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ORIGINAL ARTICLE

# Actinomycosis Mimicking Gynecological Malignancy: Imaging Patterns in Seven Cases

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## ABSTRACT

Pelvic actinomycosis is uncommon and believed to be related to the use of intrauterine devices (IUDs). It may present as a complex gynecological mass either uterine or adnexal with or without local pelvic spread or with peritoneal dissemination, all features which mimic gynecological malignancy. We describe seven women with proven actinomycosis who presented to a single cancer center gynecological cancer multidisciplinary team meeting (MDTM) to illustrate these imaging appearances and highlight discriminant features of actinomycosis. A minority of women had concurrent use of an IUD. Involvement of the pararectal space was a feature of pelvic disease extension. We describe the value of image-guided core biopsy (IGCB) in confirming the diagnosis.



**Keywords:** Arteriovenous fistula, Fistula, Hemodialysis, Infection, Patency, Primary failure, Rates, Steal syndrome, Thrombosis, Vascular access.

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## INTRODUCTION

Otto Bollinger described bovine actinomycosis in 1877 and in 1879, James Israel described the first human involvement. Actinomyces israelii is a gram-positive, anaerobic, non-acid fast filamentous bacterium. It is a common commensal in the oral cavity, vagina, and large bowel.[1] Pelvic actinomycosis is an uncommon infection, most commonly described in association with use of IUDs[2,3] diverticular disease, cholecystitis, abdominal surgery, and penetrating trauma.[4,5] We describe our experience of seven women with pelvic actinomycosis mimicking gynecological malignancy at a tertiary oncology center which, to the best of our knowledge, is the largest such series yet reported.


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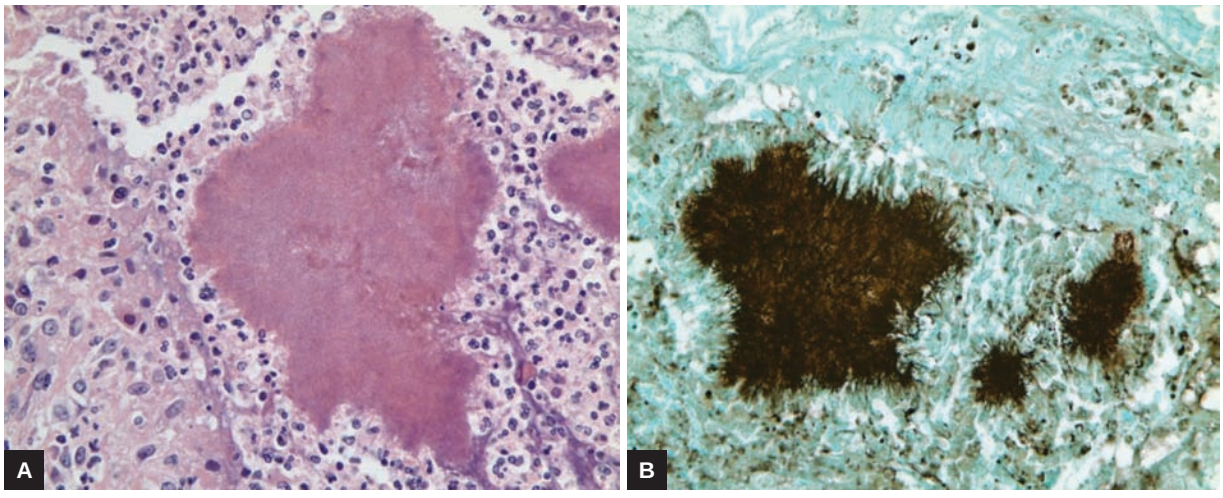
## MATERIALS AND METHODS

### Clinical

Over a 5-year period, seven cases of abdomino-pelvic actinomycosis were identified prospectively by one of the authors during attendance at the weekly MDTM. Five cases were histologically proven and two were assumed to be actinomycosis, based upon resolution of imaging abnormalities following specific antibiotic therapy. These two cases had no evidence of malignancy on multiple core biopsies which showed only a mixture of acute and chronic inflammation. No other organism was isolated from vaginal or uterine swabs. Because of a strong clinical and imaging suspicion of the diagnosis, the women were treated as actinomycosis with penicillin with excellent clinical recovery and complete or partial resolution of the imaging abnormalities. No other cases of proven pelvic urogenital actinomycosis were identified in a search of the pathology department database for this period.

