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Xanthogranulomatous Appendicitis with Pseudodiverticulum Formation- A Rare Form of Appendiceal Inflammation: A Case Report and Brief Review of Literature

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Abstract: ***Xanthogranulomatous appendicitis (XA) is a rare form of inflammatory condition involving the appendix. Here we present a young adult male presenting with typical features of appendicitis upon histopathological examination of the appendectomy specimen found to have a diverticulum and microscopy revealed xanthogranulomatous inflammation (XI) surrounding pools of mucin, abscess formation, and pseudodiverticulum formation. Ziehl-Neelsen staining was negative for acid fast bacilli and Periodic Acid Schiff (PAS) was negative for Whipple disease. No calcific bodies were found. No mucinous lesions of the appendix were found.***

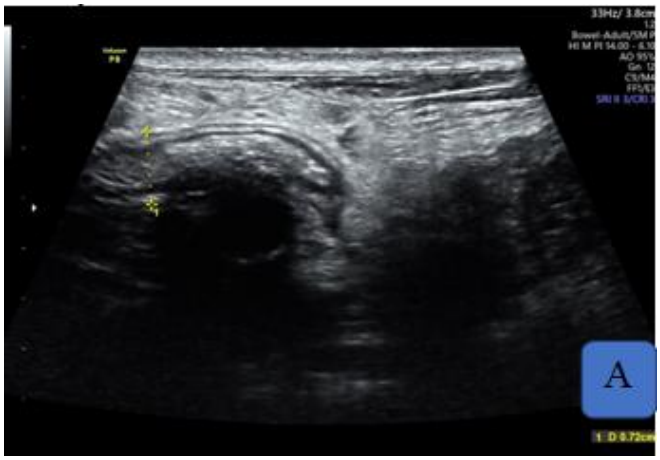
Keywords: Xanthogranulomatous appendicitis, Xanthogranulomatous inflammation, Pseudodiverticulum, Xanthogranuloma, and Appendicitis.

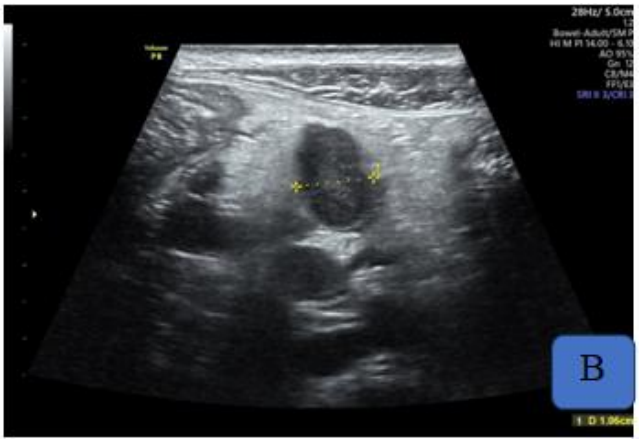
1. Introduction

Xanthogranulomatous inflammation is a type of chronic inflammation commonly seen in gallbladder and kidneys. [1, 2]Later on it was described in other organs such as lungs, pancreas, liver, ovary, urinary bladder and eyes. [3-5] This type of inflammation is uncommon in Appendix. It shows formation and accumulation of foamy histiocytes along with granulomas. Herein, we present a case of xanthogranulomatous appendicitis (XA) with a pseudodiverticulum formation.

2. Case Report

A 21-yr-old male presented with complaints of pain in the right iliac fossa radiating to the back for only one day. He also complained of dysuria. On general physical examination, he is afebrile, with stable vitals. Abdominal examination revealed pain in the right iliac fossa. His respiratory system, cardiovascular system and central nervous system examination were unremarkable. His ultrasound showed dilated appendix with features suggestive of inflammation with positive probe tenderness sign. Inflammation of the mesoappendix and enlarged ileo-colic lymph nodes were also noted (Image 1). Blood work up revealed, elevated total leukocyte count, 16.5 $x10^9$/L (3.5-9.5) with increased neutrophil count, 89.9 % (40-75). RBC, Platelets were within normal limits. Blood glucose, serum electrolytes and liver function tests were within normal limits, except for a mild increase in alkaline phosphatase, 159.41 U/L (normal range 25-140). Infectious disease screening for HIV, HBSAG and HCV were negative. His appendix was surgically removed. His post-operative recovery was unremarkable.





