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Extensive Xanthomatous Change in an Ovarian Serous Borderline Tumor: More Than Just a Mere Coincidence

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Abstract

Serous borderline tumors of the ovary fall in between the benign and malignant category. These tumors are often diagnosed early, and the prognosis is usually favorable. However, there are variations in the histopathological findings of borderline ovarian tumors. Xanthomatous change is one such rare change in which deposition of lipid-rich material is seen morphologically as xanthoma cells within tumor tissue and reports of this are sparse. There is postulated literature on xanthomatous change being a contributing factor for progression of cancer. We present a case of a 75-year-old postmenopausal female with complaint of pain abdomen since 3 days, diagnosed radiologically as right ovarian mucinous cystadenoma/cystadenocarcinoma. Histopathology revealed a serous borderline tumor with extensive xanthomatous change. This case presents important thoughts on exploring the connection of xanthomatous change with borderline ovarian tumors, which till date is a matter of debate.

Keywords
- malignancy
- ovary
- xanthomatosis

Introduction

Foam cells are formed due to the accumulation of fat droplets inside macrophages because of imbalance in cholesterol metabolism, reflecting morphologically in tissues as xanthomatous changes. They may be detected in some major organs such as the brain, liver, and connective tissue, kidneys, and gallbladder and are most commonly associated with chronic inflammatory processes, metabolic disorders, infections, and autoimmune diseases.[1,2] In ovaries xanthogranulomatous oophoritis is a well-known entity of inflammatory etiology. In addition, few cancers like ovarian, colorectal, and renal cancers have shown presence of CD68 positive foam cells and have been proposed to be associated with tumor progression and metastasis.[3]

Serous borderline tumors (SBTs) represent a distinct subgroup of ovarian neoplasms. While generally characterized by their benign behavior, SBTs can rarely exhibit unique histopathological features, including xanthomatous change. This article aims to provide a comprehensive overview and plausible association of xanthomatous change with serous borderline ovarian tumours, supported by relevant scientific literature.

Case Report

A 75-year-old female presented to the obstetrics and gynecology outpatient department with complaints of pain abdomen and vomiting since 3 days. Sonography revealed a well-defined multiloculated cystic lesion in the region of right adnexa measuring $16.5 \times 8.6 \times 13.3$ cm (►**Fig. 1A**). The cystic component showed fine internal echoes with a solid component measuring 3.5×2.1 cm along one internal

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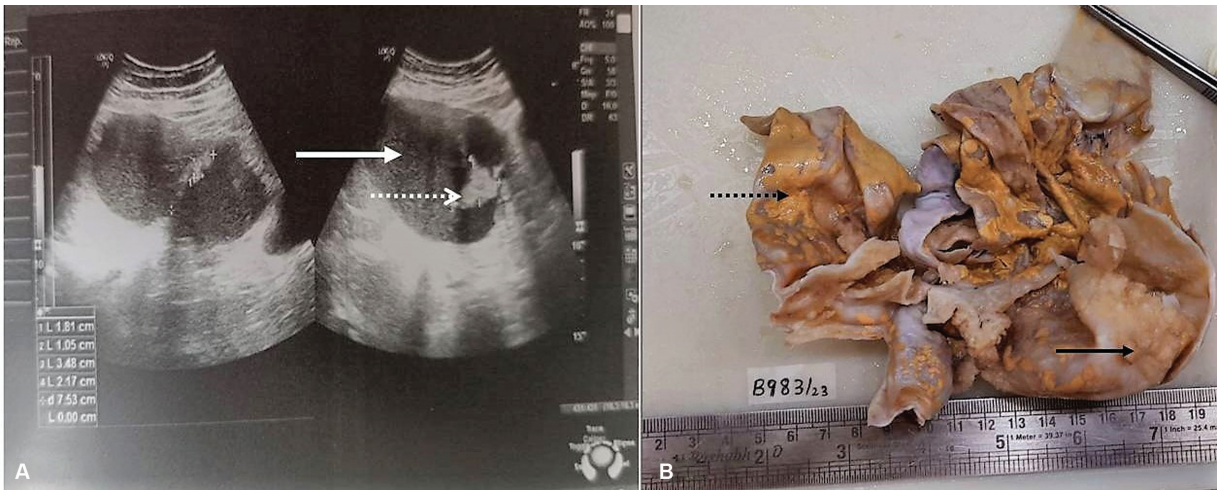

Fig. 1 (**A**) Ultrasound showing a cystic lesion (line arrow) with minor solid component and internal septations (dotted arrow). (**B**) Cut section of the ovarian cyst showing papillary excrescences (line arrow) and large areas of yellowish discoloration on the cyst wall (dotted arrow).

