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Original Research Paper

Histopathology

GRANULOMATOUS APPENDICITIS: AN UNCOMMON HISTOPATHOLOGICAL ENTITY-A SERIES OF THREE CASES.

Dr Monika B Gathwal	MD Pathology, Professor, Department of Pathology
Dr Nitika Chawla	MD Pathology, Associate Professor, Department of Pathology
Dr Ruchi Agarwal	MD Pathology, Professor, Department of Pathology
Dr Kulwant Singh	MD Pathology, Professor, Department of Pathology
Dr Chiranjeev Gathwal	MD Radiology, Professor and Head, Department of Radiology
Dr Jyoti Sangwan	PG Resident MD Pathology, Department of Pathology
Dr Sumit Kumar	Medical officer Health department, Haryana

ABSTRACT Granulomatous appendicitis (GA) is a rare pathological entity identified in 0.1% to 2% of appendicectomy specimens. Clinically mimicking acute appendicitis, its discovery on histopathology requires diagnostic differentiation to rule out serious underlying systemic or infectious pathologies, particularly in regions where tuberculosis (TB) remains endemic. We present a case series of three distinct presentations: an 18-year-old female with necrotizing granulomas and secondary anti-tubercular intervention; an 8-year-old male child with acute mucosal ulceration and transmural mixed inflammation; and a 22-year-old female displaying lymphohistiocytic mural granulomas. While individual histomorphology varied, all presented with typical symptoms of an acute abdomen and successfully underwent appendectomy. This series highlights the critical diagnostic value of histopathology, the variable features of appendiceal granulomas, and the imperative of clinical exclusion protocols.

KEYWORDS : Granulomatous appendicitis; Idiopathic granulomatous appendicitis; Necrotizing epithelioid cell granulomas; Ziehl Neelsen stain

INTRODUCTION

Granulomatous inflammation of the vermiform appendix is an uncommon histopathological variant, occurring in roughly 0.1% to 2% of all appendicectomy specimens globally. Clinically, these patients present identically to classic acute appendicitis, characterized by acute or subacute right lower quadrant abdominal pain, nausea, vomiting, or fever. Consequently, preoperative imaging and laboratory panels rarely flag the true underlying pathology, rendering definitive diagnosis heavily reliant on post-operative tissue evaluation

The detection of granulomas in appendiceal tissue introduces an expansive diagnostic dilemma. It may point to systemic non-infectious autoimmune disorders like Crohn's disease or sarcoidosis, or result from localized infectious etiologies such as Mycobacterium tuberculosis, Yersinia species, fungi, or foreign body reactions. Conversely, when comprehensive investigations fail to reveal an underlying condition, it is classified as isolated or idiopathic granulomatous appendicitis (IGA). In developing nations, the baseline threshold for suspicion remains skewed toward tuberculosis due to high endemic load. This study evaluates the unique clinical presentation, pathological observations, and management schemes of three distinct cases of granulomatous appendicitis managed within a tertiary care medical institution in India

Case reports

Case 1: An 18-year-old female presented to the Surgery OPD with a history of acute generalized abdominal pain localized to the right lower quadrant, accompanied by multiple episodes of vomiting and moderate-to-high-grade fever. On clinical examination, there was marked tenderness and rebound tenderness in the right iliac fossa. Complete Blood Count (CBC) revealed significant leukocytosis with a White Blood Cell (WBC) count of 14,200/cumm and an absolute neutrophil lineage percentage of 82%. Hemoglobin was 11.2 g/dL, and the platelet count was 2,45,000/µL. C-Reactive Protein (CRP) was elevated at 48 mg/L, and Erythrocyte Sedimentation Rate (ESR) was increased at 35 mm/hr. Serum electrolytes, renal function tests, and liver function profiles were within normal physical baseline limits. Transabdominal ultrasonography (USG) demonstrated an aperistaltic, non-compressible, blind-ended tubular structure in the right iliac fossa measuring >6 mm in diameter, highly suggestive of acute appendicitis.

During exploratory laparotomy, the appendix appeared markedly inflamed. Concurrently, multiple distinct nodules were noted on the adjacent bowel loops along with significant omental thickening. An appendectomy was performed alongside an omental biopsy and excision of the bowel nodules.

