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**Case Series**

# Xanthogranulomatous inflammation of female adnexa: diverse clinical presentations - a series of 7 cases

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## ABSTRACT

Xanthogranulomatous inflammation, a form of destructive chronic inflammation is a rare occurrence in female genital tract, especially ovary and fallopian tube. Its clinical and radiological presentation mimics ovarian malignancy which poses a diagnostic dilemma at times. Histopathology plays a pivotal role in diagnosis of this entity. We described seven cases in total, out of which two cases showed xanthogranulomatous oophoritis and five had both xanthogranulomatous oophoritis and salpingitis, all diagnosed on histopathology. Majority of the patients had abdominal pain, fever and adnexal mass on examination. Most women were treated based on the working diagnosis of malignancy or severe pelvic inflammatory disease. Histopathology remains the gold standard for diagnosis in all these cases, and with the aid of clinical and radiological details helps in ruling out other differential diagnosis.

**Keywords:** Histopathology, Xanthogranulomatous, Oophoritis, Salpingitis

## INTRODUCTION

Xanthogranulomatous salpingo-oophoritis (XGSO) is a non-neoplastic chronic inflammatory process in which there is disruption of normal anatomical structure of involved organ grossly. Most commonly affected sites by xanthogranulomatous inflammation (XGI) are kidney and gall bladder, followed by anorectum, bone, stomach, urinary bladder and testis.[1] Very few cases involving the female genital tract have been reported, among which endometrium is the commonest site involved. Ovary and fallopian tube are less frequently involved.[2] Clinically, patients usually present with symptoms similar to pelvic inflammatory disease not responding to treatment or as unilateral or bilateral pelvic mass mimicking malignancy. Diagnosis of this entity is difficult based only on clinical symptoms and gross examination. Histopathologic examination comes to the rescue in such cases and confirms the diagnosis. The involved organ is almost entirely replaced by dense cellular infiltrate of foamy histiocytes admixed with neutrophils, lymphocytes, plasma cells, fibroblasts, multinucleated giant cells and areas of fibrosis and necrosis.[3]

## CASE SERIES

### *Case 1*

A 38-year-old female presented with heaviness in left lower abdomen since 6 months associated with abdominal pain, weight loss, early satiety and bloating. On physical examination, a mass was found in the left pelvic region. Patient was a known case of hypothyroidism since 15 years, currently on treatment and also had history of renal calculi. On per vaginal examination, a large anteroposterior mass measuring 15×12 cm was present in the left fornix with restricted mobility. Ultrasonography (USG) whole abdomen showed a large multiloculated hypoechoic complex cyst measuring 11×8.4 arising from left adnexa, inseparable from left ovary and extending

medially into pouch of Douglas (Figure 1a). Right ovary showed a well-defined cystic lesion measuring 4.8×4.2 cm with presence of hemorrhagic components. Total abdominal hysterectomy (TAH) with left oophorectomy, excision of left complex adnexal cyst and right salpingo-oophorectomy (SO) was done. Intraoperatively, dense bowel adhesions were present communicating with left complex ovarian mass. Rupture of cysts drained greenish fluid and cheesy white purulent material mixed fluid. Grossly, cut surface showed greyish yellow solid cystic areas and was slough covered (Figure 1b).

***Case 2***

30-years female with bilateral endometrioma presented with pain in abdomen since 2 months. USG whole abdomen showed anechoic cystic lesions in bilateral ovaries with internal echoes and septations. Right and left ovarian cystic lesion measured 5.5×5.3 cms and 3.8×4.6 cms, respectively. Right sided ovarian mass was densely adhered to uterus and bowel. Right SO with left sided ovarian biopsy with adhesiolysis was done and specimen sent for histopathological examination. On gross examination, cut section of right ovarian cyst showed multiple grey white to grey yellow slough covered areas.

***Case 3***

43-years female presented with right lower abdominal pain and fever. Patient had poor appetite and anorexia. Physical examination revealed tenderness in the right costophrenic angle. A right adnexal mass was found on gynecological examination. Computed tomography (CT) scan revealed a well-defined solid-cystic mass in the right ovary with different signal intensities. Mass was adherent to bowel. However, CA–125 levels were normal in this patient. Malignancy was a diagnostic consideration in this case in view of the complex nature of the ovarian cyst. TAH with bilateral salpingo-oophorectomy (BSO) was performed along with ileal, sigmoid and omental biopsy and specimen sent for histopathology. Gross examination revealed a right complex tubo-ovarian mass (TOM) measuring 5×4×3.5 cms. Cut surface was grey yellow with hemorrhagic areas and cystic areas ranging in size from 0.5 cm to 0.3 cm (Figure 1c).

