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Dr. Saloni
MD Pathology, Fellow
Oncopathology, Assistant
Professor, Department of
Pathology, Guru Gobind Singh
Medical College & Hospital
Faridkot, Punjab, India

Ekta Rani
MD Pathology, Associate Professor
Department of Pathology, Guru
Gobind Singh Medical College &
Hospital, Faridkot, Punjab, India

Granulomatous mysteries of the female genital tract: A case series

Saloni and Ekta Rani

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Abstract

Introduction: Granulomatous lesions in the female genital tract are exceedingly uncommon and can involve multiple sites, fallopian tube being the most frequently affected site followed by endometrium, ovary, cervix, vagina, vulva. These granulomas arise from a range of infectious and non-infectious causes and exhibit diverse morphological patterns varying from confluent granulomas with caseous necrosis, notably in tuberculosis to well-circumscribed non-necrotizing granulomas as seen in sarcoidosis and localized endometrial granulomas in response to previous ablation or diffuse granuloma in systemic disease/infections.

Objectives: This study aimed to analyse and report the clinico-pathological characteristics of granulomatous lesions affecting the female genital tract.

Case reports: We retrospectively analysed five cases of granulomatous diseases involving female genital tract. These cases were reported in the department of Pathology over a period of one year and included two cases of granulomatous salpingitis, two cases of endometrial granulomas and one case of myometrial granuloma. Majority of cases were of tubercular etiology but had varied clinical presentation highlighting the clinical dilemma and diagnostic challenges. Age in our study group ranged from 15 to 40 years. Diffuse granulomas were noted in all cases with caseous necrosis in 3 of them. Additional histopathological findings included presence of foreign body type, Langhans type giant cells, fibrinoid palisading granuloma.

Conclusion: Effective etiological resolution requires integrative assessment combining the histopathological findings with clinical data (age, reproductive status), biochemical, radiological and microbiological evidence (PCR/GeneXpert). Such an integrated approach is essential for accurate diagnosis and appropriate patient management because of the rarity of the disease.

Keywords: Granuloma, uterus, tuberculosis

Introduction

Granulomatous lesions of the female genital tract are uncommon entities, and can involve uterus, ovaries or fallopian tubes. They arise from infectious or non-infectious causes. Among the infections, tuberculosis is the most common, especially in developing countries, followed by other reported causes like fungal and parasitic infections, actinomycosis, cytomegalovirus etc. Non-infectious etiologies include foreign bodies, prior surgical procedures/ablation, granulomas secondary to systemic diseases such as sarcoidosis, vasculitis etc [1, 2].

Granulomatous salpingitis and oophoritis are more common than uterine or cervical granulomas [1-3]. Granulomatous salpingitis and endometrial granulomas are predominantly of infectious origin, tuberculosis being the most common while ovarian granulomas are predominantly foreign body granuloma or occur secondary to systemic disorders. Myometrial granulomas are exceptionally rare, occurring either as localized reaction to previous biopsy/ablation or in a diffuse manner secondary to infections/systemic disorders [4].

In our department at GGS Medical College, Faridkot, we reported 5 cases over a period of one year from August 2024 to August 2025; including 2 cases of endometrial granulomas, two cases of granulomatous salpingitis and one case of myometrial granuloma.

Case reports

Case 1

A 15-year-old sexually inactive female presented to the outpatient department with complaints of pain abdomen for 2 months and abdominal distension for the last 15 days, along with a past history of episodic fever for 2 months. Sonographic findings and CA-125 levels of 470 U/ml raised a suspicion of an ovarian tumor. MRI suggested bilateral ovarian endometriotic cysts.

Corresponding Author:

Dr. Saloni
MD Pathology, Fellow
Oncopathology, Assistant
Professor, Department of
Pathology, Guru Gobind Singh
Medical College & Hospital
Faridkot, Punjab, India

Ascitic fluid examination revealed benign cytology with raised ADA levels (66.3 U/L). Intraoperatively, a few enlarged lymph nodes were also observed along with fused fimbriae. Received biopsy from fimbriae measuring 1.5x1.5x1cm along with few lymph nodes largest measuring 1.8cm in greatest dimension. Histopathological examination of the lymph nodes and biopsy from the fimbriae showed necrotizing granulomatous pathology (Figure 1). GeneXpert detected high load of *Mycobacterium tuberculosis* complex. Chest X-ray showed no lung lesions. No lymphadenopathy was observed clinically. Family history of tuberculosis was negative.

