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Pelvic actinomycosis: a forgotten cause of pelvic pain

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Abstract

Actinomycosis is an invasive and suppurative anaerobic infection, which can develop in the pelvis. This occurs most commonly as a result of prolonged use of an intrauterine device. The constellation of signs and symptoms associated with its typical clinical presentation include palpable mass, weight loss and malaise. It can be misdiagnosed as a result and often as a malignant process. Left unrecognised, pelvic actinomycosis can lead to sequelae such as severe abscess, fistula formation and even infertility. Removal of the intrauterine device and a prolonged course (6–12 months) of antibiotic treatment form the cornerstone of management. Surgery can be required in select cases. This article provides an overview of pelvic actinomycosis, including its background, presentation, investigations and management.

Key words: Abscess; Actinomycosis; Contraception; Infection

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Introduction

Actinomycosis is a rare, opportunistic and potentially invasive bacterial infection caused by *Actinomyces* spp. (Smego and Foglia, 1998). Infection has been described at many different anatomical sites including oral-cervicofacial (50%), pulmonary-thoracic (20%), abdominopelvic (20%) and the CNS (<10%) (Wong et al, 2011; Bonnefond et al, 2016; Veenakumari and Srivedi, 2017). It typically carries an insidious presentation and therefore often delivers a real diagnostic conundrum to the clinician. Over time, it has earned itself the title of the 'great mimic' or 'great pretender' given the many different signs and symptoms it can present with (Montori et al, 2015). In the setting of pelvic actinomycosis this can include palpable mass, weight loss and malaise, thus it is easily mistaken for a disseminated malignant process or an infectious disease such as tuberculosis.

Descriptions of the disease have appeared in the literature since the early 1800s (Bollinger, 1877). However, these records were predominantly bovine-related. The discovery of the first confirmed human infection is attributed to the German pathologist Emil Ponfick in 1879 (Garner et al, 2007). It was only later in the 20th century that a bacterial cause was definitively established. Before this, a fungal infection was widely believed to be the pathogenic culprit (Rudin, 1976). Early identification and implementation of appropriate multidisciplinary management usually results in an excellent prognosis. However, failure to recognise and delays to diagnosis can lead to serious adverse sequelae such as infertility and even death. Such is the enigma of the clinical picture caused by this fungal-like pathogen, cases can present to a multitude of hospital specialities.

While there is clear consensus that the disease is rare, epidemiological data are conflicting regarding the true prevalence – it is estimated to lie between one case per 40–119 000 head of population (Cintron et al, 1996). Minsker and Yegorova (1974) reported over 2000 cases at their institution over an 11-year period. There has also been a plethora of case series and case reports over the past decade to support the need for awareness and understanding of this disease process in both the primary and secondary care setting. This article provides an overview of pelvic actinomycosis, including its background, presentation, investigations and management.

Pathogenesis

Actinomycetes are Gram-positive anaerobic bacilli (Valour et al, 2014). These facultative anaerobes can be found as normal commensals in the endogenous flora of the genital and

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alimentary tract. While there exist over 30 species of this genus, *Actinomycoses israelii* (fine, beaded rods) is the most commonly isolated. *A. viscosus* (filamentous, branching rods) and *A. meyeri* (short, fine rods) are also often identified (Public Health England, 2015). Infection develops at sites of barrier alteration or breakdown and where the epithelial lining has been breached (Wong et al, 2011; Bonnefond et al, 2016). This includes sites of surgery, visceral perforation, trauma and as a result of foreign body insertion (Smego and Foglia, 1998). While the pathogen normally carries a low virulence, it is opportunistic and the disease carries a predilection for hosts with a history of poorly controlled diabetes, alcohol excess and immunosuppression such as human immunodeficiency virus (HIV) (Bonnefond et al, 2016).

Pelvic actinomycosis is most commonly (>80%) associated with prolonged use of an intrauterine device (Gupta et al, 1976). It is therefore recommended that intrauterine devices are changed at least every 5 years. Other recognised causes include after transvaginal mesh or transobturator sling procedures, especially in the setting of revision surgery (Ozel et al, 2010; Masata et al, 2014). It has also been reported following in vitro fertilisation and caesarean section (Sung et al, 2011). Up to 4% of individuals with an intrauterine device in situ have been reported to develop infection (**Figure 1**) (Montori et al, 2015). Valicenti et al (1982) reported rates of colonisation with *Actinomycoses* that had been identified at time of cervical smear testing. From a sample of 6450 intrauterine device users, 1.6% were found to be colonised. The dilemma facing clinicians is not knowing which patients go on to develop the infection. No universal protocol exists to advise on management of those patients who are asymptomatic and colonised. In most countries, removal and exchange of the intrauterine device is generally considered sufficient (Bonacho et al, 2001; Public Health England, 2015).

