidime for three weeks. There was symptomatic improvement, and the patient was discharged on oral doxycycline and chloramphenicol.
Index case	38	Sri Lanka	Fever, abdominal distension and lower abdominal pain for one month	Immature teratoma in the left ovary	Grade II immature teratoma with gliomatosis peritonei showed multiple foci of suppurative inflammation	Indirect haemagglutination for melioidosis antibody was positive, with a titre of 1:1280	Recovered completely following oophorectomy and meropenem treatment for five weeks, followed by oral cotrimoxazole for 20 weeks

~~The~~ Isolation of *B. pseudomallei* by microbiological culture from colonized sites such as urine, respiratory secretions or surface swabs is the gold standard diagnostic test (4). Serodiagnostic tests including IHA and enzyme-linked immunosorbent assay (ELISA) can be used to facilitate the diagnosis when the cultures are negative. An IHA titre of 1:10–1:40 indicates infection and 1:40–1:160 indicates active disease (4). Therefore, the presence of 1:1280 titre in this patient was highly suggestive of an active disease. Melioidosis culture performed on ovarian cyst fluid was negative in our patient. However, the culture was performed four weeks after commencing antibiotic treatment, at which time it was highly unlikely for cultures to be positive.

Unexplained low-grade fever, abdominal pain and significant travel history directed the clinician towards the suspicion of melioidosis, which was strongly supported by the positive serology test. In the absence of identifiable focal lesions elsewhere in internal organs, the ovarian teratoma was identified as the possible infection harbouring site. The suspicion was further supported by suppurative inflammation in histology sections, which is the characteristic finding in melioidosis, and by the fact that the patient dramatically improved both clinically and serologically following the oophorectomy.

Only three cases of melioidosis involving gynaecological tract were reported in the literature, which are summarized in table 1 (2, 8, 9). All four cases, including the index case, have been reported in Southeast Asia. The ages ranged from 31-55 years. Two patients, including the index case, had ovarian involvement. One patient had a positive vaginal swab culture while another one had a history of surgery for ovarian cystadenocarcinoma and had a positive culture of mucinous material of pseudomyxoma peritonei. All patients had clinically improved, though one had experienced an early foetal loss.

Superinfection is considered as one of the rarest complications in teratomas. A few cases of infection with coliforms, actinomyces, brucella, salmonella and schistosomiasis have been reported in teratomas (10). However, there were no reported cases of teratomas superinfected with melioidosis.

Conclusion

Melioidosis is endemic in Sri Lanka. Therefore, a high index of suspicion should be raised in all patients with unexplained febrile illness in the local setting. Extensive clinical evaluation, including travel history, and timely and appropriate testing is mandatory for correct diagnosis. Effective treatment requires the commencement of an appropriate and sensitive antibiotic according to the clinical severity. Although histology is not diagnostic, melioidosis should be considered as a differential in suppurative inflammatory reactions in suspicious cases.

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