CASE REPORT

Case Report: Xanthogranulomatous salpingo-oophoritis associated to endometriosis – are these different histologic expressions of the same disease? [version 1; peer review: awaiting peer review]

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Abstract
Xanthogranulomatous inflammation is characterized by the presence of foamy histiocytes associated with other inflammatory cells like lymphocytes, plasma cells and neutrophils. It is a rare inflammatory process, which has been more frequently described in chronic pyelonephritis and cholecystitis. Xanthogranulomatosis usually triggers a large distortion of the affected organ, which is secondary to the severe inflammatory response that characterizes this type of lesion. Only a few cases of xanthogranulomatous salpingo-oophoritis have been published to date. Here, we report the case of a xanthogranulomatous salpingo-oophoritis in a patient with endometriosis, suffering from chronic pelvic pain and long-standing infertility. The association between endometriosis and xanthogranulomatous inflammation is extremely rare and can possibly represent a severe histologic expression of this common disorder.

Keywords
salpingitis, endometriosis, infertility, xanthogranulomatous salpingo-oophoritis
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Introduction
Xanthogranulomatous salpingo-oophoritis (XGSO) is an uncommon form of salpingitis, which is associated with a prominent acute and chronic inflammatory infiltrate with admixed foamy histiocytes\(^1\)–\(^4\). The presence of this xanthogranulomatous inflammation has been described in several organs, most commonly in kidney or gallbladder, in association with chronic pyelonephritis or cholecystitis, respectively\(^1\). It is, however, an extremely rare finding in pelvic organs.

XGSO has most commonly been associated with pelvic inflammatory disease, but it has also been described in the presence of intrauterine contraceptive devices, extensive endometriosis, ineffective antibiotherapy, abnormalities in lipid metabolism and with the administration of contrast agents\(^1\)–\(^5\). Few cases of XGSO in patients with leiomyomata have also been published\(^1\),\(^4\),\(^6\). Subclinical bacterial infection seems to intervene and several agents have been implicated, such as \textit{Actinomyces}, \textit{Staphylococcus aureus}, \textit{Enterococcus faecalis}, \textit{Escherichia coli}, \textit{Staphylococcus viridans}, \textit{Bacteroides fragilis}, \textit{Candida glabrata} and \textit{Group B Streptococci}\(^1\). Non-infectious causes have also been pointed. Nevertheless, the aetiology of XGSO remains unknown.

Patients with XGSO usually present with signs of pelvic inflammatory disease, notably, pelvic pain, fever and abnormal bleeding. Treatment with antibiotics and/or surgery is required and the diagnosis of this condition is only possible after histological examination\(^1\),\(^2\).

The differential diagnosis includes: pseudoxanthomatous salpingitis and granulomatous salpingitis. The presence of acute and chronic inflammatory infiltrate differentiates XGSO from pseudoxanthomatous salpingitis, which is characterized by xanthoma cells and pigment without prominent inflammatory component, and from granulomatous salpingitis, where granulomas are present\(^3\),\(^4\).

Here, we report the case of a XGSO in a patient with chronic pelvic pain and infertility associated with endometriosis.

Case report
A 35-year-old woman, with no other relevant previous medical or surgical history, presented with 6 years of primary infertility and severe dysmenorrhea and dyspareunia for nearly a year. No other symptoms were described, like dyschezia, dysuria or abnormal vaginal bleeding. The patient had been previous diagnosed with stage III pelvic endometriosis. This diagnosis was histologically established after two abdominal diagnostic laparoscopies in the context of the infertility evaluation. In the last surgery, a left side salpingectomy and adhesiolysis were performed, with limited post-operative improvement.

The patient was then referred to our Chronic Pelvic Pain Unit due to clinical worsening. On pelvic examination, a painful area located at the right uterosacral ligament was identified by bimanual exam, without pelvic masses. No other physical abnormalities were detected. A pelvic transvaginal ultrasonography was performed, identifying a large uterus with sonographic signs of adenomyosis. Magnetic resonance imaging showed an hyposignal at T1 and T2 sequences, suggestive of an endometriotic infiltration lesion at the right uterosacral ligament location. This finding correlated with the painful area detected at bimanual exam.

