Patient with protracted abdominal pain

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Introduction

Actinomycosis is very often misdiagnosed as typically, the associated laboratory and radiological findings are non-specific. Therefore, clinicians should always have a high index of suspicion in cases in which there is a chronic, indolent development of a mass lesion with sinus tracts, that progresses through the tissue planes, and which relapses following short courses of antibiotics.[1] Early diagnosis may prevent invasive investigations and radical surgical procedures as the patient can then simply be treated with oral penicillin.[2]

Case report

A 38-year-old woman presented with a three-month history of vague lower abdominal pain with associated nausea, vomiting and excessive weight loss. In addition to these symptoms, she also developed pain and paraesthesia in her right leg, not precipitated by any specific movement. Eight years prior, she had been diagnosed with an ovarian cyst which had been progressively enlarging, based on sonographic evaluation. Having obtained the history, the patient was determined to be para 2, gravida 2, and to have had an intrauterine device inserted as a contraceptive measure on three previous occasions between 1999 and 2011.

Laboratory investigations confirmed that the patient had normocytic normochromic anaemia, with a haemoglobin level of 10.2 g/dl (12.5-16 g/dl), a mean corpuscular volume of 86.4 fl (78-100 fl) and a mean corpuscular haemoglobin of 25.7 pg (27-31 pg). Both the platelet and white cell counts were elevated, at 613 x 10^9/l (140 to 370 x 10^9/l) and 25.9 x 10^9/l (4-10.5 x 10^9/l), respectively. Renal function and electrolytes were within normal ranges, but the alkaline phosphatase was slightly elevated at 145 U/L (42-98 U/L), and the serum albumin was low at 15 g/l (35-52 g/l). The patient was confirmed to be human immunodeficiency virus (HIV)-1 negative by the HIV Combi Assay® (Roche Diagnostics, Mannheim, Germany).

A speculum examination of the cervix revealed three circular haematomatous lesions. A pelvic mass of 8 cm x 5 cm x 4 cm was also demonstrated on abdominal ultrasound. A provisional diagnosis of ovarian cancer was made and the decision was taken to perform a staging laparotomy. Ascites was aspirated and submitted for adenosine deaminase levels, and measured at 11.3 U/l (> 30 U/l is suggestive of tuberculosis). In addition, samples were submitted for mycobacterial culture and microscopy, which were negative in both instances.

During this procedure, a "frozen pelvis" was discovered with extensive adhesions between the bowel, uterus and right Fallopian tube, as well as a semi-solid adnexal mass, measuring 5 cm x 4 cm x 6.4 cm. The differential diagnosis was established to be ovarian carcinoma, and infection with *Mycobacterium tuberculosis*. Unfortunately, tissue samples were not submitted for mycobacterial culture which would have been the investigation of choice in this setting. A bilateral adnexectomy and subtotal hysterectomy, with resection of small and large bowel parts, including the appendix, was performed and submitted for histological examination.

Macroscopically, nodular lesions with central necrosis could be demonstrated in the right adnexa only. Despite numerous leiomyomas, similar nodular lesions were not found in the uterus. On microscopic examination of haematoxylin and eosin stain of the right adnexa with ovary, multiple collections of filamentous bacteria, with surrounding inflammatory response and granuloma formation, could be demonstrated (Figure 1 a and b). These collections of bacteria were Gram-positive, positive for periodic acid-Schiff (Figure 1 c and d)

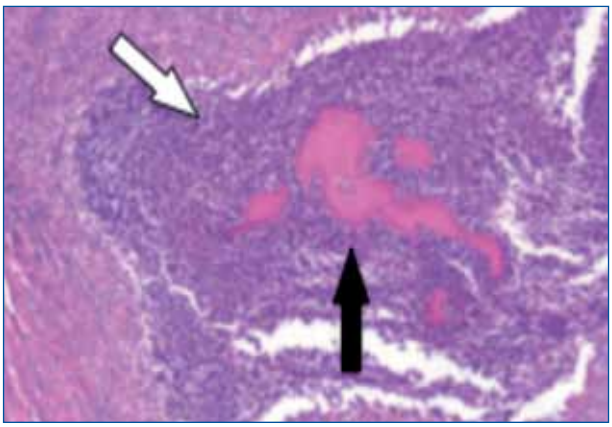

Figure 1 a: Haematoxylin and eosin stain showing infiltration by Actinomycetes (black arrow), with surrounding inflammatory cell infiltrate and granuloma formation (white arrow)

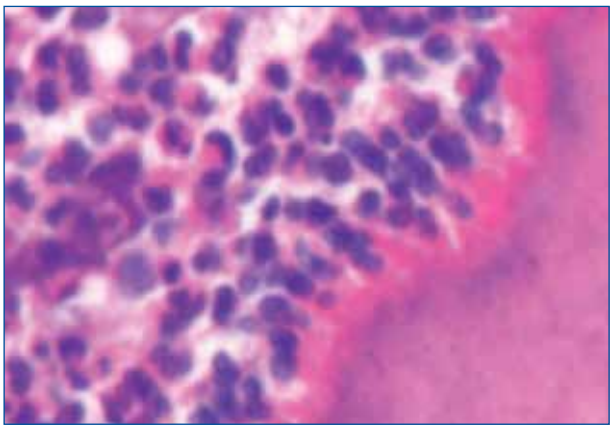

Figure 1 b: Closer view of the haematoxylin and eosin, showing the filamentous nature of the infiltrate

