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Granulomatous Inflammation of the Gall Bladder: A Diagnostic Challenge

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Abstract: ***Granulomatous inflammation of gall bladder (GB) is rare. There are a few reports of tuberculosis (TB) involving GB[1]. Non Caseating granulomas in GB after cholecystectomy may be suggestive of Sarcoidosis, though TB may be suggested as a close alternative diagnosis[2]. Sarcoidosis may be considered in the differential diagnosis when noncaseating granulomas are identified in GB and rest of the clinical features and laboratory parameters are suggestive.***

Keywords: Tuberculosis; Granulomas; Cholecystectomy, Lymphadenopathy, Gallstones

1. Case Presentation

A 42 year old male presented with right upper quadrant (RUQ) pain of 3 days. There was early satiety and mild abdominal bloating. There was no fever or jaundice. Work up revealed normal hemogram, mild hyperbiliubinemia and normal enzymes. Serum calcium (10.3 mg%) and serum angiotensin converting enzyme(ACE) was elevated (54.3 U/L). Imaging revealed gall bladder calculus, pararotic, peripancreatic and mediastinal adenopathy. There was past h/o (3 yr ago) mediastinal adenopathy with normal serum ACE. Endobronchial ultrasound (EBUS) showed granulomatous inflammation, but as diagnosis remained doubtful, thoracotomy and lymphnode biopsy was done which showed granulomatious inflammation. Sarcoidosis and tuberculosis were considered in the differential diagnosis. No definitive treatment was offered by the physician during that time and suggested observation. During the present admission surgery was offered for symptomatic gall stones. Laprascopic cholecystectomy and peri portal lymphode excision was done. Histopathology of gall bladder showed non caseating granulomas and lymph nodes showed confluent granulomas without any necrosis. Post operative course was uneventful and patient remained symptom free during the follow up of 1 month. A diagnosis of Sarcoidosis was made in view of non caseating granulomas in lymph node and gall bladder, evidence of generalized lymphadenopathy, elevated ACE and serum calcium. The cause for RUQ pain was symptomatic gall stones which probably was an associated condition. Rarity in this case is the documentation of noncaseating granulomas in the GB wall by histopathology (Fig 1).

2. Discussion and Literature Review

Sarcoidosis is a multi system disease characterized by non caseating epithelial cell granulomas. Diagnosis is based on compatible clinical presentation, non necrotizing granulomatous inflammation in one or more tissues and the exclusion of alternative causes of granulomatous disease[3]. The organs involved in sarcoidosis are lungs, skin, lymphnodes, heart, nervous system, kidney, liver, spleen, eyes, musculoskeletal system and bone marrow[4]. Based on the organ involved, a wide variety of differential diagnosis needs to be considered. Hence biomarkers (Table 1), CT pattern scores and PET-CT are usually utilised for improved diagnosis and assessment of organ involvement[5]. After a diagnosis of Sarcoidosis is obtained, it must be decided whether the patient needs any treatment or just follow up[6]. Pulmonary Sarcoidosis is staged based on Scadding (1961) into 5 stages (0-V); stage I being only mediastinal and hilar adenopathy and stage II involves lymphadenopathy with pulmonary infiltrates[7].

Spontaneous remission is common in stage I & II (55-90%) but not in stage 3 (10-20%). Observation seems reasonable in asymptomatic and mild cases. Step by step strategies are considered for high risk cases. In our case, the disease appeared stable for 3 years and the acute abdominal pain caused by gall stones seemed like an associated condition which required cholecystectomy. As laparoscopic approach had to be performed, peri portal lymphadenectomy was also done. Both gall bladder and lymph nodes showed non caseating granulomas suggesting sarcoidosis. In view of indolent course of the disease, no active intervention was suggested in the immediate post operative period; but a close follow up at regular intervals was suggested.

Diagnosis in doubtful cases may be based genetic tests which may include HLA class II antigens, HLADRB1*03, HLADRB1*11, HLADRB1*12, HLADRB1*14 and HLADRB1*15[9].

Additionally a ten gene Sarcoidosis diagnosis signature was constructed consisting of GBP1, LEF1, IFIT3, LRRN3, IFI44, LHFPL2, RTP4, LD27, EPHX2 and CXL10, which could improve the accuracy of early diagnosis[5.]

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There are very few case reports of Sarcoidosis involving gall bladder[10].

In our case, the cause of abdominal pain is gall stones which led to the confirmatin of Sarcoidosis involving gall bladder. But reports of granulomatous inflammation or extrinisic compressiion of cystic duct by enlarged lymph nodes may also lead to acute cholecystitis. Diagnosis of Sarcoidosis involving gall bladder is almost always after cholecystectomy.