Case 2

A 28-year-old female with complaints of abdominal pain and abdominal distension for the last 4 months presented to the Obstetrics OPD. Sonography showed a huge cystic adnexal mass with omental nodularity. CA-125 levels were 168U/ml. With a clinical suspicion of ovarian tumor, she underwent salpingo-oophorectomy. Grossly, we received a unilateral salpingo-oophorectomy specimen with omentectomy. Cystic ovarian mass measured 10x10x4cm with an intact capsule and no solid areas. Histopathology of cystic ovarian mass showed features of Serous cystadenoma. The fallopian tube and omental nodules were incidentally found to show necrotizing granulomatous pathology with occasional acid fast bacilli, suggestive of tubercular etiology (Figure 1).

Case 3

A 40-year-old multiparous woman came with complaints of prolonged vaginal discharge for the last 1 year and episodic low backache. Per speculum examination showed whitish discharge with no cervical erosion/ulcers. Ultrasonography revealed a thickened endometrium measuring 16mm. Grossly, we received

an endometrial biopsy comprising of multiple grey brown soft tissue pieces collectively measuring 1.5x1x0.5cm. Histopathological examination showed necrotizing granulomatous endometritis, possibly tubercular etiology, which was subsequently confirmed by GeneXpert studies (Figure 2).

Case 4

A 35-year-old lady, married for the last 4 years, with primary infertility. She was asymptomatic otherwise and sonography showed no abnormality. She underwent an endometrial biopsy as a part of work-up for infertility. Grossly, we received multiple grey-brown to grey-tan soft tissue pieces collectively measuring 2x1x0.5cm. Microscopy revealed granulomatous endometritis without necrosis and occasional scattered Langhans type giant cell (Figure 2). Stain for AFB was negative. Patient was lost to follow up.

Case 5

A 40-year-old lady presented with abnormal uterine bleeding for the last 6 months. Sonography revealed an intramural fibroid. Previous history of myomectomy performed one year ago was recorded. This time, she was planned for total abdominal hysterectomy with bilateral salpingo-oophorectomy. We received a specimen of uterus with cervix and adnexa. Cut section uterus showed trabeculations in the myometrium along with a blood clot measuring 5x3.5x3cm in the endometrial cavity displacing the endometrial lining (Figure 3). No fibroid was identified. The adnexa appeared unremarkable. Microscopy showed many non-necrotising granulomata in the myometrium with foreign body type of giant cells around refractile material. Occasional granuloma showed central fibrinoid necrosis with surrounding palisading epithelioid histiocytes (Figure 4).

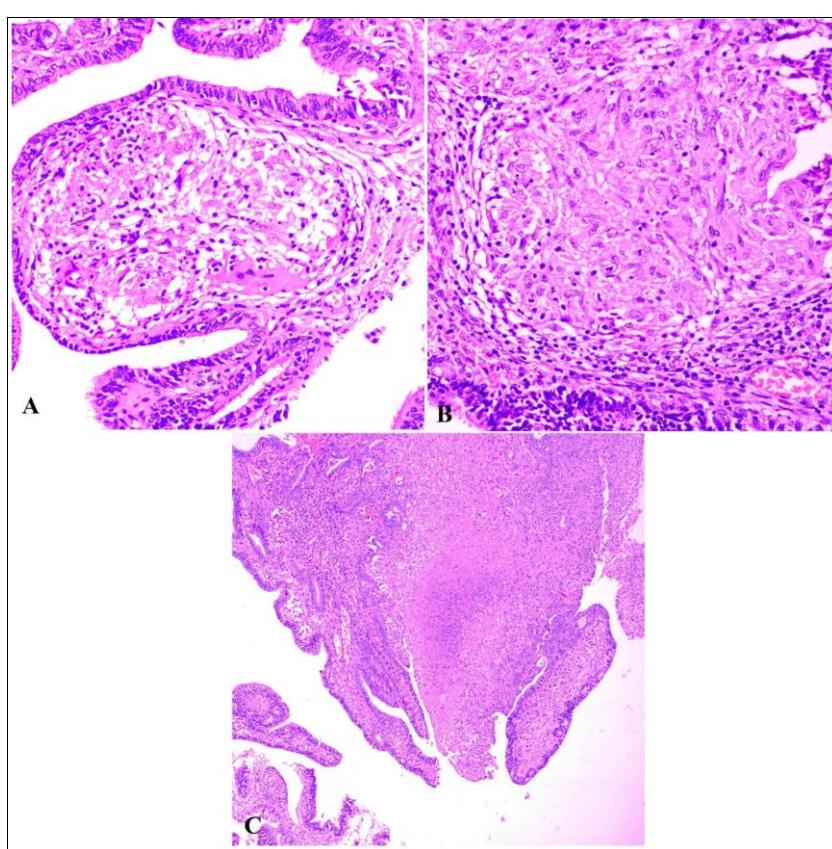


Fig 1: Case 1,2 A) Tubal wall showing subepithelial granuloma (Haematoxylin & Eosin stain; X200). B) Circumscribed granuloma with peripheral lymphocyte cuff (Haematoxylin & Eosin stain; X400). C) Focus of caseous necrosis in wall of fallopian tube ((Haematoxylin & Eosin stain; X100).