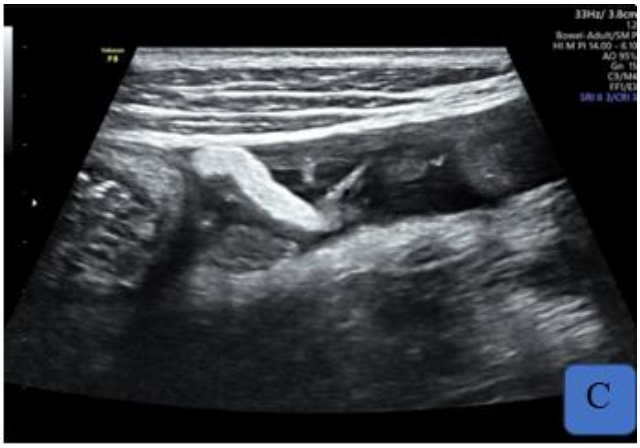


Image 1: Ultrasonographic images, (A) dilated (> 6 mm) blind ending bowel loop in right iliac fossa having gut signature suggestive of inflamed appendix. (B) enlarged ileo-colic lymph nodes (short-axis diameter more than 10mm) and hyperechoic adjacent mesentery suggestive of inflamed peritoneal fat. (C) free fluid in right iliac fossa (arrow) suggesting peritoneal inflammation due to appendicitis. Original images.

Gross examination of the specimen revealed, exudate covering the external surface of the appendix with congested blood vessels. On the cut section a diverticulum is identified just above the tip of the appendix (Image 2), wall of the appendix appeared oedematous. Lumen was identified. Light microscopic examination of the sections revealed expansion of the lamina propria by neutrophils, lymphocytes, plasma cells, eosinophils, and lymphoid follicles with reactive germinal centre extending into the submucosa. The submucosa showed lipoid infiltrate. Sections from the tip of the appendix and the diverticulum showed outpouching of the mucosa and submucosa into the serosa without a muscular layer (Image 3). The mucosa covering the pseudodiverticulum was focally ulcerated, lined by granulation tissue and filled with mucous. There was also an accumulation of foamy histiocytes, epithelioid cells, lymphocytes, neutrophils surrounding the pools of mucin (Image 3). No mucinous lesion of the appendix was noted in the sections. Acid fast stain did not reveal any bacteria (Image 4). PAS stain did not reveal intracytoplasmic aggregates which are seen in Whipple disease (Image 4). No calcific bodies noted. Thus diagnosed as Xanthogranulomatous appendicitis (XA).