septation and another solid component measuring 1.8×1.0 cm showing significant internal vascularity. Both ovaries were not visible. Computed tomography abdomen showed a well-defined multiloculated cystic lesion in the region of right adnexa, measuring $16.8 \times 12 \times 11.4$ cm. Also seen were enhancing mural nodules and septations. Right ovary was not visualized separately. Left ovary was atrophic, postmenopausal state of uterus was noted with tiny subcentimetric nodes along the right external iliac vessels, largest measuring 5×3 mm, with peritoneum showing a small calcified focus measuring 10×7 mm. A preliminary diagnosis of mucinous cystadenoma/cystadenocarcinoma arising from the right ovary was conferred. CA125 was 27.1 U/mL. The surgical oncology team proceeded with a staging laparotomy and the right ovarian mass was sent for imprint cytology intraoperatively, which was reported as borderline epithelial ovarian tumor based on nuclear atypia and stratification. Also noted was good number of foamy histiocytes. This was followed by total hysterectomy and bilateral salpingo-oophorectomy along with omentum, para-aortic, pelvic nodes, and paracolic peritoneal sampling. External surface of the cyst appeared smooth and drained yellow serous fluid on cutting open. Inner surface showed multiple papillary excrescences and large patchy areas of yellowish discoloration (►**Fig. 1B**). Uterus cervix along with left adnexa and omentum were grossly unremarkable. A total of 17 lymph nodes were isolated along with a small chalky white peritoneal deposit measuring 1 cm across.

Microscopy of the ovarian cyst revealed a SBT with sheets of foamy macrophages suggestive of xanthomatous change, at places in continuity with the serous epithelial lining (►**Fig. 2A, B**). There was no associated inflammation or features suggestive of any tissue degeneration. On staining xanthomatous areas with progesterone receptor marker, areas of xanthomatous change were negative, whereas positive control sections of the corpus luteal cells stained positive (►**Fig. 2C, D**). Left ovary showed corpus albicans. All lymph nodes were free of tumor with peritoneal deposit showing encapsulated fat necrosis with dystrophic calcification. Endometrium showed senile cystic atrophy and cervix chronic cervicitis. Peritoneal washings were negative for tumor deposits. Additionally, serum lipid profile of the patient was within normal limits with absence of dermatological manifestation of xanthoma. A final diagnosis of serous borderline tumor with extensive xanthomatous change was conferred.

Discussion

Xanthomatous change is a phenomenon characterized by presence of lipid-laden macrophages, also known as foam cells. These foam cells exhibit abundant cytoplasmic lipid droplets, giving the affected tissue a distinct yellowish discoloration. Visceral aggregates of foamy macrophages which are unassociated with inflammation and/or hemorrhage are decidedly rare and almost exclusively encountered in the gastrointestinal tract, especially in the stomach.[4] Foamy macrophages have been identified in a variety of pathological conditions, including atherosclerosis, tuberculosis, sarcoidosis, and some cancers where they play a key role in the formation and progression of the disease.[2] Though gross and microscopic identification of xanthomatous change is straightforward, its association and characterization with ovarian tumors is a matter of debate. Differential diagnosis includes xanthogranulomatous oophoritis, which is a well-defined entity associated with chronic inflammation, underscoring the importance of meticulous assessment and elaborate history taking.[5,6]

Pathogenesis of xanthomatous change and its clinical implication in SBTs remain incompletely understood and is hypothesized to result from altered lipid metabolism within the tumor microenvironment.[7] SBTs account for approximately 15 to 20% of all epithelial ovarian tumors and commonly affect women in their reproductive years. Histologically, they are characterized by complex papillary architecture, mild nuclear atypia, low mitotic activity, and stromal microinvasion < 5 mm in greatest dimension. Although most SBTs follow an indolent course, a subset can demonstrate

