International Journal Dental and Medical Sciences Research
Volume 3, Issue 3, May - June 2021 pp 338-346 www.ijdmsrjournal.com ISSN: 2582-6018

Diagnostic Dilemma In A Case Of Obstructive Jaundice Presenting With Gall Bladder Mass Masquerading As Gall bladder Cancer - A Rare Case Report With Review Of Literature.

Dr. Yatindra Kashid [1], Dr. Rajat Kumar [2], Dr. Pooja [3], Dr. Mukta Pujani [4], Dr. Vaishali Saxena[5], Dr. Vimal Bhandari [6].

[1] Associate Professor, [2] Senior Resident, [3] Senior Resident, [4] Professor, [5]Assistant Professor, [6] Professor, [1, 2, 5, 6,] Departments of General Surgery, [3] Radiology and [4] Pathology, ESIC Medical College and Hospital, Faridabad, Haryana.

Corresponding Author - Dr. Yatindra Kashid, *Flat no - 15, Shivji Sankul, Bela deSouza road, Jail road, Nashik road, Nashik, Maharashtra State, India. Pin –422 101. Email - yatindrakashid@gmail.com*

Submitted: 01-06-2021 Revised: 13-06-2021 Accepted: 15-06-2021

ABSTRACT:- Xanthogranulomatous cholecystitis (XGC) is an unusual and destructive form of chronic cholecystitis. It is an uncommon lesion which may form a tumor-like mass in inflamed gallbladders. Preoperative diagnosis is difficult and is often mistaken for gall bladder cancer. Despite much clinical experience, diagnosis and management of this disease remains suboptimal with an incidence of around 1- 3% . Its importance lies in the fact that imaging studies and intra-operative appearance may mimic tumor of the GB. The definitive diagnosis depends on the histopathologic examination. Xanthogranulomatous inflammation of gallbladder wall can extend and infiltrate adjacent organs which can be mistaken for malignancy on preoperative investigations and, intra-operatively, often leads to extensive surgical resections [1].

We present here a case of obstructive jaundice presenting with gall bladder mass masquerading as gallbladder cancer leading to diagnostic dilemma and also discuss the management of such cases.

Running title - Xanthogranulomatous cholecystitis.

Keywords - Xanthogranulomatous cholecystitis, Carcinoma gall bladder.

I. INTRODUCTION:-

Xanthogranulomatosis is an idiopathic, rare process in which lipid-laden histiocytes are deposited at various locations in the body such as skin, kidney, retroperitoneum, intracranium, gastrointestinal tract, genital organs, and gallbladder[2,3]. The nomenclature was done by McCoy et al [4] in 1976 though it was first described in 1970 by Christensen et al [5] and Amazon et al [6] had noted a pseudo-tumoral form of chronic cholecystitis that was characterized by the presence of xanthoma-like foam cells and scarring and that contained ceroid (wax-like) nodules in an inflamed gallbladder wall. They used the terms fibro-xantho-granulomatous inflammation and ceroid granulomas of the gall bladder, respectively, which are now known as synonyms of XGC [5,6]. Regarding pathogenesis, the chronic outflow obstruction provokes mucosal ulceration and/or rupture of Rokitansky-Aschoff sinuses and extravasation of mucin and bile into subepithelial tissue. Extravasated bile provokes inflammation, and macrophages phagocytose bile lipids and cholesterol to form ceroid-laden and foamy histiocytes (xanthoma cells). The chronic phase is characterized by repair of the inflammatory reaction, resulting in fibrosis [7].

II. CASE REPORT :-

A 75 years - old female, known case of type-II Diabetes mellitus and Hypertension was admitted at our institute, with history of yellowish discoloration of eyes and urine for duration of 15 days and high grade fever for a duration of two days. She also had history of passing clay coloured stools.

On examination the patient was deeply icteric. Abdominal examination revealed tender globular lump in right hypochondrium suggestive of gall bladder. There was no hepatomegaly or ascitis. Clinical picture suggested obstructive jaundice with acute cholecystitis with cholangitis with DM and Hypertension. The patient was started on intravenous antibiotics - injection Piperacillin with Tazobactum, Amikacin, and Metronidazole.