3. Conclusion

Gall bladder granulomas are very rare and the usual differential diagnosis is tuberculosis and sarcoidosis. Finding of granulomas may be more commoner in tuberculosis than Sarcoidosis. There is a sparse literature available on GB involvement by Sarcoidosis and diagnois may have to be based on clinical features and advanced lab findings.

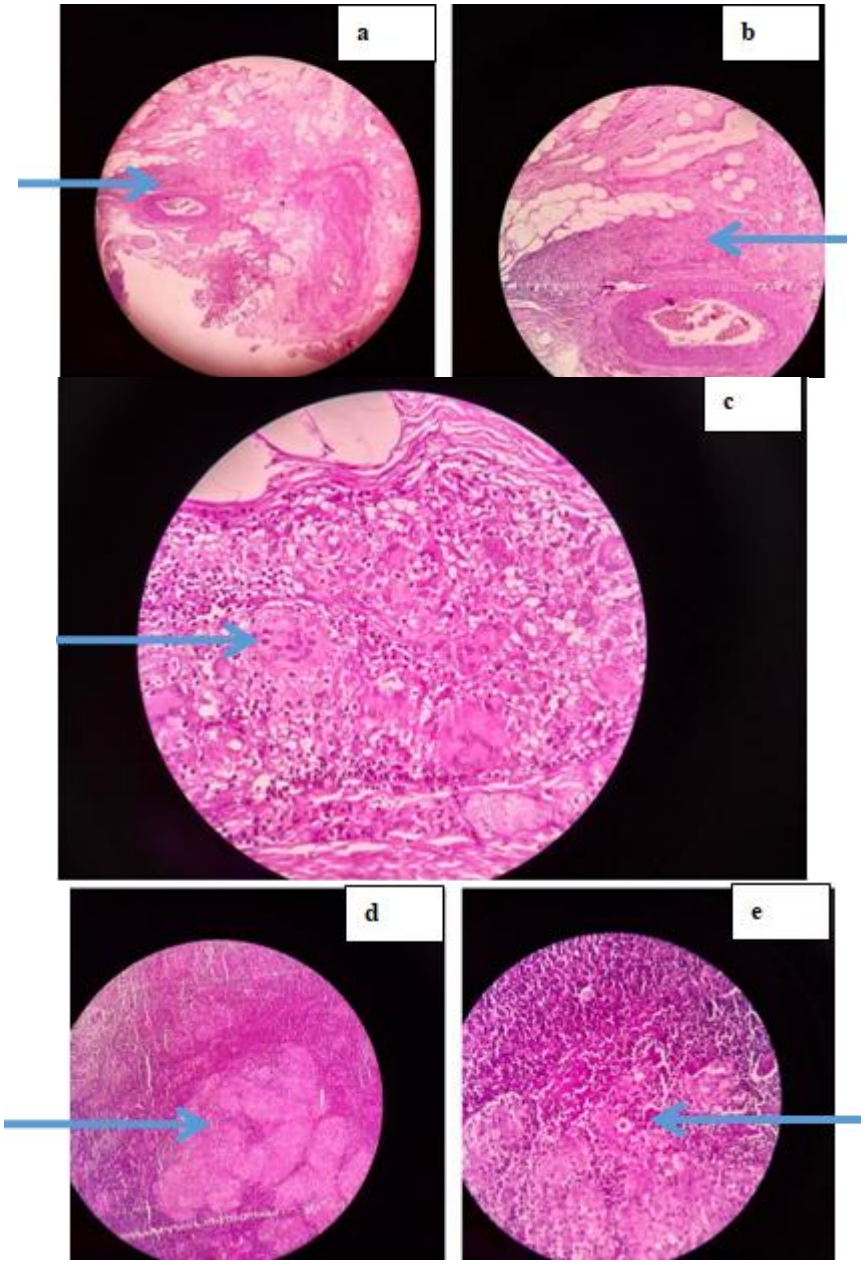

Figure (1): A, B, C are from Gall bladder showing isolated non caseating granuloma near the large blood vessels. On higher power examination giant cell showing faint intracytoplasmic calcification.

Image D and E are from cystic duct lymphnode showing non caseating granuloma with one of giant cells showing astroid body.

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Table 1: Biomarkers of Sarcoidosis

Macrophages	Monocytes	T Cell	B cell
ACE	Elevated	SSIL2r	Bcell activating factor
SSIL2r			Naive & memory cells
Lysozyme			Regulatory B cells
CD163			
YKL40			
Neopterin			
Amyloid A			
CCCL18			

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