The average age at presentation was 43 years (32–54 years). One woman had an IUD in place at presentation and two women had prior use of IUDs. All seven were referred to the regional MDTM with a provisional diagnosis of gynecological malignancy. Five women were suspected to have adnexal cancer and two to have suspected cervical cancer. One woman had prior grade II cervical carcinoma, treated by hysterectomy. Four women presented from our own local gynecology team and three were referral cases having already been discussed in other local cancer unit MDTM. No patient had a history of fever. The tumor marker CA-125 was raised in only two cases while the inflammatory marker C-reactive protein was raised in four of the seven cases. In five cases, the white cell count was raised (12.4–18.9 × $10^9$/L) and in all cases, differential white cell count showed neutrophilia.

One woman was thought to have pelvic inflammatory disease (PID) after initial MDTM review and was treated in her local hospital as such. While undergoing antibiotic therapy, she required exploratory surgery for unremitting pain and for drainage of pelvic suppuration. Another woman with a complex pelvic mass suspected to represent ovarian cancer developed small bowel obstruction necessitating emergency surgery a few days after discussion in the MDTM. Both these patients were found to have actinomycosis on examination of the surgical specimens. Diagnosis in the remaining five patients was made by




**Figs 1A and B:** (A) The H&E stain shows sulfur granules, which are circumscribed masses of bacteria in branching filaments with a radial/palisading pattern at the periphery. (B) The Grocott stain shows the filaments to better effect. The granules are surrounded by a mixed inflammatory infiltrate, mainly neutrophil polymorphs with some histiocytes

image-guided biopsy or gynecological biopsy directed by imaging features. These women avoided surgery.

Confirmatory histology was thus obtained using IGCB in three women, from operative specimens for two women and image-guided biopsy for the other two women. They both had an abnormal cervix and uterus on imaging as well as on clinical examination, but with no clinical evidence of malignancy. After MDTM discussion, they underwent cervical and parametrial biopsy and/or uterine curettings, which showed inflammatory material only. Subsequent imaging in these two women showed resolution of abnormalities after antibiotic therapy.

Image-guided biopsies were taken following local anesthesia under either ultrasound (US) or computed tomography (CT) guidance; US-guided biopsy was diagnostic. For one woman, CT-guided biopsy was initially performed and showed nonspecific chronic inflammatory changes, but a repeat US-guided biopsy was diagnostic of actinomycosis. For IGCB, an 18-gauge cutting needle incorporating a spring-loaded device was used, producing a core of up to 1.8-cm-long specimen. Biopsies were taken from the infracolic omental cake (1), liver (1), and a pelvic mass.[1] The number of biopsy cores that were taken was at the discretion of the operator, but the aim was to provide material equivalent of two full biopsy cores. The IGCB was only performed after MDTM review and when there was imaging evidence of dissemination of the disease process.

The institutional review board granted a waiver to review the case notes in further detail in a retrospective fashion.

## Pathology

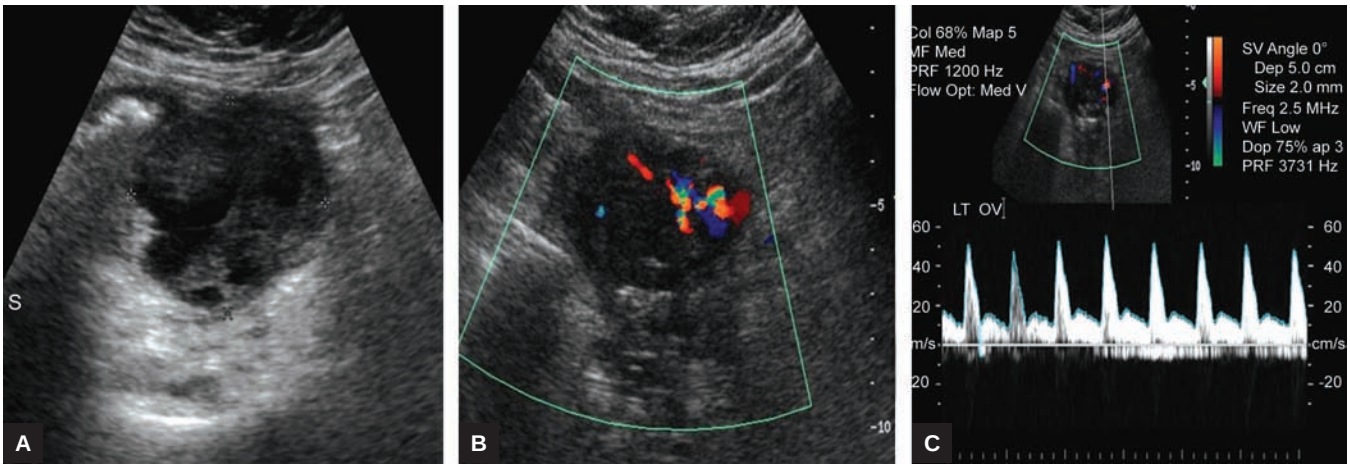
The sections were initially routinely processed in paraffin and stained with hematoxylin and eosin (H&E), followed by Gram, Grocott, Hexamine silver, and extended periodic acid–Schiff stains. Actinomyces colonies were readily identified as distinct "sulfur granules" on histological examination and these were typically surrounded by inflammation, granulation tissue, and fibrosis. This formation of an inflammatory mass may mimic a malignant tumor on macroscopic examination. The diagnosis of actinomycosis was made on microscopic examination of the specimen by the presence of sulfur granules and the absence of neoplastic cells. The sulfur granules comprised a central eosinophilic core surrounded by radiating gram-positive bacterial filaments (Fig. 1A). The diagnosis of actinomycosis was confirmed by the highlighted slender filaments of actinomyces on silver and Gram stains (Fig. 1B).