International Journal Dental and Medical Sciences Research
Volume 3, Issue 3, May - June 2021 pp 338-346 www.ijdmsrjournal.com ISSN: 2582-6018

She was also treated with injection Vitamin K, Analgesics, Pantoprazole and intravenous fluids.
Her lab reports were – Haemoglobin - 13 g / dl, WBC - 22,000 cells per cubic mm.
Liver Function Tests - Total Bilirubin - 16mg/dl with Direct Bilirubin - 14.2mg/dl and Indirect Bilirubin - 1.8 mg/dl. Alkaline phosphatase was - 260IU/L. Prothrombin Time was normal.
USG was reported as, Cholelithiasis with chronic cholecystitis with IHBR dilatation (left > right). CECT abdomen was reported as, distended GB with concentric lobulated wall thickness approximately 11 mm. A heterogeneous appearing mass lesion was seen in the fundal region with overlying capsular retraction and was seen reaching upto hepatic flexure of colon with loss of fat planes. The mass lesion measured approx 3.2 X 4.2 X 3.2 cm. The CBD was dilated and measured approx 14.6 mm with smooth distal tapering. There was central upstream bilateral IHBR dilatation (Fig 1 to 6).

Differential Diagnosis of Carcinoma gall bladder with adjacent large bowel infiltration and distal CBD stricture was made.

Patient's Tumour marker - CA-19-9 level was more than 500 IU /ml.
The patient underwent Endoscopic Retrograde Cholangio Pancreatography (ERCP), with findings of :- Ampulla - Normal. Selective CBD cannulation was done. Cholangiogram showed dilated IHBR and proximal CBD with long segment stricture in mid and lower CBD. Wide billiary sphincterotomy done. Stricture dilated with SBDC 7 - 10F. Stent placed in CBD across the stricture into right biliary system. Copious flow of white bile noted. However, despite ERCP and CBD stenting, the Patient still had persistent high bilirubin levels.