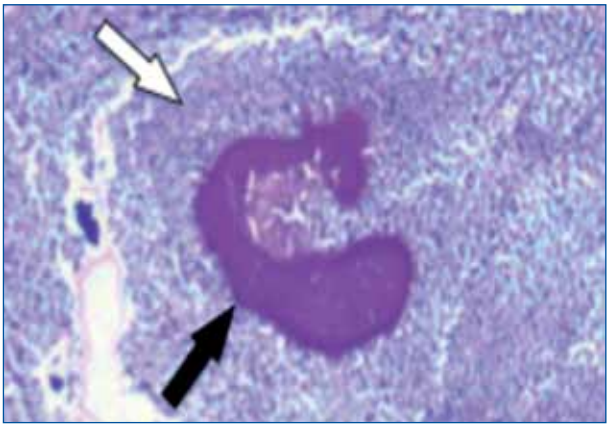

Figure 1 c: Periodic acid-Schiff stain, showing Actinomycetes infiltration (black arrow), with surrounding inflammation (white arrow)

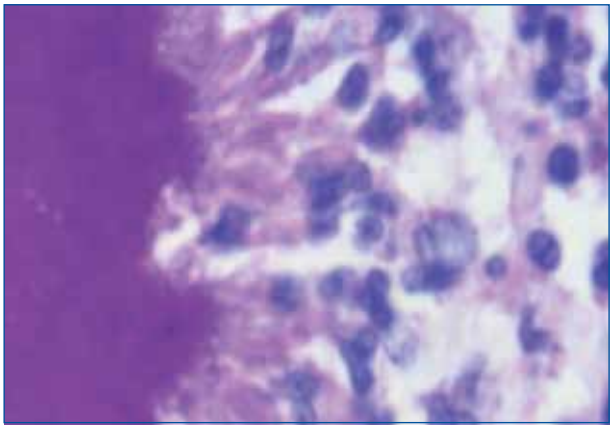

Figure 1 d: Closer view of the filamentous infiltrate on the periodic acid-Schiff

Figure 1 a-d: Microscopic appearance of lesions found in the right ovary of the patient

and Grocott's dye positive, and negative with Ziehl-Neelson stain. The remainder of the samples that were evaluated microscopically did not show the same pathology, except for the serosal surface of the appendix. A diagnosis of ovarian actinomycosis was made and the patient was treated with parenteral penicillin.

Discussion

Actinomycosis is a chronic suppurative granulomatous condition that is caused by a group of Gram-positive filamentous anaerobic bacteria. Species that are commonly associated with human infections are *Actinomyces israelii, A. naeslundii, A. odontolyticus, A. viscosus, A. meyeri* and *A. gerencseriae*.[3] At times referred to as "the most undiagnosed disease",[4] this infection can mimic a wide range of conditions and is often missed, if not actively excluded.[1] It should be included in the differential diagnosis of most cases of unconfirmed malignancy as it has been described in this context on numerous occasions.[4,5]

Clinical manifestations

Reported prevalence varies significantly in different geographic regions,[6,7] although South African data are lacking. Immunosuppression, as a result of various conditions, has largely been cited as a risk factor for this condition.[1,8] Generally, six clinical forms have been described, with highly varying prevalence.[1] The most common form is orocervicofacial actinomycosis, which is present in up to 50% of cases.[9] Typically, this is associated with previous dental manipulation or trauma, as well as poor dental hygiene.[10] Thoracic actinomycosis is the second most common form, accounting for approximately 15-20% of cases.[9,11] However, the clinical picture can vary greatly, delaying the initial diagnosis.[12] This is usually secondary to the aspiration of oropharyngeal secretions, but can also be secondary to direct extension from cervicofacial or abdominal infection. Haematogenous spread has also been described.[6]

Abdominopelvic actinomycosis accounts for an estimated 20% of cases, of which the majority present with