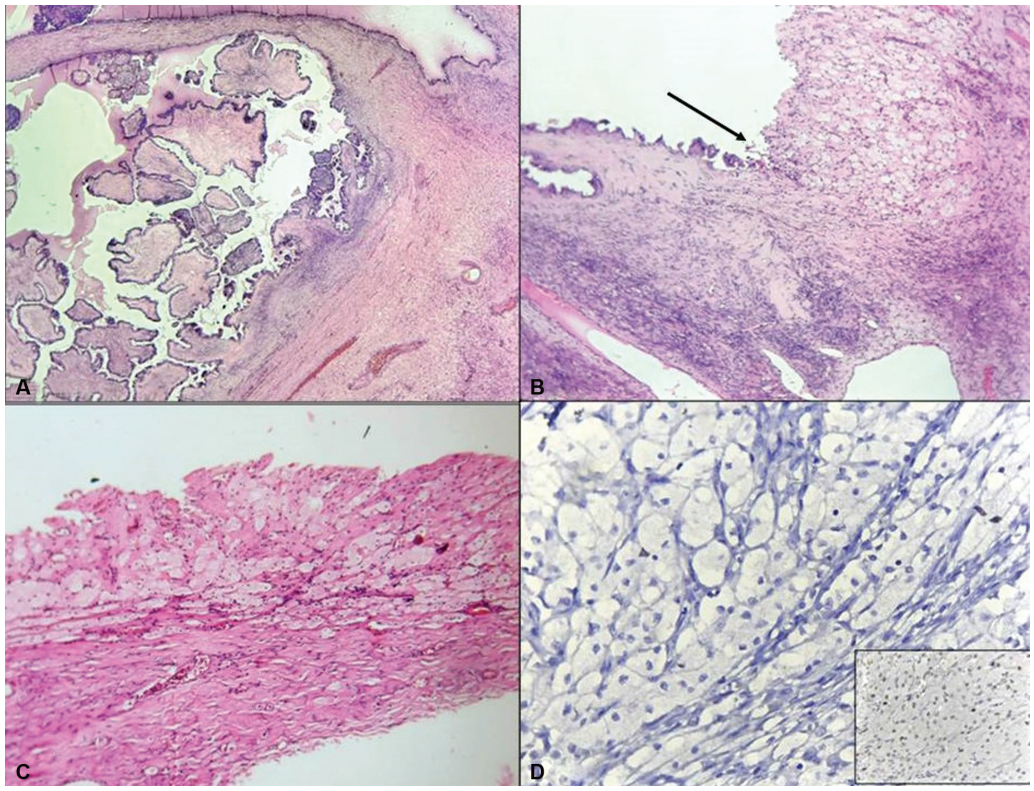

Fig. 2 (**A**) Microscopy of the ovarian serous borderline tumor (×100 hematoxylin and eosin [H&E]). (**B**) Microscopy showing junction of the serous borderline epithelial lining and foamy macrophages (×100 H&E). (**C**) Microscopy showing sheets of xanthomatous cells resting on ovarian cyst wall (×100 H&E). (**D**) Microscopy showing sheets of xanthomatous cells negative for PR (progesterone receptor) and inset showing corpus luteum positive for PR receptor (×100).

microinvasion or invasive carcinoma, necessitating careful assessment.[8] Formation of foam cells can impair macrophage immune function and contribute to pathogenesis. Studies have shown that foam cells tend to lose immune functions, produce proinflammatory cytokines, induce tissue damage, and sustain survival of intracellular pathogens, contributing to maladaptive immune responses.[2] Additionally, they have been found to be involved in angiogenesis, which is essential for tumor growth and metastasis.[9]

Alternatively, foamy cells may be postulated to represent corpus luteum in its normal course of degradation. Some studies have suggested that regressing corpus luteum shows autophagocytic luteolysis of steroidogenic cells which present as foamy macrophages and stain positive for CD 68.[10] In the present case this could imply the presence of a corpus luteal cyst coexisting with the SBT. However, there was no viable corpus luteum nor the progesterone marker stained positive in xanthomatous cells, rendering the relationship of these cells as continuum of corpus luteual degeneration doubtful.

Further research is needed to elucidate the true impact of xanthomatous change on prognosis and clinical management of patients with SBTs as literature on the same is sparse. Studies focusing on molecular and genetic characteristics of xanthomatous change in SBTs are needed to improve our understanding of this intriguing pathological entity.

Conclusion

Extensive xanthomatous change unassociated with inflammation is a rare and enigmatic feature infrequently encountered in serous borderline ovarian tumors as in the case presented. While the clinical significance of xanthomatous change in SBTs remains uncertain, its presence may warrant closer surveillance and reporting as its contribution to cancer pathogenesis is a matter of debate till date.

Note

If the manuscript was presented as part at a meeting, the organization, place, and exact date on which it was read. A full statement to the editor about all submissions and previous reports that might be regarded as redundant publication of the same or very similar work. Any such work should be referred to specifically, and referenced in the new paper.

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Conflict of Interest

None declared.

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Authors Contributions

A.K., A.S. and H.S.E. - Data collection and analysis.
A.S. and V.M. - Literature search and review.

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