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Case Report

Xanthogranulomatous endometritis mimicking endometrial carcinoma: A case report and review of literature

Xiao-zhou Du, MD[a,], Miao Lu, MD[b], Janice Safneck, MD[b], Patricia Baker, MD[b], Erin Dean, MD[c], Jeffrey Mottola, MD[d]*

[a] *Department of Radiology, University of Manitoba, GA220-820 Sherbrook Street, Winnipeg, Manitoba R3A1R9, Canada*

[b] *Department of Pathology, Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba, 401 - 727 McDermot Avenue, University of Manitoba, Winnipeg, Manitoba R3E 3P5, Canada*

[c] *Department of Obstetrics, Gynecology and Reproductive Sciences, Section Head, Division of Gynecology Oncology, University of Manitoba, RS4 - 810 Sherbrook Street, Winnipeg, Manitoba R3A 1R8, Canada*

[d] *Department Head, CT and MRI, Health Sciences Centre, Department of Radiology, University of Manitoba, GA220-820 Sherbrook Street, Winnipeg, Manitoba R3A1R9, Canada*

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ABSTRACT

Xanthogranulomatous endometritis (XGE) is an extremely rare chronic inflammatory condition, which may be associated with endometrial hyperplasia, endometrial carcinoma, or cervical stenosis. Imaging features can be easily misdiagnosed as an aggressive malignancy. We present a case of XGE, which is the first case of XGE with serial multimodality imaging examinations, in addition to clinical, surgical and pathologic correlations. As such, this unique case illustrates the evolution of this rare disease.

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Introduction

Xanthogranulomatous inflammation is an uncommon type of chronic inflammation characterized by foamy lipid laden histiocytes admixed with other inflammatory cells [1]. The most common sites of xanthogranulomatous inflammation are the kidneys and the gallbladder [2,3]. Xanthogranulomatous endometritis is extremely rare with just over 20 cases reported in the English literature. This form of endometritis

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* Corresponding author.
E-mail addresses: umdux@myumanitoba.ca (X.-z. Du), vivianmiaolu@gmail.com (M. Lu), Janice.Safneck@umanitoba.ca (J. Safneck), pmbaker@dsmanitoba.ca (P. Baker), edean@cancercare.mb.ca (E. Dean), jmottola@me.com (J. Mottola).

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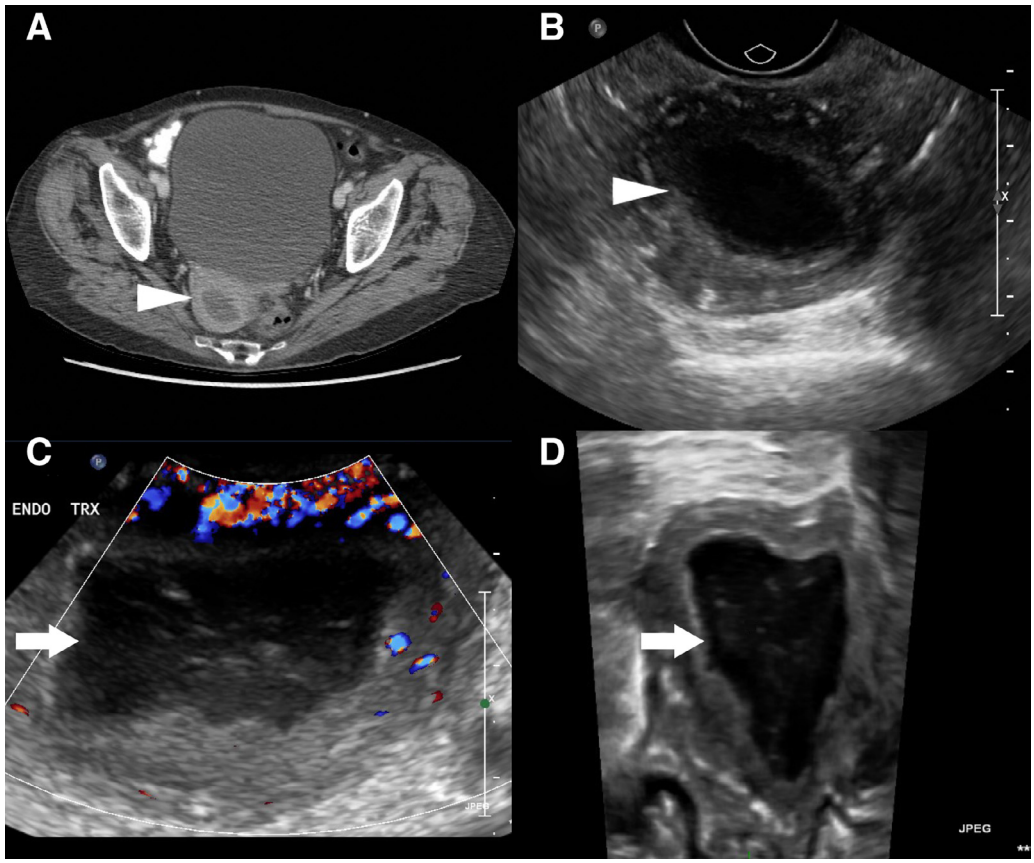