## Imaging Features

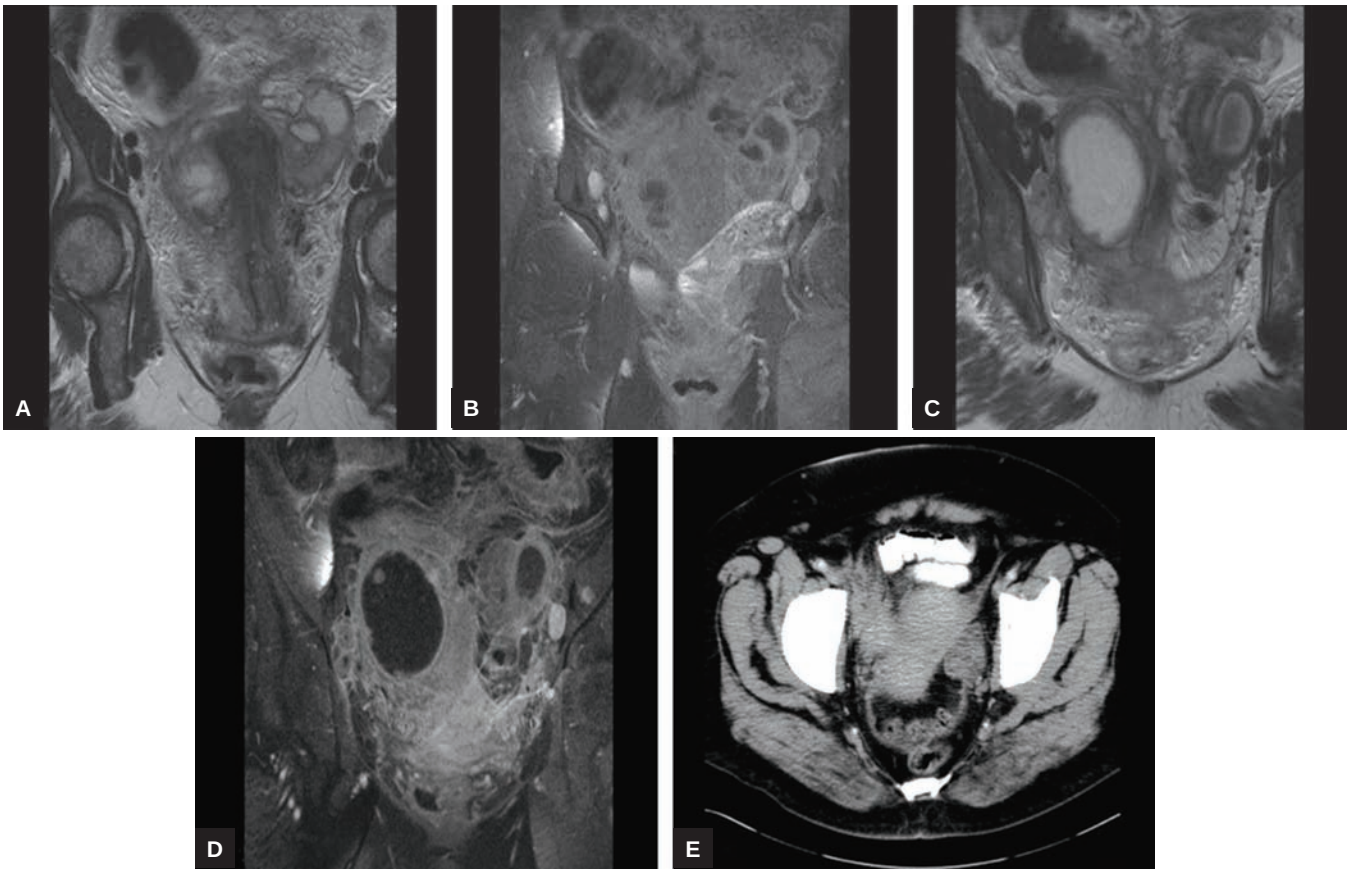
The presentations mimicking as gynecological malignancy are summarized in Table 1.