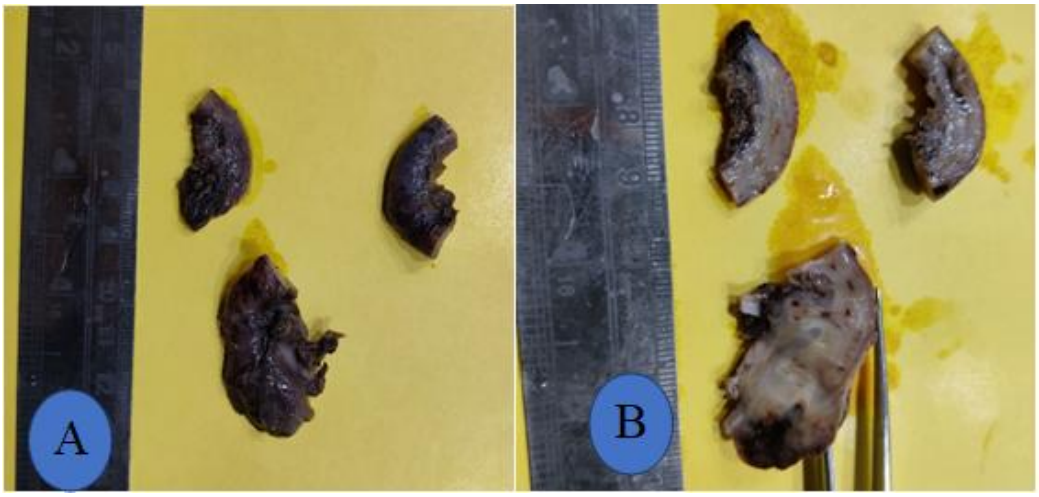
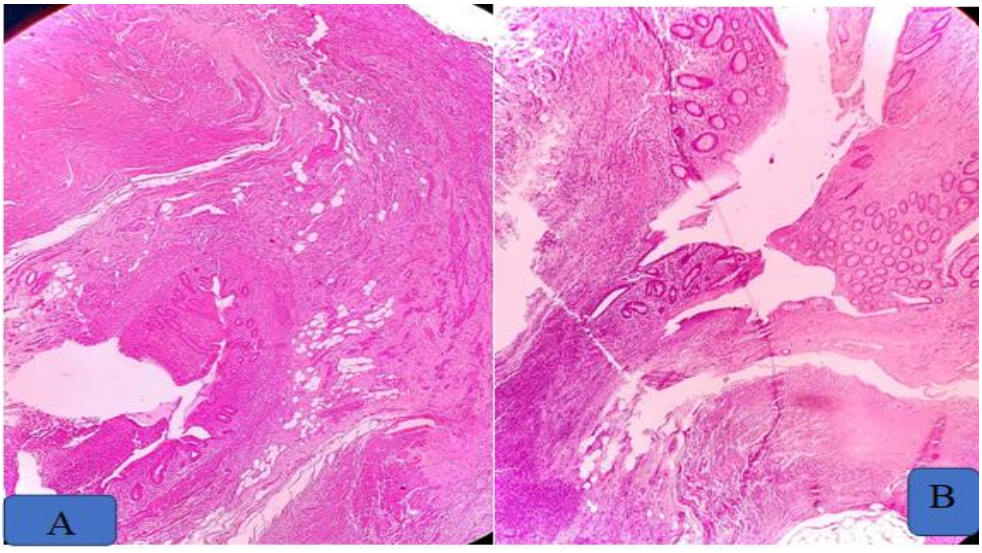


Image 2: Gross specimen; (A) external surface shows exudates and congestion. (B) Cut section of the specimen shows oedematous wall with a diverticulum formation at the tip of the appendix. Original images