Fig. 1 – On initial presentation in 2009, imaging investigations revealed an endometrial fluid collection on CT (A), which was anechoic with posterior acoustic enhancement on endovaginal ultrasound (B) (white arrowhead). On endovaginal (C) and 3-D sonography (D) of the uterus in November 2012, the fluid collection had increased in volume and progressed in complexity, with new internal echogenic debris (white arrows). No vascular flow was present on color Doppler interrogation. The findings in 2012 were suspicious for hematometra and/or debris.

typically occurs in postmenopausal women who may have endometrial hyperplasia, endometrial carcinoma and/or cervical stenosis. We report a unique case of xanthogranulomatous endometritis with clinical, surgical and pathologic correlation, which demonstrates the evolution of the disease process over a number of years.

Case

A 74-year-old woman (Gravida 6, Para 4) with poorly controlled type 2 diabetes and a remote history of treated breast cancer, presented intermittently from 2009 through 2014 to the emergency department with diffuse abdominal pain. Computed tomography (CT) and ultrasound imaging demonstrated simple appearing fluid filling the endometrial canal in 2009 (Fig. 1A and B). The fluid collection enlarged over the next 4 years, measuring 2.8 × 2.5 × 1.3 cm (38 cc, anteroposterior by transverse by craniocaudal) in June 2009, 3.7 × 3.5 × 2.7 cm (146 cc) in September 2012, and 4.2 × 3.7 × 3.2 cm (208 cc) in March 2013. On endovaginal ultrasound in November 2012, the fluid collection demonstrated new dependent internal echogenic debris, suspected to represent hematometra or necrotic material (Fig. 1C and D). The patient failed to comply with the recommendations for gynecology follow up.

In May 2014, the patient represented with 4-day history of diffuse abdominal pain, leukocytosis, microhematuria and *Escherichia coli* pyuria. The patient also complained of intermittent blood tinged vaginal discharge for approximately 4 months. A contrast enhanced CT of the abdomen demonstrated a 7.4 × 5.8 × 4.8 cm irregular, heterogeneously enhancing uterine mass (Fig. 2A and B). In addition, there was mild left hydronephrosis related to a 2.2 × 2.8 × 2.6 cm (68 cc) rim enhancing lesion adjacent to the left ureter and psoas muscle (Fig. 2C and D), noncontiguous with the uterine mass. The clinical and laboratory findings favored pyelonephritis and the patient improved on intravenous antibiotics. Based on the CT findings, a primary endometrial carcinoma with peritoneal spread was suspected.

On speculum examination, the patient's cervix was flush with her vaginal wall and was not easily identified. Endometrial sampling was unsuccessful as the cannula was not able to be passed through the cervix. CT-guided biopsies of the uterine mass were undertaken, and demonstrated acute inflammatory exudate and fragments of spindle cells, without evi-