Taking in consideration these clinical and imagiological findings, it was decided to perform a laparoscopy. Several adhesions between the uterus and the anterior rectum were identified. The right Fallopian tube was attached to a 2cm nodule in the right ovarium, which was highly suggestive of severe endometriotic infiltration (Figure 1 and Figure 2). In addition to extensive adhesiolysis, a right salpingectomy and oophorectomy were also performed.

The right fallopian tube was 3.9cm in length, 0.4 cm in diameter and had a golden yellowish colour. The lumen was dilated, with thickened plicae and wall. The serosal surface was irregular, suggesting focal bilateral adhesions. The ovarian mass consisted of an irregular brown to yellowish nodule of tissue with 2cm of diameter. Both the fallopian tissue and the ovarian nodule were paraffin embedded and haematoxylin-eosin stained slides were examined.

Histopathological examination of the fallopian tube showed abundant infiltration of the lamina propria by foamy histiocytes mixed with some inflammatory cells, including lymphocytes,
plasma cells and occasional neutrophils, and there was no intervening stroma, conditioning tightly packing of the fallopian tube plicae. The histiocytes were intimately contiguous to the muscle wall and the subserosa of the fallopian tube and there was serosa fibrosis, with appearance of focal adhesions (Figure 3–Figure 7). The histiocytes appeared to contain abundant lipid material. Red cell extravasation was identified throughout the lesion. A similar finding was present in the ovarian nodule, where this pattern of inflammation was in close relation to normal ovarian tissue. No microorganisms were identified using periodic acid–Schiff, methenamine silver, acid-fast bacilli and Gram stains. Immunohistochemical stain was performed on paraffin-embedded sections and demonstrated strong CD68 staining in foamy histiocytes (Figure 8). No pigments, multinucleated giant cells, granulomas or foci of endometriosis were present in both specimens. The fallopian tube epithelium has reactive aspect, without proliferative foci. These findings were diagnostic of XGSO.

Figure 3. Fallopian tube architecture is distorted with infiltration of lamina propria and muscle wall by histiocytes.

Figure 4. Fallopian tube muscle wall is disrupted by abundant infiltration of histiocytes and other inflammatory cells.

Figure 5. This mixed inflammatory infiltrate distinguishes this entity from the pseudoxanthomatos salpingitis.

Figure 6. Infiltration of lamina propria by foamy histiocytes and other inflammatory cells without intervening stroma.

Figure 7. Infiltration of Fallopian tube lamina propria by abundant foamy histiocytes, lymphocytes and occasional neutrophils.
This patient had a significant symptomatic improvement after surgical treatment with sustained clinical response. A close follow-up with regular gynaecological appointments was performed, and no symptomatic recurrence, nor surgical adverse outcomes were detected to date.

Discussion
Endometriotic lesions are characterized by the presence of blood and endometrial shedding, representing a favourable trigger for the development of chronic inflammation and fibrosis. Classically, this disorder causes pelvic dysfunction and anatomical distortion that both lead to chronic pelvic pain and infertility. The pathologic finding of xanthogranulomatous inflammation may represent a severe form of endometriotic lesions, which could explain the recurrence of symptoms in this patient.

Idrees et al. described a progressive spectrum of pathologic changes, from pure endometriosis to mixed endometriotic and xanthogranulomatous inflammation, and finally to only XGSO lesions. The endometrioid implant shedding and the chronic inflammatory process characteristic of endometriosis could explain the xanthomatous process and the accumulation of excessive foamy histiocytes. In this case, we observed a complete replacement of the endometriotic tissue, which was previously documented in prior surgeries, by foamy histiocytes. The current finding of a destructive xanthogranulomatous inflammatory process, in the absence of endometriotic foci, make us speculate that, probably, endometriosis reached a “burnout phase”, as postulated by other authors. Moreover, no other predisposing conditions to the development of XGSO were identified.

In conclusion, a long history of histologically documented endometriosis with multiple previous surgical treatments may lead to the development of a chronic exaggerated inflammatory response, as found in XGSO. A xanthogranulomatous inflammation may represent a rare but aggressive expression of such a common disorder, as is endometriosis.

Consent
Written informed consent for publication of their clinical details and images was obtained from the patient.

Data availability
All data underlying the results are available as part of the article and no additional source data are required.

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Figure 8. CD68 immunostain in fallopian tissue demonstrates strong staining in foamy histiocytes.
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