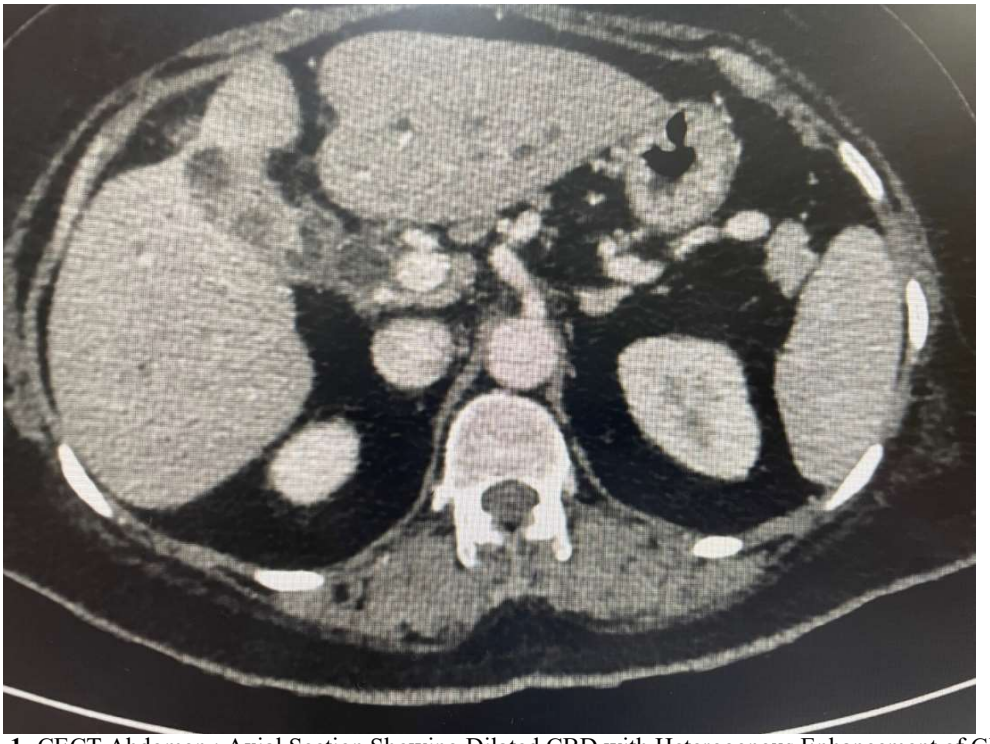


Fig. 1- CECT Abdomen : Axial Section Showing Dilated CBD with Heterogenous Enhancement of GB.

International Journal Dental and Medical Sciences Research
Volume 3, Issue 3, May - June 2021 pp 338-346 www.ijdmsrjournal.com ISSN: 2582-6018

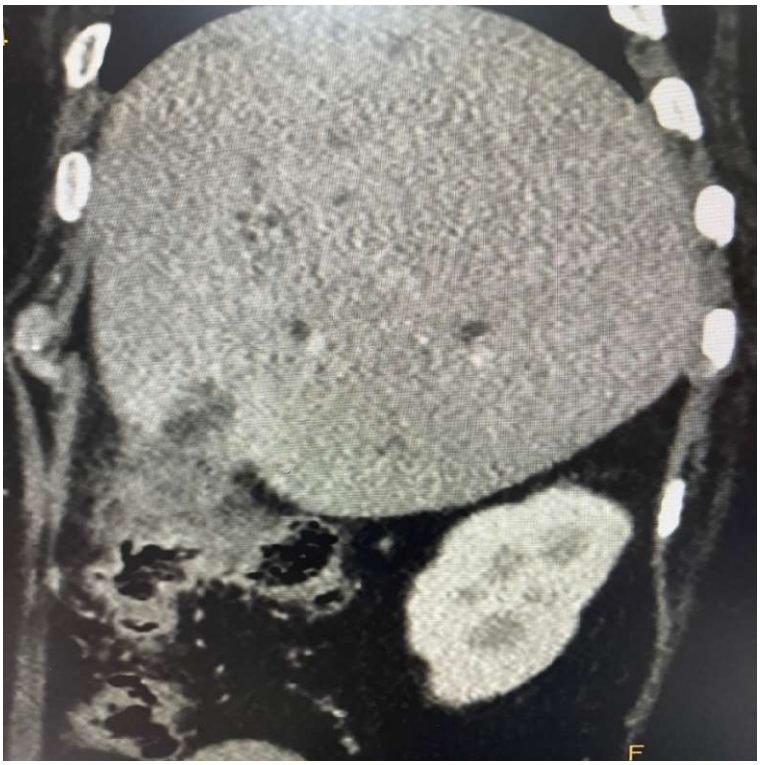


Fig. 2- CECT Abdomen Saggital Section Showing Heterogenously Enhancing Mass Lesion In Fundus of GB With Loss of Fat Planes with Hepatic Flexure of Colon.