**Table 1:** Imaging features in seven cases of actinomycosis

| *Imaging feature* | *Number of cases* |
|---|---|
| *Features of primary cancer* | |
| Adnexal mass | 5 |
| Uterine/cervical mass | 2 |
| *Features of local extension* | |
| Lymphadenopathy | 2 |
| Pelvic sidewall involvement | 2 |
| Pelvic fluid collections | 2 |
| Involvement of sigmoid mesentery | 1 |
| Involvement of pararectal spaces | 3 |
| Hydronephrosis | 2 |
| *Features of dissemination* | |
| Ascites: pelvic | 2 |
| Ascites: upper abdominal | 0 |
| Omental masses | 2 |
| Liver surface deposit | 1 |

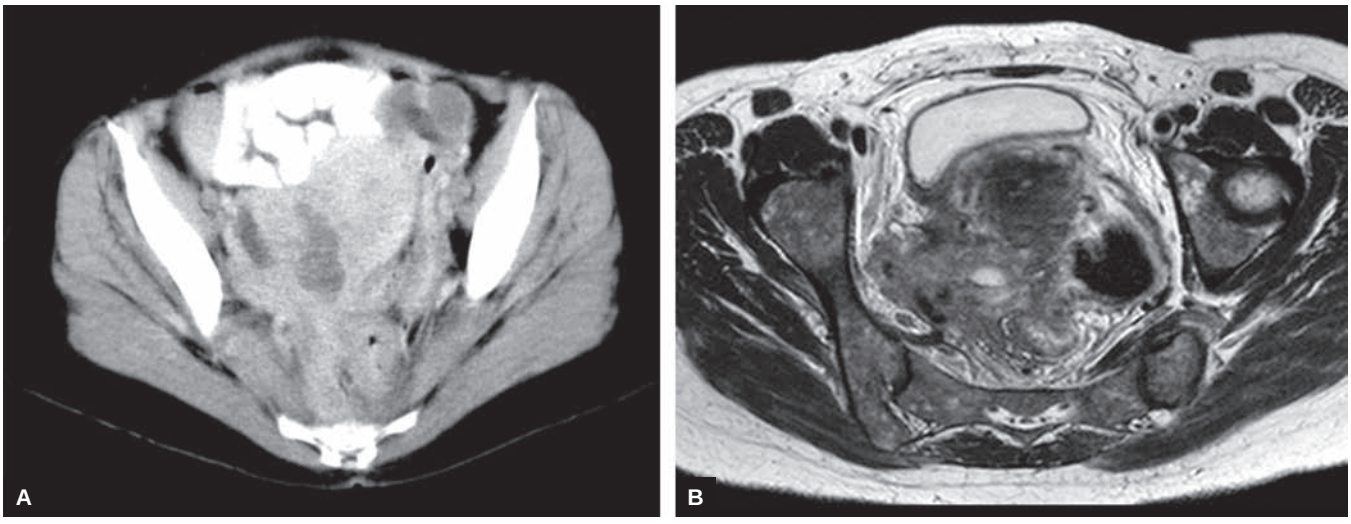



**Figs 2A to C:** (A, B) A sonographically complex solid-cystic mass in the left adnexa which shows abnormal color flow in the solid component and is thus suspicious for a malignant mass; (C) the spectral Doppler shows low-resistance velocity waveforms suggestive of malignancy