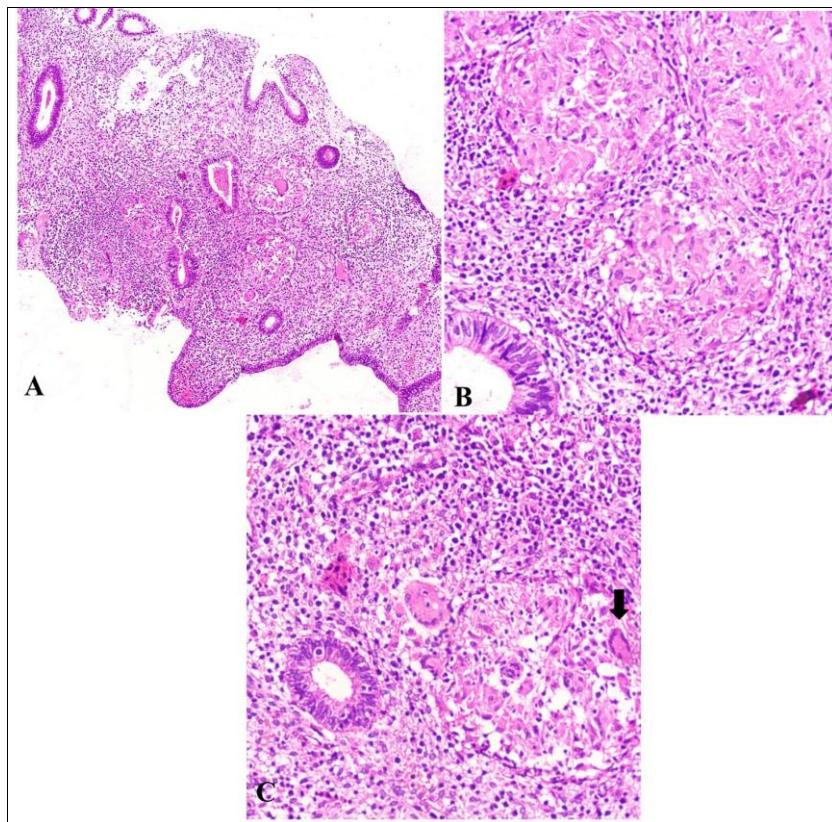


Fig 2: Case 3,4 A) Scanner view of endometrial biopsy with tubular glands and granulomata ((Haematoxylin & Eosin stain; X40). B) Multiple confluent granuloma in stroma (Haematoxylin & Eosin stain; X200). C) Occasional scattered Langhans type of giant cells, pointed by arrow (Haematoxylin & Eosin stain; X200).



Fig 3: Hysterectomy specimen showing blood clot in the endometrial cavity with grey yellow areas in myometrium. No fibroid seen grossly.