On histopathological examination, microscopy of the appendiceal sections revealed a dense, transmural chronic inflammatory infiltrate. Multiple well-formed epithelioid cell granulomas characterized by central caseous-like necrosis and occasional Langhans-type multinucleated giant cells were seen extending through the submucosa, muscularis propria, and subserosa. Biopsy sections of the omentum and bowel nodules similarly demonstrated fibro-adipose tissue heavily infiltrated by necrotizing epithelioid granulomas.

Ziehl-Neelsen (ZN) staining for Acid-Fast Bacilli (AFB) utilizing 20% H_2SO_4 was non-contributory (negative). However, a detailed post-operative history revealed that the patient had close, prolonged domestic contact with her maternal grandmother, who had recently succumbed to pulmonary tuberculosis. Based on the histopathological presence of caseous necrosis and strong epidemiological link, the patient was initiated on a standard regimen of anti-tubercular medication (ATT). Unfortunately, the patient was subsequently lost to clinical follow-up

Case 2: An 8-year-old male child presented to the emergency department with a 24-hour history of severe right iliac fossa

pain, anorexia, and localized abdominal tenderness. Vital signs were stable, and physical examination revealed localized guarding at McBurney's point. Lab work showed mild leukocytosis with a WBC count of 11,800/cumm (Neutrophils 74%, Lymphocytes 21%). Hemoglobin was 12.1 g/dL. CRP was slightly elevated at 14 mg/L. Routine urinalysis was completely normal, ruling out lower urinary tract etiologies. Abdominal ultrasonography confirmed a distended appendiceal lumen measuring 6.8mm with increased vascularity of the wall, confirming acute appendicitis. A chest X-ray was performed as part of the pediatric workup and revealed clear lung fields with no hilar lymphadenopathy.

An emergency open appendicectomy was performed without intraoperative complications. Gross examination of the cut section of the resected appendix revealed focal mucosal hemorrhagic spots and discrete grey-white patchy areas.

Microscopic evaluation showed prominent mucosal ulceration and an underlying mixed inflammatory cell infiltrate (composed of neutrophils, lymphocytes, and plasma cells) spanning all anatomical layers. Interspersed within the mucosa and submucosa were multiple well-defined, non-caseating epithelioid cell granulomas containing characteristic Langhans multinucleated giant cells. ZN staining with 20% H_2SO_4 was negative for acid-fast structures. A final diagnosis of primary granulomatous appendicitis was established. Pediatric systemic workup, including a chest X-ray and screening for inflammatory bowel disease, yielded normal results, pointing to a localized idiopathic presentation.

Case 3: A 22-year-old female presented with a two-day history of progressively worsening lower abdominal pain localized to the right iliac fossa, associated with nausea and vomiting. Complete Blood Count revealed a total WBC count of 12,500/cumm with neutrophilic dominance (78%). Hemoglobin was 12.8 g/dL. CRP was recorded at 22 mg/L. Serum quantitative β-hCG was negative (<2 mIU/mL), successfully ruling out ectopic pregnancy. Magnetic Resonance Imaging (MRI) of the abdomen and pelvis was performed, revealing a thickened, fluid-filled appendix with peri-appendiceal fat stranding, consistent with acute appendicitis.

The patient underwent an uncomplicated appendicectomy. Histopathological analysis of the resected specimen demonstrated dense lymph histiocytic aggregates forming non-necrotizing granulomas accompanied by multinucleated giant cells. These inflammatory changes involved the transmural appendiceal wall and extended directly into the surrounding periappendiceal adipose tissue. Histochemical staining for AFB using 20% H_2SO_4 was non-contributory. The diagnosis was compatible with isolated granulomatous appendicitis. Post-operative screening revealed no extra-intestinal manifestations or history suggestive of systemic granulomatous conditions.