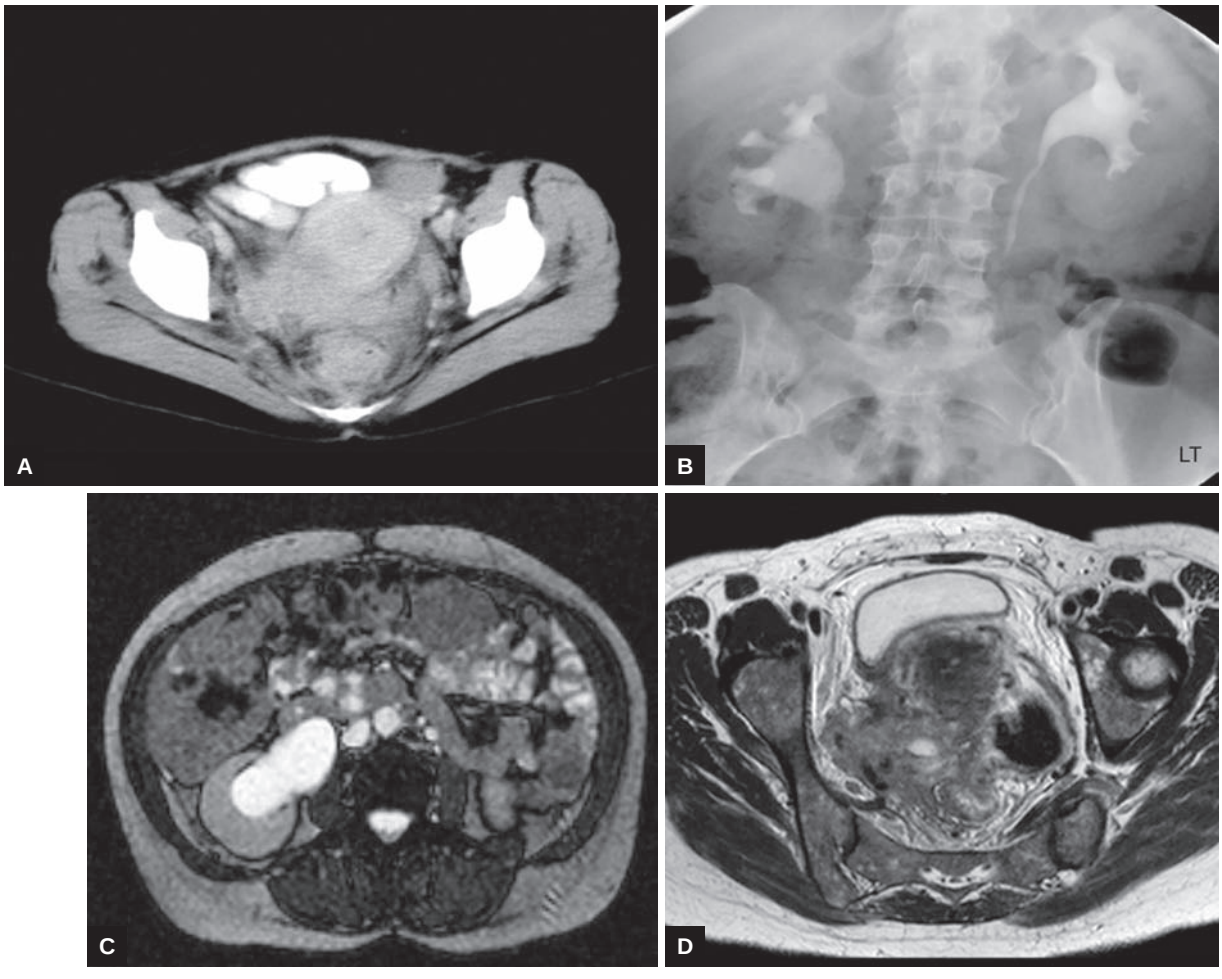



**Figs 3A to E:** (A) Coronal oblique T2-weighted MRI shows bilateral complex adnexal masses that have low signal intensity with some regions of high signal intensity and (B) the corresponding contrast-enhanced fat-suppressed T1-weighted MRI shows enhancement of the multilayered wall around cystic spaces. A 10 mm lymph node with enhancement is seen in the left iliac chain. Note the generalized "stranding" of the fat of the pelvic peritoneum in (A) which enhances on (B) suggestive of a diffuse infiltrative process. (C) Coronal T2-weighted MRI shows mural nodules in the cystic part of the right adnexal mass and (D) the corresponding contrast-enhanced fat-suppressed T1-weighted MRI which shows enhancement of the mural nodules along with the thick cyst walls on the right side. Note also right iliac lymphadenopathy showing small foci of necrosis. (E) Contrast-enhanced CT at an earlier time shows the infiltrative pattern of extension of disease from the right adnexal mass along the broad ligament and sigmoid mesentery. Simultaneous extension to the right pelvic sidewall and sigmoid mesentery is an odd pattern with primary ovarian malignancy

There were complex adnexal masses with solid components which showed abnormal Doppler flow on US and abnormal gadolinium enhancement at magnetic resonance imaging (MRI) (Figs 2 and 3). The solid components included mural nodules or mural thickening and irregularity exceeding 3 mm in thickness. Pelvic lymphadenopathy was seen in two women, one with solid lymphadenopathy and the