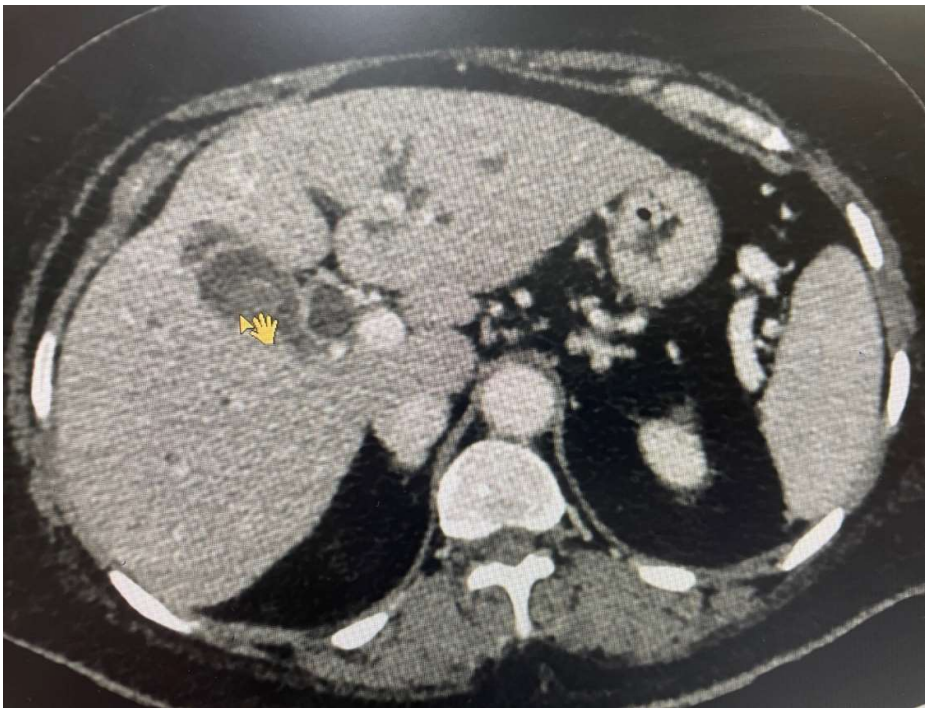


Fig. 3 – CECT Abdomen Showing Hyperdense Calculus In Gall bladder Lumen.

International Journal Dental and Medical Sciences Research
Volume 3, Issue 3, May - June 2021 pp 338-346 www.ijdmsrjournal.com ISSN: 2582-6018

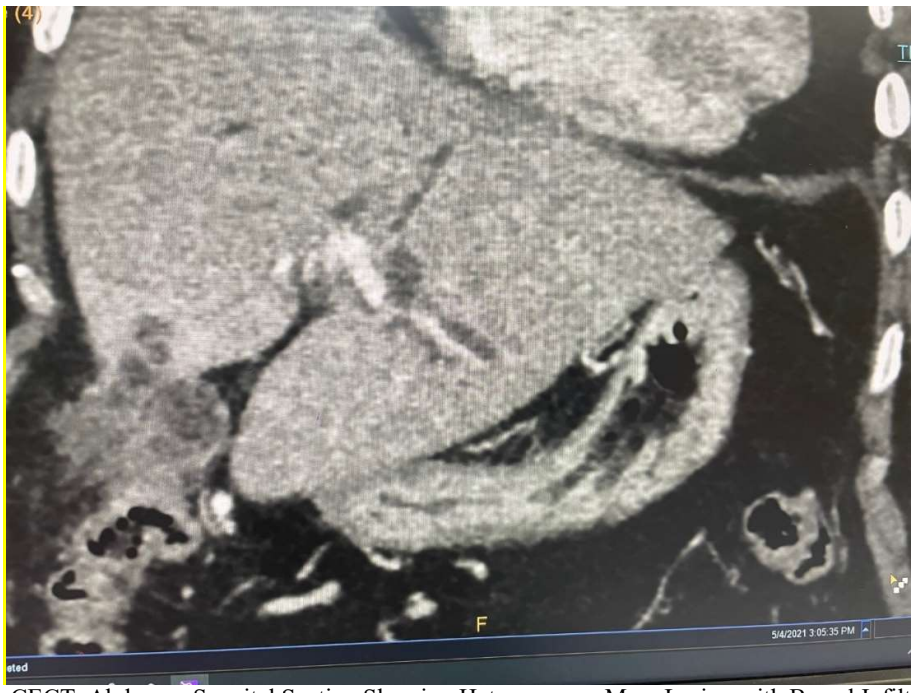


Fig. 4- CECT Abdomen Saggital Section Showing Heterogenous Mass Lesion with Bowel Infiltration.