***Case 4***

32 years old woman presented with lower abdominal discomfort since 15 days and associated with fever and vomiting since 2 days. Physical examination revealed tenderness in the lower abdominal region. Gynecological examination revealed large ill-defined mass measuring 7×8 cms in the left adnexal region confirmed by USG as solid mass with heterogenous areas with fluid collection. Left ovary was not visualized. Subsequently, bilateral salpingectomy was carried out. During intraoperative examination, pus drained out from bilateral fallopian tubes. A provisional clinical diagnosis of tuberculosis was provided. Specimen sent for histopathology. Serosal surface of both tubes were covered with exudate.


**Figure 1: (A) USG whole abdomen showed a large multiloculated hypoechoic complex left adnexal cyst, extending into pouch of Douglas; (B) gross appearance of left tubo-ovarian mass showed grey yellow solid cystic cut surface and thickened cyst wall; (C) resected specimen of right complex ovarian mass showed grey yellow solid areas with focal cystic areas; (D) resected specimen of left tubo-ovarian mass showed grey yellow to grey brown solid areas; (E) cut surface of right ovarian cyst showed grey yellow necrotic areas; and (F) serial cut sections of left fallopian tube showed grey yellow necrotic areas.**

***Case 5***

40-years female, P3L3 presented to gynecology OPD with pain in abdomen since 4 months with increased intensity since past 3 days. On per vaginal examination, right sided fornicial fullness was present. On magnetic resonance imaging (MRI), both ovaries were not visualised and multiple lobulated cysts were present in bilateral adnexa with presence of septations and thick peripheral hypointensity. Laparotomy with TAH was carried out with removal of right sided TOM with left sided salpingectomy. Intraoperative examination revealed a right sided TOM measuring 4×6 cms, which was densely adherent to posterior surface of uterus, lateral pelvic wall, small bowel and part of rectum. A thick purulent fluid was aspirated from the mass. Cut section of mass was grey white to grey yellow with few hemorrhagic areas along with presence of

cysts ranging in size from 2×2×0.5 cms to 0.5×0.5×0.5 cms, filled with mucoid and cheesy necrotic material (Figure 1e). Left sided fallopian tube was dilated and on cut section, showed focal grey yellow necrotic areas (Figure 1f).

***Case 6***

46 years female P2L2A1 presented with complaints of abdominal pain since 2 months. On per vaginal examination, uterus was normal in size and a left fornicial mass was felt with restricted mobility, which turned out to be left sided TOM measuring 6.7×5.3 cms on USG. Laparotomy with TAH was done in view of left TOM. On gross examination, left tube and ovary were adhered to each other and showed presence of exudative material on external surface. Left TOM measured 5.5×4×3 cms. Cut section showed grey yellow with focal dark brown solid areas (Figure 1d).

***Case 7***

46 years female P2L2 with history of previous caesarean section presented with abnormal uterine bleeding since 3 months. On USG, uterus was bulky with thickened endometrium. Multiple fibroids identified, largest was found to be an intramural fibroid measuring 8×9 cms. Gynecological and radiological examination did not reveal any obvious adnexal mass lesion. On gross examination, multiple fibroids were present distorting the endometrial cavity. External surface of bilateral ovaries and fallopian tubes was unremarkable, however cut section of left ovary showed focal grey yellow areas (Table 1).

***Histopathology***

Microscopic examination of all seven cases showed extensive replacement of normal ovarian and tubal parenchyma by sheets of foamy histiocytes and mixed inflammatory infiltrate comprising of lymphocytes, plasma cells and admixed with few neutrophils and eosinophils (Figure 2a). The foamy histiocytes have characteristic morphology i.e. abundant vacuolated cytoplasm and vesicular nuclei (Figure c). Multinucleated giant cells were observed in two cases and stroma showed fibroblastic proliferation (Figure 2d). Case of xanthogranulomatous salpingitis, in addition, showed short, thickened and compressed plicae by sheets of foamy histiocytes and mixed inflammatory infiltrate as described above (Figures 2e and f).