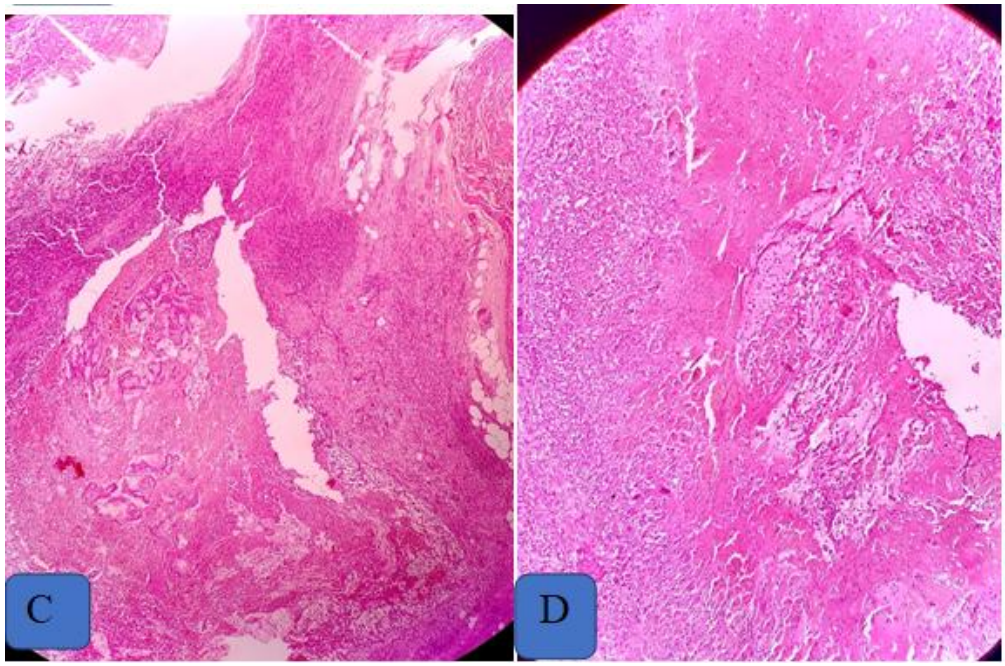


Image 3: Haematoxylin and Eosin stained sections of the appendix. (A) Appendiceal mucosa with expansion of submucosa by adipocytes and collagen fibres (4x). (B) Herniation of the mucosa and the submucosa through the muscularis externa. Note there is discontinuation of the muscularis externa (4X). (C) Focal ulceration of the appendiceal mucosa in the pseudodiverticulum, surrounded by pool of mucin and inflammatory cells (4X). (D) Higher magnification shows pools of mucin surrounded by foamy histiocytes and giant cells (10X). Original images.

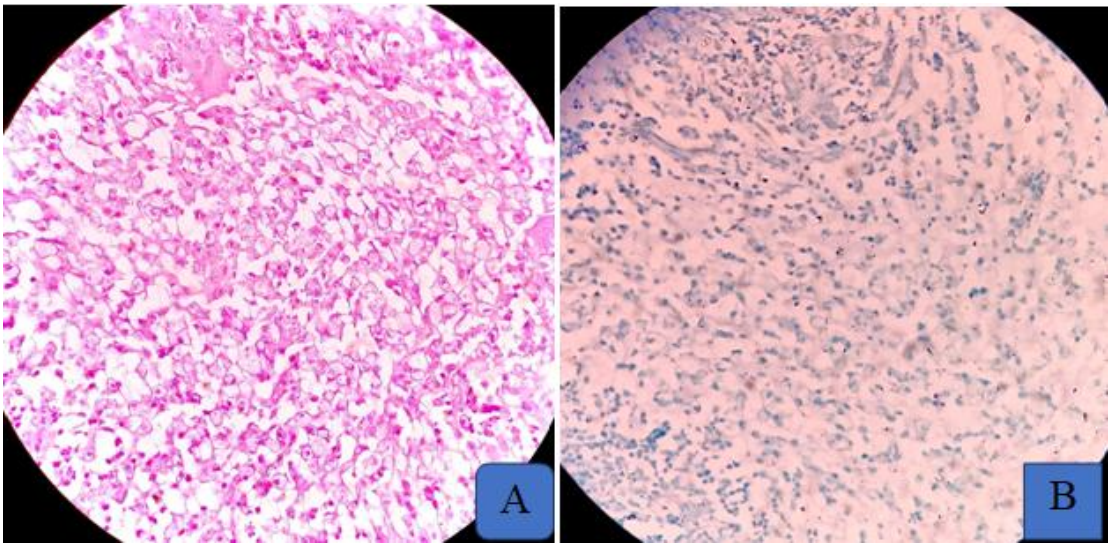


Image 4: (A) PAS staining revel no intra cytoplasmic inclusions (40X). (B) AFB staining is negative for acid fast bacilli (40X). Original images.