As part of the history taking, it is vital to determine how long the intrauterine device has been in place. Interestingly, there is no evidence to indicate that a specific type of intrauterine device carries a greater risk of developing pelvic actinomycosis (Garner et al, 2007).

Presentation

Given the array of signs and symptoms that can be associated with pelvic actinomycosis, cases may present to a number of different clinical specialties, such as gynaecology, urology, general surgery and internal medicine. The clinical presentation typically includes a palpable mass, malaise and weight loss (Bollinger, 1877) (**Figure 2**). It is therefore easily mistaken for a process of disseminated abdominal or pelvic malignancy. Other possible symptoms include vaginal discharge, pelvic pain and fever (**Table 1**). Patients do not present with ascites, which more than a third of patients with ovarian cancer present with at the time of diagnosis (Ahmed and Stenvers, 2013). Regional lymphadenopathy is not normally seen either, which can help differentiate pelvic actinomycosis from other conditions (Mohajeri et al, 2015).

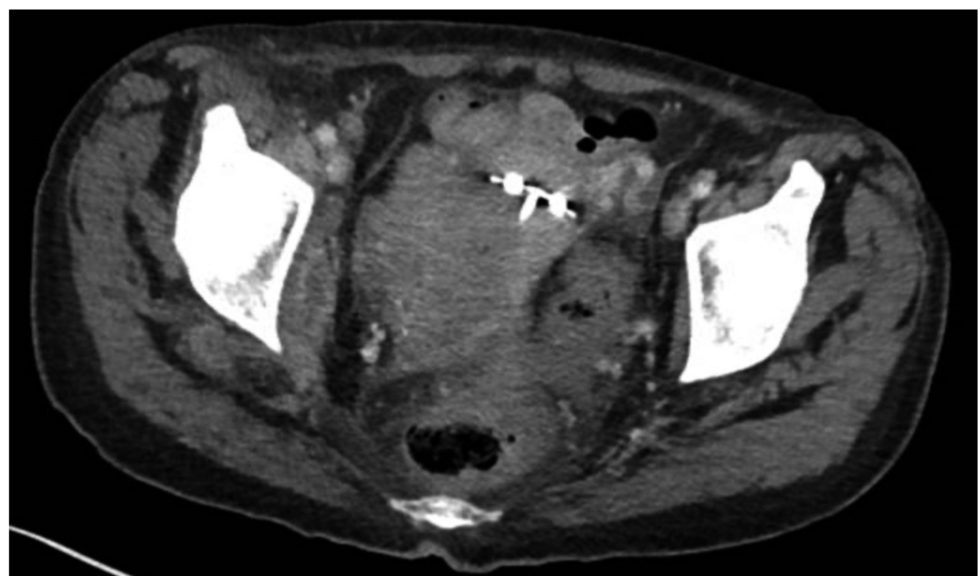

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Figure 1. Circumscribed fluid collection adjacent to an intrauterine device.