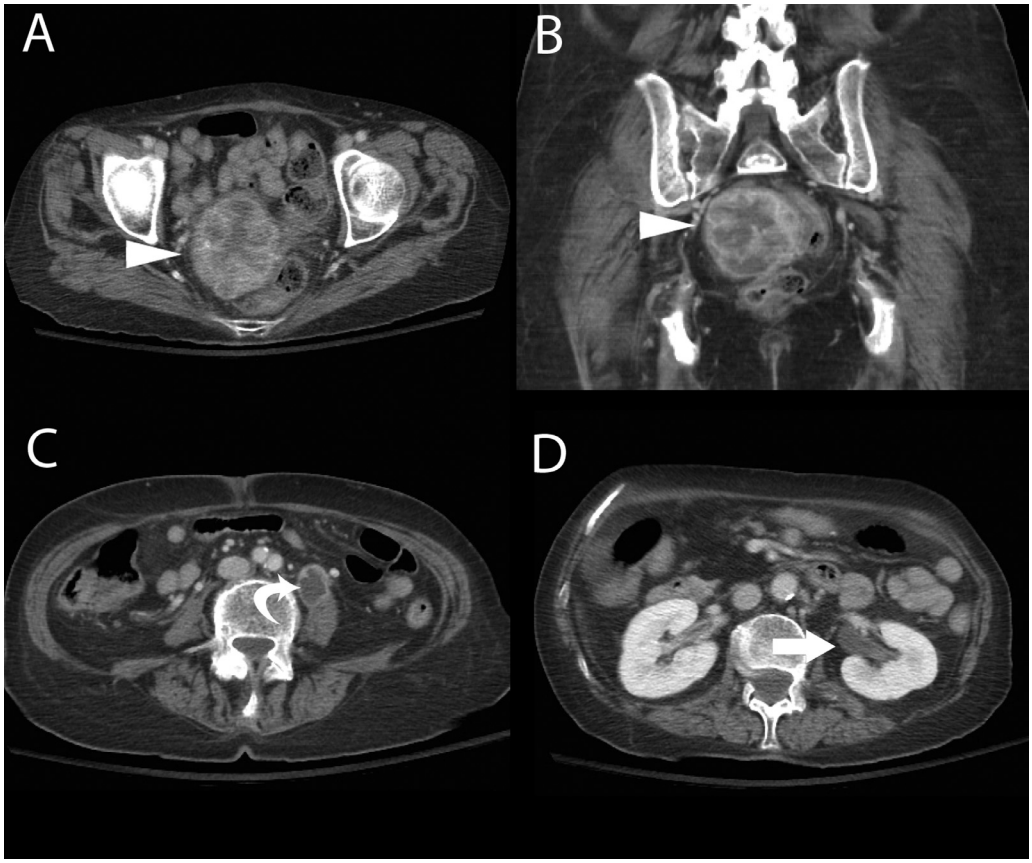

Fig. 2 – (A, B) During the acute presentation in 2014, CT demonstrated a heterogeneous uterine lesion, which had increased in size and complexity when compared to previous studies in 2012 (arrowheads). There was also a new rim enhancing abscess collection (curved arrow) apposing the mid left ureter and psoas muscle (C), causing mild hydroureteronephrosis (D, white arrow).

dence of malignancy. A total abdominal hysterectomy and bilateral salpingo-oophorectomy was performed under the assumption that the uterine lesion was most likely malignant. Intraoperatively, the uterus and adnexal structures showed no evidence of extrauterine invasion. An abscess corresponding to the rim enhancing lesion seen on CT was visualized along the left posterior peritoneum, which was surgically drained and debrided. The postoperative course was unremarkable and the patient was discharged after 3 days.

The left hydronephrosis resolved on follow-up CT examination 8 months after the operation. No postoperative complications were noted.

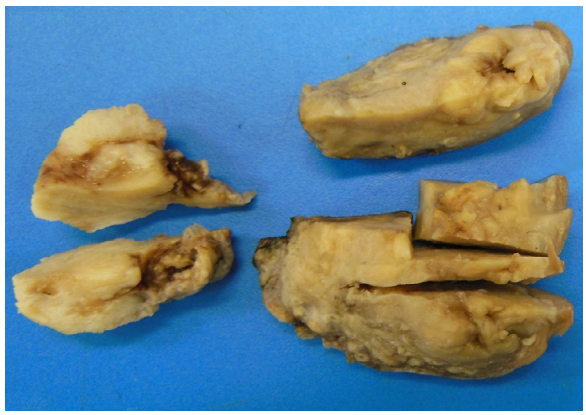

Fig. 3 – Gross specimen of the uterus demonstrated firm, tan nodular tissue which replaced the entire endometrium and involved myometrium.