3. Discussion

Xanthogranulomatous inflammation composed of foamy histiocytes and granulomas was first described by Osterlind in 1944 in the kidney. [5, 6] Since then this entity has been described in various organs, including GIT, male genital tract, and female genital tract. Involvement of appendix by xanthogranulomatous appendicitis is quite rare.

There is no single pathophysiological factor responsible for the development of XA. It has been proposed that it is multifactorial, due to interplay between the factors like luminal obstruction, mucosal hypoxia, haemorrhage, infection by low virulent organisms, defect in lipid transport within the macrophages, immunological disturbances of leukocytes and macrophages. Bacterias implicated in the development of XA are proteus and Escherichia coli species. [4, 16, 17, 18, 19, 20]

Researchers Cozzutto and Carbone [5] observed that haemorrhage is a major factor which leads to the development of foamy macrophages, thus hypothesized that engulfed erythrocytes and platelets inundate the lysosomal system of the macrophages leading to accumulation of phospholipids thus facilitating the formation of foamy macrophages. The theory of phospholipid accumulation and a defect in the lipid transport was supported by Muichor et al. who found undigested lipid droplets within the foamy macrophages on electron microscopy. [4]

Clinically, majority of cases have been reported in adults and only a few in children. Most of them presented as acute appendicitis. [7] However, cases reported by Chuang et al and Ito et al, presented with fever, right lower abdominal pain and a mass with elevated tumour markers, which on gross mimicked an invasive carcinoma. [8 &9]

Guo and Greenson upon a retrospective comparison study between the cases of interval appendectomy within 4yrs duration and appendectomy for acute appendicitis within 72 hrs of onset of symptoms found that xanthogranulomatous appendicitis was found in 36% of patients with interval appendectomy. Meanwhile none of the patients who underwent appendectomy for acute appendicitis had this type of inflammation. [10] Majority of the case reports and studies till date proposed that XA is a response seen in appendix with long standing appendiceal inflammation and may lead to formation of a mass. [10, 11 & 12]
In 2011, Martinez-Garza et al. concluded in their case report that xanthogranulomatous appendicitis may be associated with inflammatory bowel disease. [13]

Only 39 [9 & 14] cases have been recorded in the medical literature till date and among which India has contributed 8 cases. This is the ninth case of XA reported from Himachal Pradesh, India.

Gold standard and cost effective test for appendicitis in non-pregnant adults is contrast-enhanced multidetector computed tomography. However, radiological findings are non-specific and XA is mostly identified on histopathological examination of the surgical specimens. [24, 25, 26]

A typical gross presentation of this lesion is presence of golden yellow mass-like lesion associated with abscess cavity. [5 & 15]
Common differentials which can present with foamy histiocytes and granuloma are Crohn's disease, Whipple's disease, tuberculosis and malakoplakia. Histopathology of Crohn's disease is characterized by the presence of transmural inflammation and granulomas, which is not seen in XA. Absence of concentric calcific Michaelis Gutmann bodies rules out malakoplakia. In addition Von Kossa and Perl's Prussian stains are useful to rule out the presence of Michaeli's Gutmann bodies. [21, 16, 22, 23, 10, 15] Whipple's disease shows Periodic acid Schiff positive intracytoplasmic granules or sickle forms which is absent in the histiocytes of XA. Also, in XA a Ziehl-Neelsen stain would be negative for tubercular organisms. Finally, a rare differential would be invasive carcinoma, because of fibrosis and inflammation seen in XA. [9]

4. Conclusion

In majority of studies the XA was most commonly observed in interval appendicitis. However, patients can have varied clinical presentation, where it can present as acute appendicitis or subacute appendicitis or a mass lesion. Rarely it can present as a fistula due to the destructive nature of the disease. Even though the gold standard test to detect appendicitis is contrast enhanced CT, the findings are nonspecific. Histopathological examination is required for the diagnosis of Xanthogranulomatous appendicitis.
A long term follow-up and comprehensive lab examination is required in cases with XA to identify its associated with inflammatory bowel disease.

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