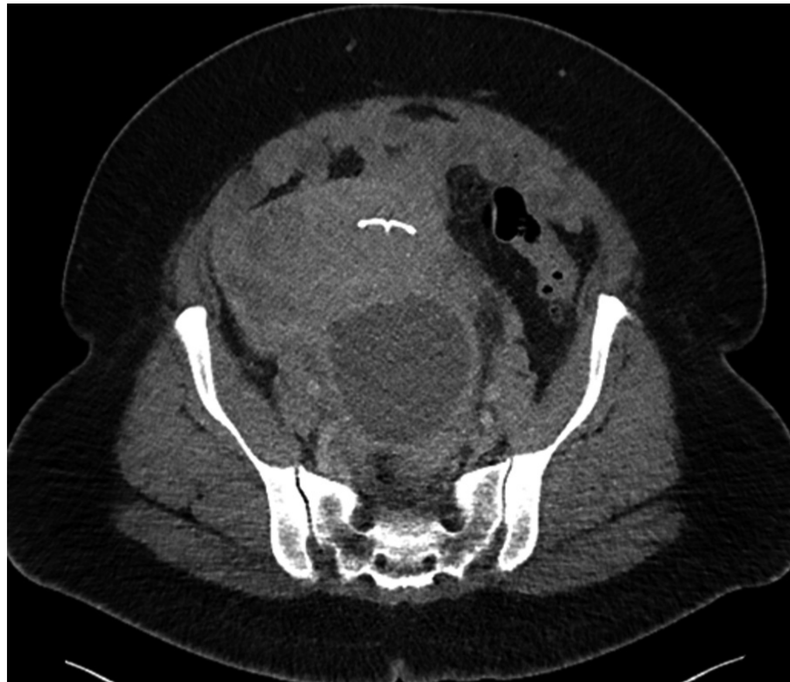

Figure 2. Pelvic mass with both cystic and solid components.

Table 1. Presenting symptoms according to site affected

Site	Symptoms
Pelvic	■ Abdominal mass ■ Abdomino-pelvic pain ■ Vaginal discharge ■ Dyspareunia ■ Intermenstrual bleeding ■ Dysuria ■ Weight loss ■ Malaise ■ Fever
Oral-cervicofacial	■ Swelling to mandibular or peri-mandibular region ■ Pain on mastication ■ Weight loss ■ Malaise ■ Fever
Pulmonary-thoracic	■ Dry or productive cough ■ Haemoptysis ■ Dyspnoea ■ Chest pain ■ Weight loss ■ Malaise ■ Fever
CNS	■ Headache ■ Loss of consciousness ■ Loss of vision ■ Limb weakness ■ Weight loss ■ Malaise ■ Fever

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In a series published by Triantopoulou et al (2014), symptom duration ranged between 5 days and 8 months and the average length of time the intrauterine device had been in situ was 7 years. Given the association with intrauterine devices, most patients will be of reproductive age. However, patients can have an intrauterine device for a protracted period because it has been forgotten. In such cases patients can be much older. Prabhala et al (2016) reported a 76-year-old with the condition who was found to have had the device for over 40 years.

While patients with chronic symptoms may present via primary care, sequelae such as abscess formation leading to sepsis can cause these patients to present to the emergency department and surgical specialities in an acute on chronic form. Sung et al (2011) reported that 50% of the cases which presented to their institution over a 15-year period required emergency surgery as a result of having symptoms of peritonitis.

Other clinical presentations of actinomycosis

While this review focuses on pelvic actinomycosis, it is valuable for the clinician have an awareness and knowledge of other possible presentations of this disease process. In oral-cervicofacial disease (the most common site affected), patients can present with soft tissue swelling(s) of the submandibular or perimandibular region(s) (Wong et al, 2011). These are usually slow growing over a number of months and fluctuant upon palpation. Mastication is generally associated with pain. The history may reveal recent dental surgery. Dental caries, gingival trauma and poor dentition are all risk factors. Haematogenous or local spread of oral-cervicofacial disease can lead to infiltration of the CNS. In CNS cases, patients may display new onset of focal neurological signs suggestive of a space-occupying lesion (Smego, 1987).

Patients with pulmonary-thoracic actinomycosis may present with dyspnoea, a dry or productive cough and even haemoptysis. Pre-existing lung conditions such as bronchiectasis and chronic obstructive pulmonary disease render patients at higher risk.

Patients with abdominal actinomycosis may present with a history of bowel change and bloating as a result of stricture formation caused by the disease (Garner et al, 2007). Peri-anal abscesses can also occur and cause further diagnostic difficulty as Crohn's disease can be initially suspected. Where the colon and/or ano-rectum are affected, the principal cause is usually intrauterine devices. If the ileo-caecal area is affected, this is most commonly after previous appendiceal perforation. The patient usually presents with right iliac fossa mass and there may be fistula formation.

Cutaneous actinomycosis has also been reported (Wong et al, 2011). These cases typically occur after local trauma, for example at the site of a surgical scar. History may reveal a chronic lesion, which fails to heal. There may be discolouration to the area as well as sinus formation.

Constitutional symptoms such as fever, weight loss and malaise are common to all the anatomical sites affected by actinomycosis (Smego and Foglia, 1998).