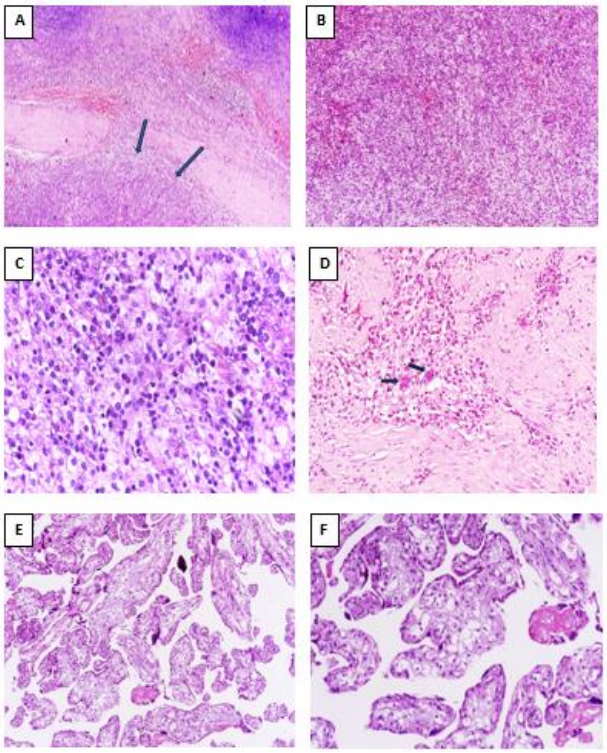


**Figure 2: (A) Photomicrograph showing focally preserved ovarian parenchyma and infiltration by sheets of foamy histiocytes (H&E, x40); (B) foamy histiocytes interspersed with mixed inflammatory infiltrate (lymphocytes, plasma cells, few neutrophils) [H&E, x100); (C) foamy histiocytes showed abundant vacuolated cytoplasm and vesicular nuclei, admixed with mixed inflammatory infiltrate (H&E, x400); (D) stroma showed fibroblastic proliferation with presence of few multinucleated giant cells (H&E, x200); (E) distorted architecture of fallopian tube showing thickened plicae and infiltration of lamina propria by sheets of foamy histiocytes (H&E, x100); and (F) lamina propria expanded with foamy histiocytes and admixed with focal mixed inflammatory cells (H&E, x200).**

**Table 1: Clinico-pathological features of cases.**

| S. no. | Age | Clinical entity | Associated risk factors | Presen-ting compla-int | Gynecolog-ic exami-nation | Investigations | Surgery | Histopathology | |
|---|---|---|---|---|---|---|---|---|---|
| **1** | 38 | Left XG SO | - | Abdom-inal pain | Left fornicial mass with restricted mobility | **USG –** Large multiloculated left sided complex cyst extending into pouch of Douglas | TAH with left oophorecto-my and excision of left | | Multi nucleat-ed giant cells |

Continued.

| S. no. | Age | Clinical entity | Associated risk factors | Presen-ting compla-int | Gynecolog-ic exami-nation | Investigations | Surgery | Histopathology | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | complex adnexal cyst | Sheets of foamy histiocytes admixed with mixed inflammatory infiltrate comprising of lymphocytes, plasma cells, few neutrophils and eosinophils | |
| **2** | 30 | Bilater-al XGO | Bilateral endometr-ioma | Abdom-inal pain | Right fornicial fullness and tenderness | **USG -** Anechoic cystic lesions in bilateral ovaries with internal echoes and septations, right sided ovarian mass densely adhered to uterus and bowel | Right SO with left ovarian biopsy and adhesioly-sis | | Multi nucleat-ed giant cells |
| **3** | 43 | Right XG SO | - | Abdom-inal pain | Tenderness in right costophren-ic angle | **CT -** Well-defined solid-cystic mass in the right ovary, adherent to bowel | TAH with bilateral SO and ileal, omental and sigmoid biopsy | | |
| **4** | 32 | Bilater-al XG salping-itis with left XGO | - | Abdom-inal pain, fever, vomiti-ng | Tenderness in lower abdomen | **USG –** Solid mass with heterogenous areas with fluid collection | Left sided mass excision with bilateral SO | | |
| **5** | 40 | Bilater-al XG SO | - | Abdom-inal pain | Right sided fornicial fullness | **MRI -** Multiple lobulated cysts were present in bilateral adnexa with presence of septations and thick peripheral hypointensity, both ovaries were not visualised | Laparoto-my with TAH with removal of right sided TOM and left sided salpingect-omy | | |
| **6** | 46 | Left XG SO | - | Abdom-inal pain | Left fornicial mass with restricted mobility | **USG –** Left TOM | Laparoto-my with TAH | | |
| **7** | 46 | Left XGO | Previous LSCS | Abnor-mal uterine bleed-ing | No adnexal mass lesion palpated | **USG –** Bulky uterus with thickened endometrium and multiple fibroids | TAH with BSO | | |

