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Xanthogranulomatous Inflammation in Gynecology: A Rare and Perplexing Clinical Entity

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ABSTRACT

Xanthogranulomatous inflammation is a chronic inflammation whose diagnosis remained a dilemma for gynecologists and pathologists. Its involvement of female genital tract is rare and involves ovaries, tubes, uterus and cervix. Etiopathogenesis is not clear and hypothesis like infective etiology, radiation, cancer, etc., have been proposed. Clinical symptoms and signs may vary depending upon location of this inflammation like abdominal pain, swelling, fever, purulent discharge, tub ovarian mass, etc., USG and CECT pelvis may show solid cystic tub ovarian mass, uterine collection and swelling, etc. Patients with pyometra or having infective etiology may respond to antibiotic, but who have large tub ovarian mass need surgery. Diagnosis is confirmed by histopathology.

Keywords: Xanthogranulomatous inflammation, Female genital tract

Abbreviations: XGI: Xanthogranulomatous Inflammation

INTRODUCTION

Xanthogranulomatous inflammation (XGI) is a rare form of chronic inflammation that is characterized histopathologically by a marked proliferative fibrosis, parenchymal destruction, and infiltration of foamy histiocytes mixed with hemosiderin laden macrophages and foreign body giant cells. It has been reported in multiple organs, most commonly in the kidney, gall bladder, salivary glands and bones. It is less commonly seen in the female genital tract [1-3].

DISCUSSION

Various other terms have also been used like pseudoxanthoma and histolytic endometritis. Histolytic endometritis was coined by Buckley and Fox in 1980 [4]. Malakoplakia is another rare variant of histiocytic endometritis which shows Michaelis-Gutmann bodies, i.e., intra and extracellular calcified spherules. Immunohistochemistry for xanthogranulomatous inflammation is positive for Vimentin and CD 68.

LOCATION

This type of inflammation is most commonly seen in pyelonephritis and cholecystitis, although it has more recently been described in other locations like bronchi, lung, endometrium, vagina, fallopian tubes, ovary, testis, epididymis, stomach, colon, ileum, pancreas, bone, lymph nodes, bladder, adrenal gland, abdomen and muscle.

In female genital tract it has been reported in following organs:

1. Adnexa including ovaries and tubes as tub ovarian mass

2. Uterus including myometrium, perimetrium [5] and as xanthogranulomatous endometritis [6]

3. Cervix

Etiopathogenesis

Although the exact etiology of the disease is not known, however, various theories have been proposed in literature. Suppurative infections, organ obstruction and hemorrhage trigger leads to tissue damage within the involved organs, usually eliciting a microscopic response. XGI causes destruction of the involved organ and could be misinterpreted as a locally invasive cancerous lesion. Biedermann et al. [7] supports the Infective etiology theory as long-standing infections with mycoplasma hominis in a

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patient of tubo-ovarian abscess leads to peritonitis. Various other organisms have been isolated from the bacterial culture such as *E. coli*, *Proteus* spp., *Staphylococcus aureus*, *Bacteriodes fragilis* and *Salmonella typhi*. Inoue et al. [5] reported the case of XGI of perimetrium, myometrium and endometrium because of abscess from the perimetrium and infiltrating deep into the posterior uterine myometrium which also supports the infective etiology. XGI may be influenced by various factors like tumor tissue or dead tumor cells due to necrosis, presence of abundant amount of intrauterine hemorrhage and cervical stenosis [8]. XGI associated with post-menopausal pyometra due to cervical stenosis or as a result of cervical carcinoma has also been reported. Theory of endometriosis, intrauterine contraceptive device, inborn errors of lipid metabolism and drug have also been proposed. Endometrial carcinoma that had been irradiated with external beam and/or intracavitary implants is also associated with xanthogranulomatous inflammation. Similarly, xanthogranulomatous cervicitis has been reported in a patient of cervical cancer in specimen of radical hysterectomy who was treated initially with external beam irradiation for the cervical cancer [9]. Uterine artery embolisation may also predispose this condition causing ischaemia or chronic obstructive process leading to congestion and infection [10]. XGI with ovarian hemangioma [11], diverticulitis [12], uterine leiomyoma [13] association with diabetes mellitus [14], talcum powder [15] and as an unusual complication of typhoid [16] has also been reported **(Figure 1)**.