Diagnosis

While there are no specific laboratory tests, standard blood tests usually show leucocytosis, anaemia and raised levels of inflammatory markers. Adding to the diagnostic challenge is that patients may have had their level of CA-125 tumour marker checked and these levels can be elevated (normal <32 kU/litre) in the context of this particular infection (Garner et al, 2007). Cross-sectional imaging such as computed tomography is recommended. This can reveal a poorly defined mass with heterogenous enhancement after contrast administration. This enhancement is related to the granulation tissue and fibrosis (Ha et al, 1993). Progression of the infection can lead to a 'frozen pelvis' appearance which can resemble malignancy or endometriosis (Martínez et al, 2014).

Radiographic features are usually non-specific and non-diagnostic (Table 2). These include free fluid and indurated pelvic fat (Mohajeri et al, 2015). Central abscess formation can lead to formation of sinus tract(s) and subsequent fistulas with other organs or cutaneously (Ha et al, 1993). Haematogenous spread can lead to nodule formation at extra-pelvic sites such as the liver, which can further cause the clinician to suspect malignancy as the underlying disease process. Even with cross-sectional imaging fewer than 10% of cases are accurately diagnosed preoperatively (Lewis et al, 1978; Harris et al, 1985). Even while a suspicion

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of the condition may be raised at the time of surgery, the intraoperative appearances also display no specific features to suggest actinomycosis. Therefore pathological examination is relied upon in the majority of cases. Sinha et al (2016) carried out a prospective study of pathology specimens for 100 hysterectomies performed at their institution. In two cases who had undergone this surgery for clinically diagnosed dysfunctional uterine bleeding the underlying cause was revealed to be actinomycosis.

Diagnosis can therefore be formally confirmed through histopathological evaluation (Weese and Smith, 1975). Samples can be obtained by either image-guided biopsy or directly at the time of surgery. Cervico-vaginal smear with Papanicolaou (Pap) staining is another method of sampling (Veenakumari and Srivedi, 2017). Histological evaluation typically reveals suppurative changes to the tissue and sulphur granules (requires haematoxylin-eosin stain) with the classical yellowish appearance (Wong et al, 2011). These tiny clumps, which are made up of clusters of bacteria held within a biofilm, are present in approximately 75% of actinomycosis infections (García-García et al, 2017). They are not truly pathognomic of actinomycosis as they can be found in other infections such as nocardiosis and chromomycosis, but they are considered highly suggestive (Wong et al, 2011). The Gram stain reveals Gram-positive bacilli (Public Health England, 2015). Microscopy of the pus sample can identify the causative organism. However, because of the slow-growing nature of actinomycosis, a prolonged incubation period in anaerobic conditions is mandated (Westhoff, 2007). Colonies of *A. israelii* characteristically show a 'molar tooth' formation on the agar plate (Hotchi and Schwarz, 1972). It can take up to several weeks to achieve an adequate and satisfactory culture on agar (37 °C). Combined with the fastidious need to secure the sample quickly into an anaerobic environment, the failure rate for successful isolation using this controlled technique exceeds 50% (García-García et al, 2017).

Treatment

Early involvement of the microbiologist is recommended. Prolonged antibiotic treatment forms the mainstay of the management (Minsker and Yegorova, 1974). Insufficient treatment courses are frequently associated with relapse. Indeed, a failure to respond to multiple courses of antibiotics and persistence of symptoms can be the trigger for a diagnosis of actinomycosis to be considered. A penicillin-based regimen delivered parenterally is recommended for up to 6 weeks. The first-line treatment option is penicillin G (Wong et al, 2011) at a high dosage (18–24 million units a day) to facilitate tissue penetration. Amoxicillin is a potential alternative. This can then be switched to oral treatment (2–4 g/day) for 6–12 months (Wong et al, 2011). Treatment regimens lasting up to 18 months have been described (Garner et al, 2007). *Actinomycoses* spp. are resistant to metronidazole and aminoglycosides (Public Health England, 2015). Clindamycin or linezolid is an alternative in patients with penicillin allergy (Yang and Im, 2018). Erythromycin can be selected if the patient is pregnant (Ruiz et al, 2017). The intrauterine device must also be removed – this is an essential step. Alternative forms of contraception should be discussed with the patient.