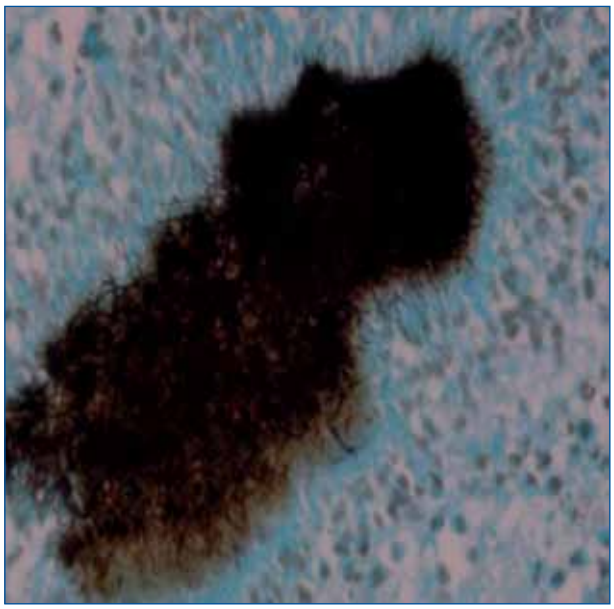

Figure 2 a: Grocott's dye-positive

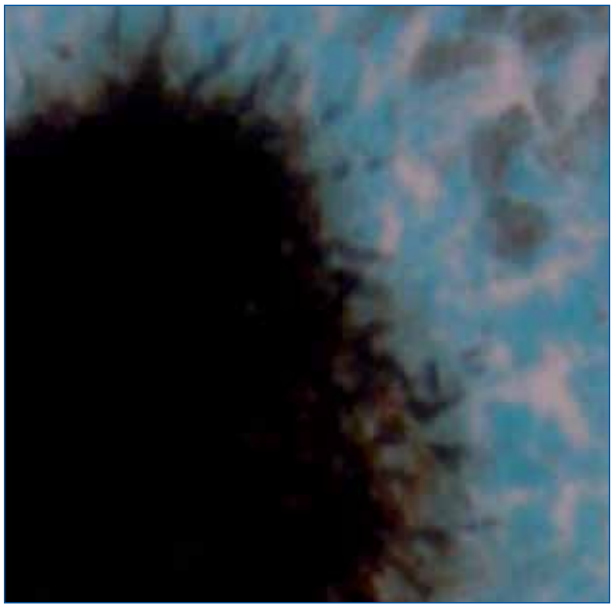

Figure 2 b: A closer view of Grocott's dye positivity, showing filaments

appendicitis.[13,14] In most instances, it has been postulated to be secondary to gastrointestinal perforations, neoplasia or surgery.[1] Direct extension can occur into the pelvis,[1] although most of the primary pelvic cases occur in association with intrauterine contraceptive devices (IUDs).[15,16] Despite this classic association, more than 30-million patient years of IUDs have been reported worldwide.[16] Currently, there are less than 100 case published reports in the English literature.[4] Very rarely, the central nervous system can be involved via either direct extension or haematogenous spread.[1] Of these cases, brain abscesses seem to be the most common presentation. Meningitis, subdural empyema and epidural abscesses are less common.[17] Rare manifestations include musculoskeletal[18,19] and disseminated disease.[18]

Diagnosis

Typically, initial findings in affected patients are non-specific and include anaemia, leucocytosis and features of inflammation, like a raised C-reactive protein or erythrocyte sedimentation rate.[3,11,16] Elevated alkaline phosphatase, as described in this case, has been noted in cases of hepatic actinomycosis.[20]

Radiological findings suffer the same non-specificity that is returned by general laboratory testing. Typically, these findings are similar to those of inflammation or malignancy.[11] As a rule, lymphatic spread does not occur. Therefore, regional lymphadenopathy is a rare finding.[21] No radiological features are considered to be specific for actinomycosis[19,20,22] and the diagnosis is rarely established preoperatively based on the radiological findings.[4]

Histopathology can greatly facilitate in establishing a diagnosis of actinomycosis. The demonstration of sulphur granules, consisting of Gram-positive filamentous organisms, is highly supportive of this diagnosis.[1] However, up to 46% of cases have no sulphur granules[23] and sulphur granules may also be present in a range of other conditions, including nocardiosis,[17] streptomycosis, chromomycosis, eumycetoma and botryomycosis.[24] Typically, actinomycosis stains positive with both periodic acid-Schiff stain and Grocott's dye, as both are specific for carbohydrates that are found in the cell wall.[23,25-33] These two positive stains distinguish actinomycosis from nocardiosis and streptomycosis.[34] The differential diagnosis will also include infection with mycobacteria. Therefore, it is suggested that a Ziehl-Neelson stain is also performed. This will be negative in cases of actinomycosis.[23]

The gold standard for diagnosis remains direct isolation of the organism from a clinical sample.[1] However, the culture is fraught with difficulties and is successful in less than 50% of cases.[20] Difficulties include administration of the antibiotic therapy prior to sampling, overgrowth by other microbes, as well as analytical difficulties.[21] Sulphur granules remain the optimal sample to obtain, but tissue may also be submitted. Once sampled, the specimen should be transported to the laboratory urgently[35] to enable rapid inoculation of the culture media and incubation in anaerobic conditions.[5] Culture should be followed by identification of the organism, as this condition is caused by a heterogeneous group of bacilli. This can be carried out through biochemical testing (commercially available kits),[36] molecular genetic methods,[37] fluorescent in situ hybridisation[37] or mass spectrometry.[38]

Conclusion

The current epidemiology of actinomycosis in South Africa has not been studied thoroughly. As immunosuppression is cited as a risk factor for acquiring this infection, clinicians should have a high index of suspicion in cases in which there is the chronic, indolent development of a mass lesion with sinus tracts, that progresses through the tissue planes and which

relapses following short courses of antibiotics. Early diagnosis may prevent invasive investigations and radical surgical procedures as these patients can simply be treated with oral penicillin.

Conflict of interest

The authors do not report any conflict of interest.

Declaration

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