DISCUSSION

Granulomatous appendicitis remains a major diagnostic challenge due to its identical clinical presentation to typical acute suppurative appendicitis. It is typically discovered incidentally during post-operative histopathological review. The formation of epithelioid granulomas represents a specialized chronic T-cell-mediated immune response attempting to sequester persistent, non-degradable antigenic stimuli. Laboratory investigations in GA mirror those of classic acute appendicitis, typically manifesting as leukocytosis and elevated acute-phase reactants (CRP and ESR), as documented in all three of our cases. These findings indicate systemic inflammation but lack the specificity required to deduce a granulomatous process prior to surgical resection.

The etiologic distribution of GA varies heavily by geographic region. In Western nations, an incidental finding of an appendiceal granuloma is frequently considered an early or isolated manifestation of Crohn's disease, with approximately 5% to 10% of these patients eventually developing systematic gastrointestinal involvement. In contrast, within developing and tuberculosis-endemic regions, gastrointestinal tuberculosis is a primary differential consideration. Appendiceal tuberculosis is a rare form of extra-pulmonary TB, often arising secondary to swallowed infected sputum or hematogenous spread, though it can occasionally present as a primary localized lesion.

Histopathologically, the presence of caseous (central) necrosis within epithelioid granulomas strongly points toward a mycobacterial infection, as observed in Case 1. While a positive ZN stain or polymerase chain reaction (PCR) confirms the diagnosis, negative staining does not exclude tuberculosis, particularly in paucibacillary tissue specimens. Thus, a comprehensive history of tuberculosis exposure, coupled with inflammatory panels and chest imaging, is vital for guiding therapeutic management.

Non-necrotizing (non-caseating) granulomas, as seen in Case 2 and Case 3 present a broader differential diagnosis. They can represent localized idiopathic granulomatous appendicitis (IGA), a delayed reaction to a fecolith or prior subclinical perforation, or early-stage Crohn's disease. Emerging data indicate that true idiopathic granulomatous appendicitis has a highly favourable prognosis, with simple appendectomy serving as a definitive cure in the vast majority of cases. Nevertheless, these patients require careful clinical follow-up and monitoring to rule out subsequent manifestations of inflammatory bowel disease.4

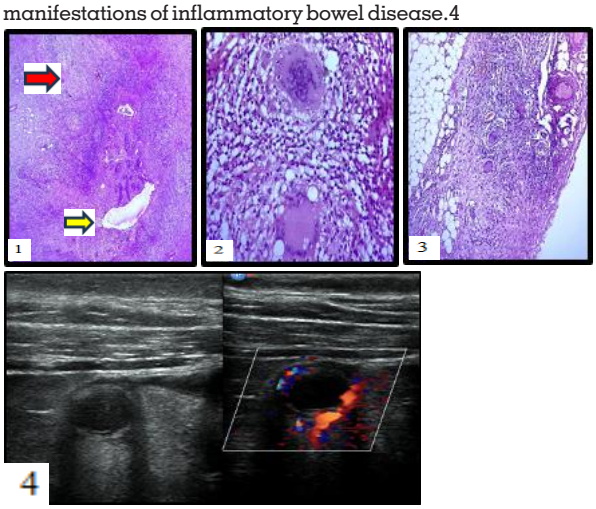

Fig 1: Photomicrograph Showing appendiceal lumen and granuloma with multinucleated giant cells (H&Ex10). (yellow arrow- lumen, red arrow- granuloma) Fig2: Photomicrograph showing an epithelioid cell granuloma with Langhans-type giant cells in the wall of appendix(H&Ex200). Fig3: Photomicrograph showing granulomatous inflammation with giant cells in peri appendiceal adipose tissue (H&Ex40). Fig4: Ultrasonography shows a dilated, non-compressible appendix with peri appendiceal inflammatory changes and increased vascularity on Doppler, suggestive of acute appendicitis.

CONCLUSION

Granulomatous appendicitis is a rare condition that perfectly mimics ordinary acute appendicitis in clinical settings. Definitive diagnosis is exclusively histopathological. Because the finding of an appendiceal granuloma can be the harbinger of systemic conditions (such as Crohn's disease) or specialized infections (such as tuberculosis), a multi-disciplinary approach involving lab values, imaging,

comprehensive clinical history, and targeted diagnostic testing is mandatory to optimize patient management.

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