Surgical intervention

Surgical drainage and/or reconstruction may be resorted to in cases of severe abscess or fistula involvement. Hydronephrosis can occur as a result of mass effect from the

Table 2. Radiological features

Suggestive of actinomycosis	■ Free fluid ■ Indurated pelvic fat ■ Enhancing mass ■ Hydronephrosis ■ Sinus tracts ■ Fistula(s)
Not suggestive of actinomycosis	■ Ascites ■ Lymphadenopathy

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'pseudotumour' (Figure 3). The decision to proceed to early decompression of the upper tracts via ureteral stenting or percutaneous nephrostomy is determined on a case by case basis. It is indicated in those cases of pain, renal impairment or subsequent urinary sepsis caused by the obstruction (Marella et al, 2004). If a ureteral stent has been placed, the surgeon can plan for removal once prolonged antibiotic treatment has been completed.

Prognosis and follow up

Published mortality rates associated with actinomycosis range between 0 and 28% (Smego and Foglia, 1998; Sharma et al, 2002). However, the worst outcomes are consistently seen in patients with CNS disease. Only a few deaths have been reported associated with pelvic actinomycosis, and these all occurred as a result of sepsis in patients with multiple pre-existing medical comorbidities (Cintron et al, 1996). In the majority of cases, including those which present to secondary care, early identification allows for good treatment response and excellent long-term outcome (Garner et al, 2007). However, as a result of delays and the bacteria's mechanism of tissue invasion, serious sequelae can occur such as tubo-ovarian abscess, destruction of parenchyma and subsequent infertility (Rudin, 1976; Wong et al, 2011; Veenakumari and Srivedi, 2017). The difficulties and delays in diagnosis therefore have the potential for high morbidity associated with pelvic actinomycosis. Patients should be followed up through the duration of their prolonged antibiotic treatment and beyond. There is no universal follow-up protocol, but it is generally agreed among experienced centres that it should be continued for several years given the risk of recurrence. There are very limited data to suggest the rate of recurrence.

Conclusions

Pelvic actinomycosis is a rare but curable disease. However, given its insidious presentation, if left unrecognised it can cause severe sequelae. Prolonged antibiotic treatment and removal of the intrauterine device are the cornerstone of treatment. Familiarisation with this topic by clinicians in both primary and secondary care is recommended.

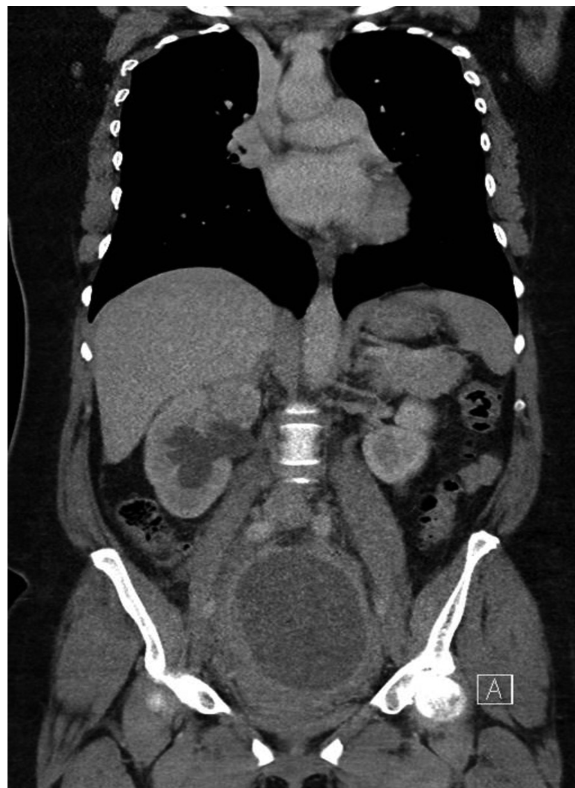

Figure 3. Right hydronephrosis can be seen on coronal view.

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Key points

- Actinomycosis is an invasive and suppurative anaerobic infection, which can develop at many different anatomical sites including the pelvis.
- Pelvic actinomycosis is most commonly caused by prolonged use of an intrauterine device.
- Features of weight loss, malaise and palpable mass can lead it to be misdiagnosed as a malignant process.
- Removal of the intrauterine device is essential and alternative contraception methods should be discussed with patient.
- Early recognition and prolonged antibiotic therapy with a penicillin-based regimen is the mainstay of management.

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Conflicts of interest
The authors declare no conflicts of interest.

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Curriculum checklist

This article addresses the following requirements from the general internal medicine training curriculum:

- Managing an acute unselected take
- Managing an acute specialty-related take
- Managing medical problems in patients in other specialties and special cases.

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