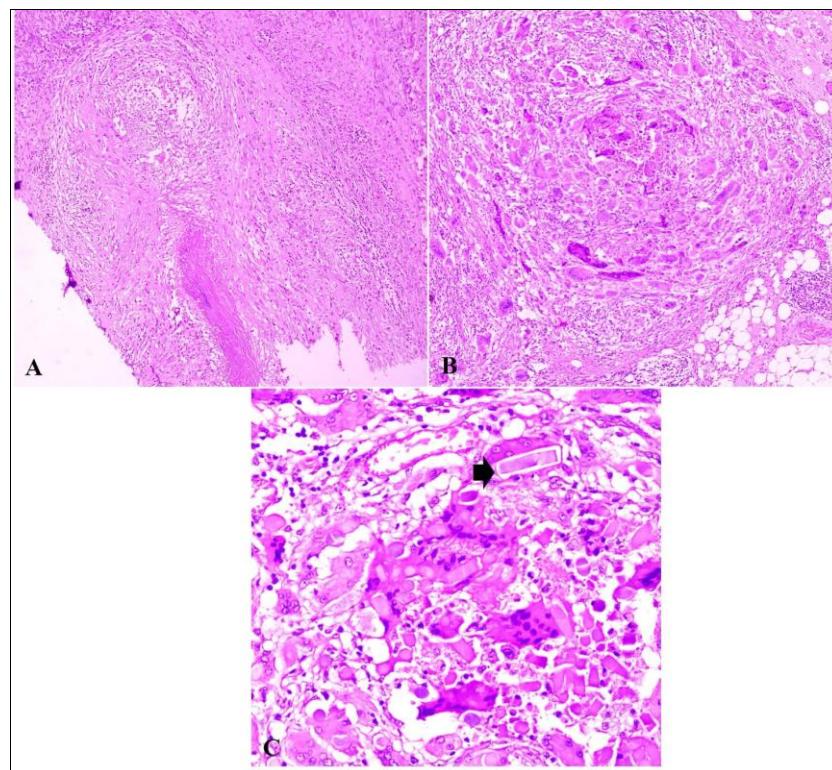


Fig 4: Case 5 A) Myometrium showing palisading granuloma with central fibrinoid material. (Haematoxylin & Eosin stain; X200). B) Foreign body granuloma with numerous giant cells. (Haematoxylin & Eosin stain; X200). C) Refractile material in the granuloma with surrounding foreign body type giant cells, pointed by arrow head (Haematoxylin & Eosin stain; X400).

Discussion

Granulomatous inflammation of the female genital tract represent a rare and diagnostically challenging spectrum of diseases arising from diverse infectious and non-infectious aetiologies. In our series, tuberculosis emerged as the most prevalent cause as also reported in literature, especially in developing countries like India. A major risk factor for contracting genital tuberculosis is reproductive age group. As per literature, genitourinary tuberculosis in children is extremely rare [5, 6]. While genital tuberculosis can involve multiple sites, 90% of the cases are seen in fallopian tube, followed by endometrium (50-80%) and the incidence is even lesser in ovary, cervix, vagina and vulva [4, 7, 8]. Clinically patients may present with non-specific symptoms like amenorrhea, irregular menstrual cycles, infertility, vaginal discharge, and postmenopausal bleeding underscoring the need for heightened clinical suspicion [7, 9].

Tubercular salpingitis, is the leading contributor to infertility in nearly 40% cases in India [10]. However, its incidence in sexually inactive younger females (less than 18 years) is rare. Primary infection of the tubes is rare. In most cases, it occurs secondary to hematogenous spread from a primary pulmonary infection. Lymphatic spread from intestinal or urinary bladder tuberculosis may occur. Although, tubal involvement is mostly bilateral, our experience includes two cases of unilateral tubal disease. In one of our cases, tubercular salpingitis occurred in an adolescent girl without primary pulmonary involvement, which is an extremely rare presentation that challenges conventional expectations and highlights the variability of disease presentation. Diagnostic clues in this case were raised ADA levels and intra-operative fimbrial fusion. In another case, incidental tubal involvement by tuberculosis was seen in the setting of primary ovarian serous tumor, highlighting the existence of concomitant pelvic pathology.

Granulomas within the endometrium are rare but clinically

significant given its reported association with infertility. A number of infections including tuberculosis, fungal infections and CMV can lead to granulomatous endometritis. Tubercular granulomas are the most common and usually occur in perimenopausal age group. In one of our patients with primary infertility, non-necrotizing granulomas were observed while the other case showed caseating necrosis. Tubercular endometritis remains a recognised cause of infertility with reported prevalence of 1.34% to 3.9% cases in developed countries, and 1 to 19% in developing world [11, 12, 13]. Histologically, confluent granuloma with caseous necrosis, typical of tuberculosis may not be found in tubercular endometritis due to cyclical menstrual shedding of endometrium [14]. Well circumscribed non-necrotizing granulomas in endometrium can also occur as due to Sarcoidosis or secondary to foreign bodies like talc or IUD. None of our cases showed such granuloma in endometrium. Granulomas secondary to endometrial ablation are usually palisading granuloma with central fibrinoid material and giant cell reaction, mimicking a rheumatoid nodule microscopically [14, 15]. In one of our cases with palisading and foreign body type myometrial granulomata, a previous history of surgical intervention was present. There was no clinical evidence of any systemic disease or tuberculosis in this patient, suggesting that previous instrumentation triggered diffuse granulomatous response in the myometrium. Uterine granulomas involving the myometrium are rare. Though rare, tubercular involvement of myometrium is reported in literature [1, 16].

Conclusion

To conclude while reporting granulomatous diseases of the female genital tract, caution should be practiced in careful assessment of the nature of granulomas, type of necrosis, history of previous surgery and clinical evidence of any systemic disease as the spectrum of diseases is wide. There is immense diagnostic value of integrating clinical context (age,

reproductive status), biochemical levels of ADA in fluid, imaging, targeted histopathology including stains for acid fast bacilli and microbiological evidence (PCR/GeneXpert) to resolve the aetiology as management strategies differ substantially between infectious and non-infectious granulomatous diseases.

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None

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