XGSO- Xanthogranulomatous salpingo-oophoritis, USG–ultrasonography, XGO-xanthogranulomatous oophoritis, SO-salpingo-oophorectomy, TAH-total abdominal hysterectomy, CT-computerised tomography, MRI-magnetic resonance imaging, TOM–tubo-ovarian mass

## DISCUSSION

XGSO was first described in 1976 by Kunakemakorn in his case report on inflammatory pseudotumor in the pelvis involving serosa of uterus, left fallopian tube and ovary.[3] This type of inflammation involving female genital tract is very rare and is confined mostly to endometrium. Involvement of vagina, cervix, fallopian tube and ovary has been documented, although cases of XGSO have been reported from India. Till date, 46 cases are published in literature, out of which 32 cases are from India.[4] Tanwar et al reported the youngest case of XGI involving the ovary and fallopian tube, in a two-year-old.[5]

The exact etiopathogenesis of xanthogranulomatous oophoritis (XGO) is still unexplained. Many associations have been implicated like bacterial infections, endometriosis, leiomyoma, immunosuppression, chronic inflammatory conditions, IUCD use, luminal obstruction, ineffective antibiotic therapy, abnormal lipid metabolism and defective phagocytosis. Among these, the most accepted one is that of infection which is supported by the clinical evidence of infection and detection of bacteria via culture studies e.g. *Escherichia coli*, *Proteus vulgaris*, *Bacteroides fragilis* and *Salmonella typhi*.[6]

Ovarian involvement by pelvic inflammatory disease (PID) may be mild, chronic or recurrent and present as chronic peri-oophoritis, visibly grossly as periovarian and tubo-ovarian adhesions. Sometimes, it can present as chronic ovarian abscess resembling tumor like mass. The involved ovary in such cases is replaced by a solid or cystic, yellow, lobulated mass.[7]

Histiocytic inflammation of the fallopian tube results mainly from infection by different organisms or due to tissue reactions to foreign body materials. It can be pseudoxanthogranulomatous or xanthogranulomatous. It is important to differentiate between these 2 entities as the latter is linked to PID and not associated with endometriosis unlike the former.[7]

XGSO affects people between the ages of 2 and 84 with an average age of 38.5 years.[4] These patients usually present with fever, menorrhagia, lower abdominal or suprapubic pain, dysmenorrhea, dyspareunia and a tender adnexal mass, poor appetite and infertility.[2] From a clinical and radiological perspective, it can resemble a neoplastic lesion due to its appearance as a mass lesion in the pelvic cavity and infiltration of adjacent tissue. It typically poses challenges for the clinician in terms of diagnosis and management. Underlying pathogenetic mechanisms might involve bleeding and blockage which would have led to infection, tissue necrosis, release of cholesterol and other lipids, and phagocytosis of macrophages and may lead to persistent ovarian abscess. Inflammation of the ovary can also affect the nearby peritoneum, resulting in the production of adhesions.[1]

Radiological findings of XGSO shows solid complex adnexal masses with extension into adjoining tissue and thus mimic carcinoma. Additionally, the appearance of a solid mass with altered signal intensity favors malignancy, making a CT scan diagnosis of this entity problematic. Characteristic MRI findings in patients of XGSO is lacking.[8]