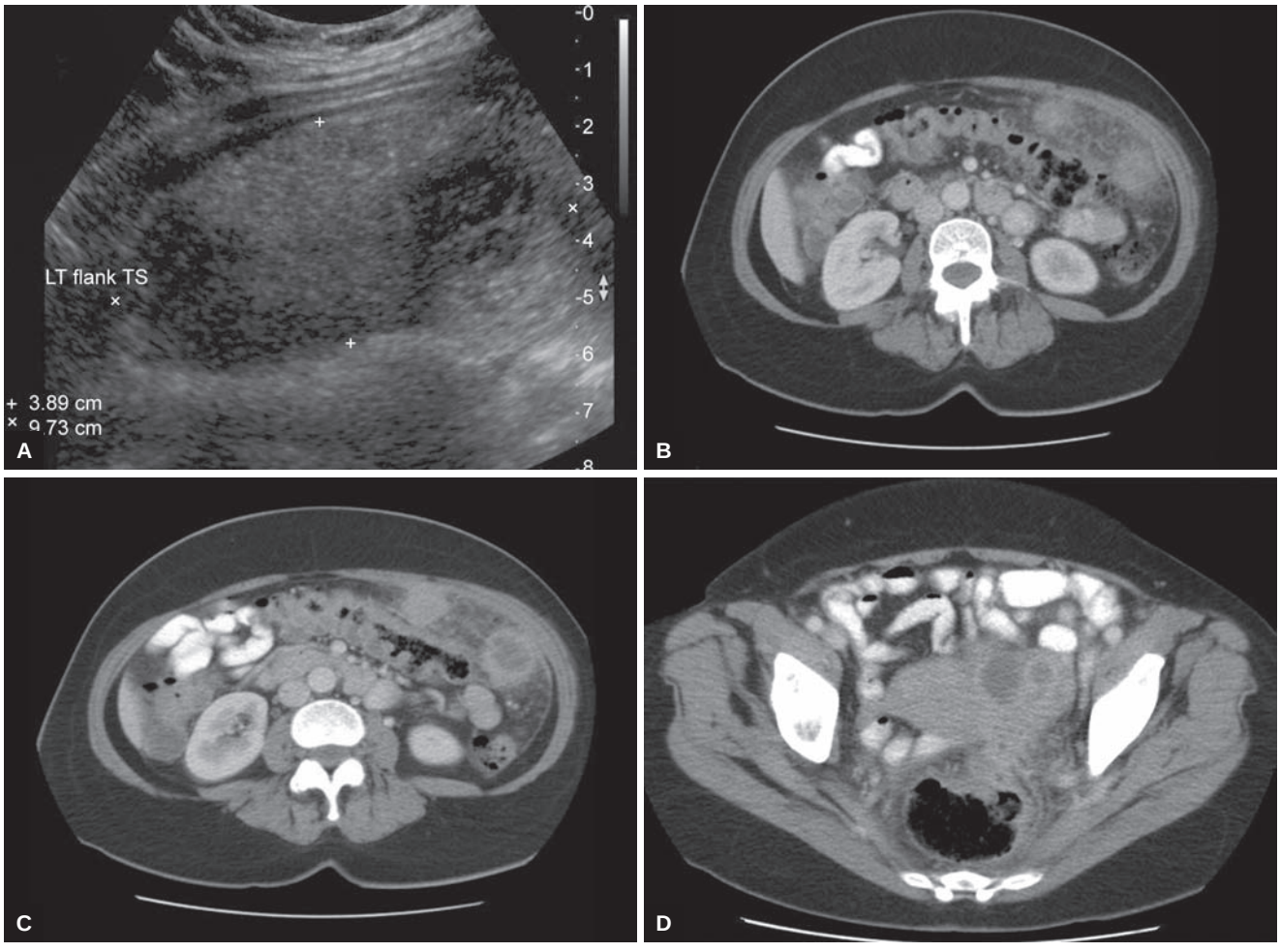

**Figs 4A and B:** (A) Contrast-enhanced CT scan shows a right adnexal mass with large areas of necrosis. Also note the right pelvic side wall involvement and a "tongue-like" direct extension though the right para-rectal space to the sacrum, again an odd feature for primary adnexal malignancy and (B) an axial T2-weighted MRI shows the same process. The adnexal mass has intermediate signal intensity with some regions of high signal intensity