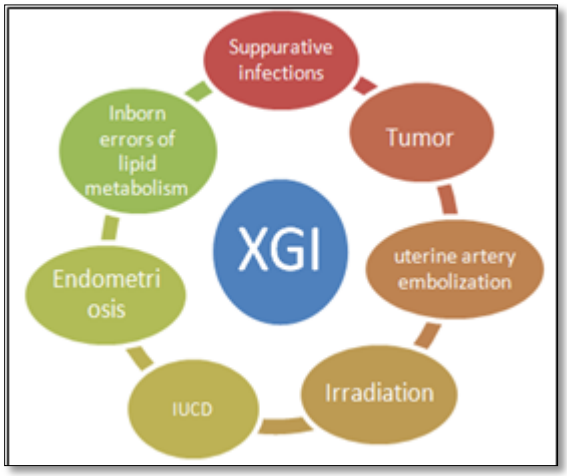

Figure 1. Various etiological factors proposed for xanthogranulomatous inflammation.

Age

It has been reported in every age group from prepubertal to postmenopausal. Tanwar et al. [17] reported XGI in a 2 year female child with right-sided xanthogranulomatous salpingooophoritis presented as mass in abdomen. Although the juvenile form is often considered to undergo regression; the adult xanthogranuloma is persistent in most of the cases [18]. The juvenile form has been described with hematologic malignancies such as B-cell acute lymphoblastic leukemia [19].

Presentation

Patients with XGI of ovaries and fallopian tubes may present with abdominal pain, swelling, low grade fever etc. Abnormal uterine bleeding, purulent discharge [3] **(Figure 2)**, pyometra or hematometra may occur in xanthogranulomatous endometritis or in cervical xanthogranuloma. On examination, lower abdominal mass may be felt. In per speculum, foul discharge from cervix, cervical lesion or cervical growth may be there. Bulky uteri, fornix fullness, tenderness in bilateral fornix are the other findings in per vaginal examination. Features and presentations may mimic ovarian cancer, endometrial cancer and cervical cancer in cases of xanthogranulmatous oophritis, endometritis and cervical xanthogranuloma, respectively. Chronic diseases like diabetes mellitus [14], tuberculosis, etc., may also be associated with it. Abeysundara et al. [13] reported a case presented with intestinal obstruction in xanthogranulomatous salpingitis and oophoritis associated with endometriosis and uterine leiomyoma. The xanthogranulomatous inflammation involving the salpingitis and cystitis simultaneously is rare but has been reported and the patient may present with urgency, frequency, lower abdominal mass and pain. Adnexal xanthogranulomatous may leads to hydroureteronephrosis by ureteric obstruction **(Table 1)**.

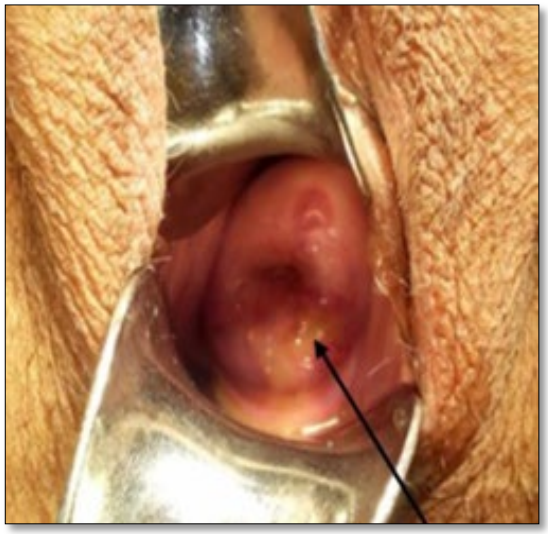

Figure 2. Ulcerated growth with purulent discharge from cervix.

Table 1. Various presentation of XGI of female genital tract.