Grossly, the involved ovary and fallopian tube are replaced by a well-circumscribed lobulated mass that is characteristically yellow in colour, solid to cystic in consistency, sometimes involving adjacent organs, thus mimicking malignancy. The mass usually is fragile, and on cut section shows areas of hemorrhage, necrosis, purulent material and cystic degeneration due to liquefactive necrosis.[9-11] In majority of the cases, mass is unilateral, with capsule adherent to surrounding structures like uterus and bowel. Demarcation of normal/residual ovary and fallopian tube from the TOM is difficult in such cases.[12]

Histomorphologically, the normal ovarian and fallopian tube structure is destroyed and replaced by foamy histiocytes (xanthoma cells), chronic inflammatory cells, multinucleated giant cells, stromal fibroplasia, and vascular proliferation, which give the appearance of a pseudotumor on gross examination. Xanthoma cells are histiocytes with a vacuolated appearance as they contain large amount of lipid-laden cytoplasm.[1,7]

Differential diagnosis includes: pseudoxanthomatous salpingitis (PXS), granulomatous inflammation and malakoplakia. PXS is linked to endometriosis and is characterized by swollen, edematous tubes with a gross appearance of yellow to dark brown polypoid mucosa, usually covered with purulent material.[13,14]

Presence of xanthoma cells, acute and chronic inflammatory infiltrate differentiates XGSO from PXS, which is characterized by distended plicae and pigment (hemosiderin and lipofuschin) laden macrophages without prominent inflammatory component, and from granulomatous salpingitis, where granulomas are present. Granulomatous conditions that come under differential diagnosis include tuberculosis and fungal infections, which are ruled out by special stains and culture studies.[15,16] In the current study, Ziehl-Neelsen stain for AFB and PAS stain was negative in all cases; thus, ruling out these possibilities.

Malakoplakia should be taken into consideration in the differential diagnosis of XGI due to the presence of foamy histiocytes.[17] XGI and malakoplakia are believed to share common pathophysiology. Malakoplakia is believed to be caused by defective phagocytic mechanism to eliminate microorganisms, which may be brought upon by a decrease in β-glucuronidase release and a low concentration of cyclic guanosine monophosphate. Phagolysosomes which contain partially digested bacteria, are the source of Michaelis Gutmann bodies. Escherichia coli is frequently the cause.[10,11] Although there are

differences between XGI and malakoplakia, it is important to note that No Michaelis Gutmann bodies were seen in any of the cases in the current study, which are diagnostic of latter. As XGSO is rarely diagnosed, other differentials which mimic this condition are malignant small round cell tumor with stromal leutinization, sclerosing tumor and secondary lymphoma/leukemia.[18]

Cases of XGO had been reported associated with different clinical conditions. Shukla et al have documented a case of XGO linked to endometriosis and primary infertility.[15] Cases of XGI of the ovary associated with ovarian hemangioma have been reported, as an unusual cause of tubo-ovarian abscess, in relation to endometriosis, uterine leiomyoma, diabetes mellitus, foreign bodies like talcum powder. Sometimes XGO can also present as an unusual complication of typhoid, and after uterine artery embolization.[12,14,19] There have also been case reports of premature ovarian failure as an uncommon consequence of XGI.[16]

Frozen sections are also helpful in the detection of XGI and further intraoperative care. Diagnosis can also be confirmed with immunohistochemistry and markers such as CD68 (positive in foamy histiocytes), CD3 (positive in T lymphocytes) and CD20 (positive in B lymphocytes).[20,21] Since the diagnosis was confirmed by the histopathological features itself, immune-histochemistry was not required in any of the cases in the current study. The treatment of choice is surgery. Awareness of this inflammatory lesion can prevent extensive surgery and overdiagnosis as malignancy.[22]

## CONCLUSION

XGSO is a rare inflammatory condition affecting the ovaries and fallopian tubes. Given its infrequency, there is limited information on its precise incidence, long-term prognosis and recurrence rates. Most of the information is available as case reports and small case series. Accurate diagnosis of XGI is crucial to determine the best course of treatment and prevent misdiagnosis of malignancy in order to avoid needless radical surgical interventions. A thorough and collaborative approach is needed to improve diagnostic standards and create more specialized treatment approaches. Association of this entity with chronic inflammation, characteristic histopathological features, and the need for surgical intervention demands further research to unveil the risk factors and better understand the underlying pathogenesis.

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