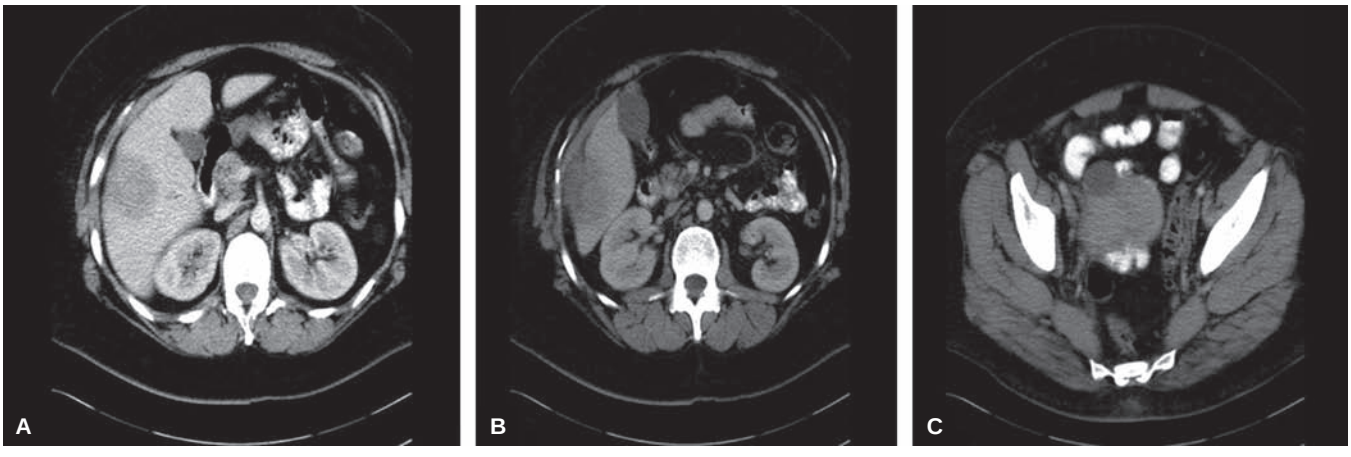

**Figs 5A to D:** The adnexal mass causing hydronephrosis on various modalities

other with multiple small areas of micro-necrosis in enlarged nodes (Fig. 3).

Local pelvic infiltration extended into sigmoid mesentery, pararectal and mesorectal spaces, or laterally to the pelvic sidewall (Fig. 4). The infiltrative process also involved the ureter causing hydronephrosis in two women (Fig. 5). When disease was predominant in the subperitoneal space of the pelvis, there was marked enhancement of the pelvic peritoneum and florid stranding of the fascial and fat spaces above and below this (Fig. 6).




**Figs 6A to D:** (A) Ultrasound of the left flank shows a low echo texture solid mass just below the anterior abdominal wall in keeping with an omental cake. (B) and (C) Contrast-enhanced CT which confirms an infiltrative mass in omentum with at least two large cavitating masses and small amount of free fluid hepatorenal pouch. (D) The CT of the pelvis shows a complex left adnexal mass with invasion of the mesorectal fat, an unusual feature of primary ovarian cancer




**Figs 7A to C:** (A) and (B) Contrast-enhanced CT shows a liver surface deposit extending as a round, solid mass into the parenchyma of the right lobe of the liver and which simulates a metastatic deposit and (C) CT at the level of pelvis of the same patient shows a predominantly solid adnexal mass. Note the absence of ascites on these images and indeed no intervening disease between adnexa and liver

Omental masses and liver surface deposits were seen in two women (Fig. 7). Notably on CT, the omental masses were nodular, more like "buns" than "cakes," and these showed central low attenuation (Fig. 6). This feature correlated histologically with central necrosis. Ascites were minimal or absent.

The MR signal characteristics were varied. There was bland T1-signal in the solid elements of pelvic

**Table 2:** Unusual imaging features in actinomycosis and comparison with PID and malignancy features

| *Features* | *Acute PID* | *Actinomycosis* | *Primary ovarian malignancy* |
|---|---|---|---|
| Primary disease site | Uniform, thick-walled predominantly cystic. Occasional thickening of peritoneal folds | Ill-defined cystic or solid masses. No respect for fascial planes in spite of smaller primary mass | Usually well defined, solid, cystic, or mixed. Fascial planes offer longer resistance to local spread for smaller masses |
| Omental disease | Usually fine peritoneal thickening and enhancement | Masses like "buns" with or without cavitations | Large omental cakes or wispy disease. Rarely cavitate prior to treatment |
| Lymphadenopathy | Reactive | Micro-abscess within nodes or solid nodes | Usually solid with exception of cervical cancer |
| Liver surface disease | Rarely seen except in Fitz-Hugh-Curtis syndrome | Liver surface disease in absence of ascites | Liver surface or parenchymal disease almost always with ascites |
| Mesorectal invasion | Rare, thickening of uterosacral fold common with posterior extension | Mesorectal invasion out of proportion to size and site of primary mass | Unusual with adnexal masses, seen more commonly in cervical cancer |
| Pelvic sidewall involvement | In the form of enlarged reactive nodes | Involvement out of proportion to size and site of primary mass | Commoner with cervical cancer than other adnexal masses |
| Hemorrhage | Rare | Seen in solid masses | Unusual feature of solid ovarian mass |

actinomycosis. T1 high signal suggestive of hemorrhage was not seen. T2-weighted images showed both low to intermediate signal in some of the solid areas, possibly suggesting a fibrotic process. High signal intensity was associated with cysts, fluid collections, or necrotic areas, and intermediate signal in the mural nodules of predominantly cystic masses. Involved pelvic floor and pelvic sidewall muscles also showed increased T2 signal. T1-weighted gadolinium-enhanced images showed intense enhancement of the solid elements or the solid components of lymphadenopathy and cystic masses and within the septae of complex cystic-solid masses. Enhancing infiltration of pelvic fat on fat-suppressed T1-weighted images was a prominent finding.