Female genital organs involved	Presentations
Ovaries and tubes	Abdominal pain, swelling, low grade fever, tuboovarian mass, hydroureteronephrosis
Uterus	Abnormal uterine bleeding, pyometra, hematometra, purulant discharge
Cervix	Ulcerative lesion, sinus formation with pus discharge

INVESTIGATIONS AND MANAGEMENT

Laboratory tests may show elevated white blood cell count and raised ESR. Transabdominal ultrasound may show enlarged uterus with thickened myometrium and fluid collection in the uterine cavity. There may be bilateral, large, multi-septated, thick-walled cystic ovarian masses which may be confused with endometriomas and/or with malignancy of ovary [10]. MRI and Contrast enhanced CT scan can also be done. In MRI, in Xanthogranulomatous oophritis, septated, cystic lesions with multiple intramural nodules in a thickened wall with high signal intensity on T2-weighted images and low signal intensity on T1-weighted images in bilateral ovaries and lesions may show mild peripheral and septal enhancement. In cervical xanthogranuloma, CECT may show bulky cervix, heterogeneously enhancing thickened lips of cervix, and endometrial cavity may be distended with fluid suggestive of pyometra. There may be obliteration of fat planes between uterus and bladder; uterus and rectum. Multiple enlarged lymph nodes like portocaval, retrocaval, precaval, aortocaval, preaortic and para-aortic may also be present [3]. Contrast-enhanced CT may mimic ovarian neoplasm by showing complex solid-cystic lesions with thick enhancing walls, internal septation and variably enhancing solid intramural nodules. CA 125 may also be elevated.

Due to non-specific presenting symptoms and radiological imaging, pre-operative diagnosis has been challenging. There are no definitive imaging characteristics for xanthogranulomatous inflammations of female genital tract till now have been established. Confirmed diagnosis is by histopathology only which is characterized by marked proliferative fibrosis, parenchymal destruction, and infiltration of foamy histiocytes intermixed with hemosiderin laden macrophages and foreign body giant cells **(Figure 3)**. Immunohistiochemical stains are also helpful in establishing the diagnosis which includes CD68 for foam cells, CD3 for T lymphocyte and CD20 for B lymphocytes.

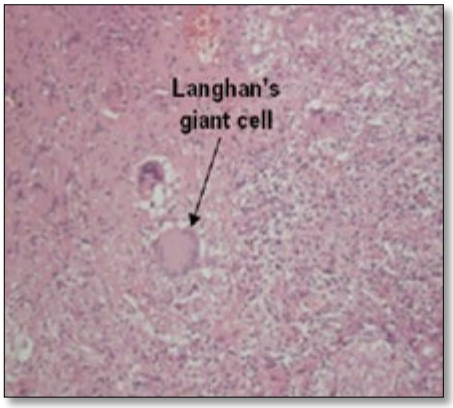

Figure 3. Histopathology of Xanthgranulomatous inflammation showing epithelioid cell granuloma with Langhan's giant cell and numerous foamy histiocytes.

In cases of salpnigoophoritis with tuboovarian mass, laparotomy is the only option left. In young patients fertility preserving surgery can be done with removal of ovarian cyst and sparing healthy ovarian tissue for ovarian stimulation [10]. Care must be taken to avoid injury to bladder, bowel and ureter as adhesions may be there. Cervical and endometrial xanthogranuloma are to be confirmed by histopathology and to be managed conservatively. Extensive sampling of tissue is required to rule out any foci of neoplastic growth such as endometrial adenocarcinoma or cervical carcinoma because presence of histiocytic endometritis does not rule out malignancy [20]. Associated pyometra should be drained and pus is to be sent for culture and sensitivity. Some cases have been reported to be by tuberculosis and relieved by anti-tubercular treatment also [3]. XGI associated with chronic infective conditions like recurrent pyometra is to be managed aggressively in the form of surgery if diagnosed pre-operatively as it has been known to progress to systemic inflammation which can be lethal also [21].

CONCLUSION

Both the gynecologists and pathologists should be aware of this entity as it may mimic carcinoma. Grossly, the findings may be necrotic, irregular mass or lesion which may confuse the gynecologists and microscopically, the foamy histiocytes infiltrating the myometrium may confuse the pathologists with clear cell carcinoma or sarcoma. Immunohistochemistry may easily distinguish the XGI from

malignancy. Malignancy may also coexist with XGI like in endometrial cancer.

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