Pathology findings

The entire endometrium was submitted for histology. Grossly, firm, tan, multinodular tissue replaced the entire endometrium (Fig. 3). No intrauterine fluid accumulation was present. On microscopic examination, sheets of abundant foamy histiocytes admixed with acute and chronic inflammatory cells were extensively present in the uterus (Fig. 4A). In some areas, the inflammatory changes involved the full thickness of the uterine wall (Fig. 4B) and extended to the cervix (Fig. 4C). Rare preserved endometrial glands were also present. Occasional multinucleated giant cells were identified but well-formed granulomas were absent (Fig. 4D). The

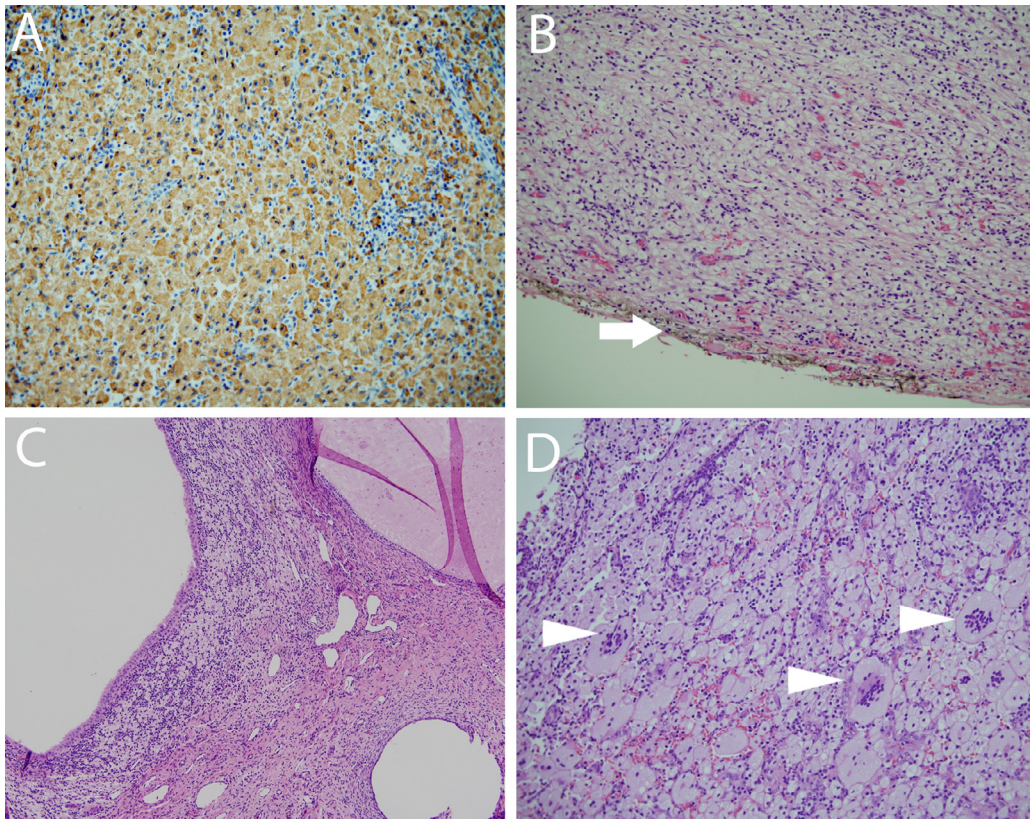

Fig. 4 – (A) Abundant histiocytes, as demonstrated by CD68 stain; Xanthogranulomatous inflammation, as shown with hematoxylin and eosin (H&E) stain, involved the full thickness of the myometrium out to the serosa (arrow) (B), and extended to the cervix (C); there were scattered multinucleated giant cells (arrowheads) (D).

histiocytes were positive for CD68 and negative for pancytokeratin, CD10, CD1a and S100. Special stains (Von Kossa, Prussian blue) did not show evidence of malakoplakia. No fungi, mycobacteria or bacteria were identified on special stains (methenamine silver, PAS, Gram, Ziehl-Neelsen). The cervix showed focal xanthogranulomatous change (Fig. 3C). The xanthogranulomatous inflammation did not involve the adnexa. A malignant process was not identified. The final diagnosis was xanthogranulomatous endometritis.