## DISCUSSION

While 20% of IUD users have actinomyces-like organisms as part of their normal genital flora,[6] pelvic actinomycosis is a very rare, but serious infections may require long-term medical (antibiotic) therapy and may necessitate intervention and surgery to manage complications. Two of our seven cases required surgery for symptoms, one for small bowel obstruction and another for unremitting pain and pelvic sepsis which did not respond to standard antibiotic therapy for PID. There are thus similarities between actinomycosis and advanced gynecological malignancy in both clinicoradiological presentation and management. Pelvic actinomycosis is a chronic suppurative and granulomatous disease which does not respect anatomical barriers.[5] This property may result in condition being mistaken for a malignant "frozen pelvis." Thus, in some cases, unnecessary radical cancer surgery has been performed.[7,8]

The unifying feature of our seven cases is that they all presented to a gynecological oncology MDTM in a Cancer Unit with suspicion of new or recurrent cancer. None had features of a septic condition, none had fever, and only mild neutrophilia was present. One was suspected to be complex PID after initial MDTM discussion and one was suspected to have ovarian cancer, but there were uncertainties in diagnosis for the five women who proceeded to core biopsy. Three were diagnosed based on IGCB and two from core biopsies which were taken by a gynecologists from sites of concern identified on MRI at the MDTM review.

Some clinical and some imaging aspects of these cases did not fit with the typical presentations of gynecological cancer. Only two cases had a raised CA-125 level. This is rare with ovarian malignancy, especially when it has spread to the peritoneum and this further raised concerns.

Imaging features which were "out of character" for malignancy were: (i) Invasion of the pelvic side wall musculature or necrotic sidewall lymphadenopathy related to an adnexal mass, features more associated with an advanced primary cervical cancer (Fig. 4); (ii) a liver surface lesion without ascites and intervening omental cake that would be expected with typical spread of primary ovarian cancer (Fig. 7); (iii) invasion of the adnexal mass into the mesorectum or pararectal spaces, compartments usually respected by untreated ovarian cancer; and (v) cavitating omental masses in a patient who had not undergone treatment (Fig. 6). These discordant imaging features (Table 2) prompted the need for a firm histological diagnosis prior to treatment.

With a firm histological diagnosis, the primary treatment plan was medical/interventional and thus five of the seven women avoided unnecessary cancer surgery. One woman had percutaneous placement of a ureteric stent and another had CT-guided insertion of

a pelvic drain early in their treatment plan. However, two women later required surgery for associated complications, including bowel obstruction and unremitting pain with radiologically inaccessible and multiloculated abscess formation. Thus, actinomycosis, even when diagnosed quickly and accurately, further mimics advanced gynecological malignancy in its protracted and complex clinical course and its requirement for multidisciplinary care.

The diagnosis is highly likely when there are some of the key imaging features we have outlined and illustrated and when core biopsies show a mixture of acute and chronic inflammation and absence of malignant cells or granulomas which might suggest tuberculosis, a condition also recognized to mimic local and disseminated gynecological malignancy. There may be histological mimics of actinomycosis. Pseudo-actinomycotic radiate granules are a recognized mimic of sulfur granules[9]; these are non-infectious and lack a distinct central core with broad, club-like peripheral projections replacing the filamentous projections of actinomyces. Conversely, the histological diagnosis of actinomycosis is often difficult because many specimens contain only a few granules. In one series, only a single granule was identified in 25% of samples. Granules may not be detected in histology samples in cases of culture-proven actinomycosis.[10,11] For two of our seven women, we did not identify sulfur granules nor obtain positive cultures, but their clinical response to antibiotic therapy was dramatic.

A variety of imaging features of pelvic actinomycosis have been previously described and our findings largely confirm these.[12-15] For our series, it was the combination of clinical concern for the diagnosis combined with some unusual imaging features (Tables 1 and 2) which prompted core biopsy. We have previously shown that IGCB is a valuable tool in the investigation of peritoneal disease in women suspected to have gynecological malignancy.[16,17] A small minority have non-malignant disease including actinomycosis and tuberculosis and malignancies with more favorable prognosis like lymphoma.[17]

## CONCLUSION

Pelvic actinomycosis has a variety of imaging patterns which can mimic locally advanced gynecological malignancy or its local, regional, and distant metastatic spread. Diagnosis can, however, be achieved prospectively after MDTM review and using IGCB, when clinical and imaging features are atypical for primary gynecological cancer (Tables 1 and 2).

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