Discussion

Xanthogranulomatous endometritis, also known as histiocytic endometritis or pseudoxanthomatous endometritis, is a rare disease characterized by chronic inflammation of the endometrium. To our knowledge, only 23 cases have been reported in English literature [4–14], of which only 7 cases contain imaging findings [4–10]. The incident age range is from 45 to 88 years. Common clinical symptoms include lower abdominal pain and vaginal discharge. Palpable pelvic mass is a common physical exam finding [4,5,9,12].

Development of XGE is believed to involve a complex interaction of multiple factors, including cervical obstruction, inflammation and the presence of lipid, resulting in generation of free radicals and lipid peroxidation [14]. Other contributing features include necrosis and hemorrhage. Previous authors have also identified cervical stenosis as a risk factor for XGE [14].

This is the first case of XGE with serial multimodality imaging examinations. Endometrial fluid had been present since at least 2009, and slowly increased in volume and complexity until early 2013. The dependent debris that developed by November 2012 was suggestive of hematometra or necrotic debris, both of which are known contributing factors in the development of xanthogranulomatous inflammation. The findings of chronic hydrometra and hematometra were consistent with cervical stenosis, as confirmed on physical examination. Between March 2013 and May 2014, the imaging appearance of the uterus dramatically altered, likely due to acute on chronic inflammation. The presence of the noncontiguous peritoneal abscess adjacent to the left ureter, which resulted in hydronephrosis, further supports acute inflammation.

Based on prior case reports, the most common radiologic feature is heterogeneous cystic uterine mass (6 out of 8 cases) [4–10]. However, this was the first case that demonstrated a chronic, complex fluid collection in the endometrial canal prior to development of acute inflammation. Four cases (including current case) extend into the perimetrium or adjacent pelvic organs [7,9,11], one of which resulted in macroscopic uterine perforation [9]. Radiologically, the inflammatory process can appear aggressive, causing destruction of normal fat planes and infiltrating into surrounding organs [9,11].

Nine reported cases of xanthogranulomatous endometritis were associated with malignancy, including 7 cases of endometrial adenocarcinoma, 1 case of mixed carcinoma, and 1 case of recurrent squamous cell carcinoma of the cervix. It should be noted that 6 out of the 9 cases were published in a single report by Russack and Lammers [14]. The remaining 15 cases (including current case) were not associated with malignancy. The nonspecific presentation and aggressive imaging characteristics make the differentiation between xanthogranulomatous inflammation and malignancy difficult, if not impossible. Although no local lymphadenopathy has been reported in the literature, reactive lymphadenopathy is theoretically possible and may not be a useful distinguishing feature.

Diabetes has been reported as a risk factor for xanthogranulomatous inflammation in gallbladder, kidneys and testis [15–18]. Leukocyte dysfunction, in terms of leukocyte adherence, chemotaxis, and phagocytosis, is more common in diabetic patients [19–21]. The presence of poorly controlled diabetes in our patient supports the notion that diabetes is a risk factor for developing xanthogranulomatous inflammation in general.

On histology, XGE should not be misinterpreted as malakoplakia, pseudodecidual change of endometrial stroma or Langerhans cell histiocytosis (LCH). In malakoplakia, Michaelis-Gutmann bodies, intracytoplasmic inclusions composed of degenerate encrusted bacteria, should be visible with stains for calcium. Pseudodecidualized stroma should be CD10 positive. In XGE, histiocytes are CD68 positive while in LCH, they are CD1a and langerin (CD207) positive. Targeted investigations in our patient did not reveal findings suggesting any of these other diagnostic entities. Although XGE may be found with endometrial hyperplasia and neoplasm, these should not pose a problem for diagnosis. In both endometrial hyperplasia and carcinoma, the gland to stroma ratio is altered in favor of glandular growth. The glands become variable in shape, show increased structural complexity, and, if premalignant/malignant, cytologic atypia. In carcinoma, glands begin to fuse and may display solid growth in keeping with an invasive process.

Conclusion

Xanthogranulomatous endometritis is a rare entity that mimics endometrial carcinoma both clinically and radiologically. Diabetes mellitus may be a risk factor for the development of xanthogranulomatous inflammation. Since xanthogranulomatous inflammation can be associated with endometrial carcinoma, surgical excision remains the standard treatment. The endometrium in its entirety should be analyzed to rule out malignancy.

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