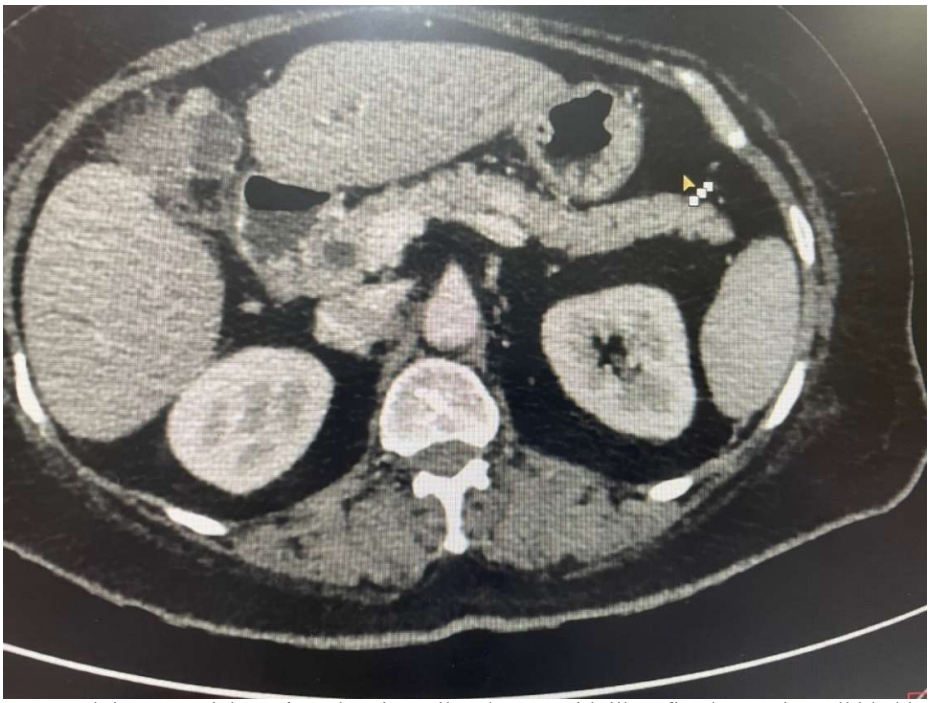


Fig. 5- CECT Abdomen Axial Section Showing Dilated CBD with ill Defined Mass in Gall bladder Fossa Showing Loss of Fat Planes With Adjacent Bowel.

International Journal Dental and Medical Sciences Research
Volume 3, Issue 3, May - June 2021 pp 338-346 www.ijdmsrjournal.com ISSN: 2582-6018

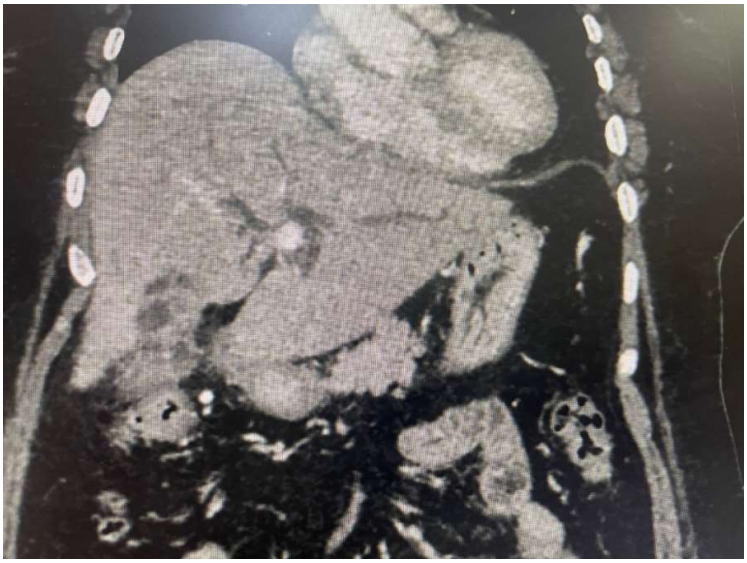


Fig. 6. - CECT Abdomen Coronal Section Showing Hypodense Locules Within The Mass.

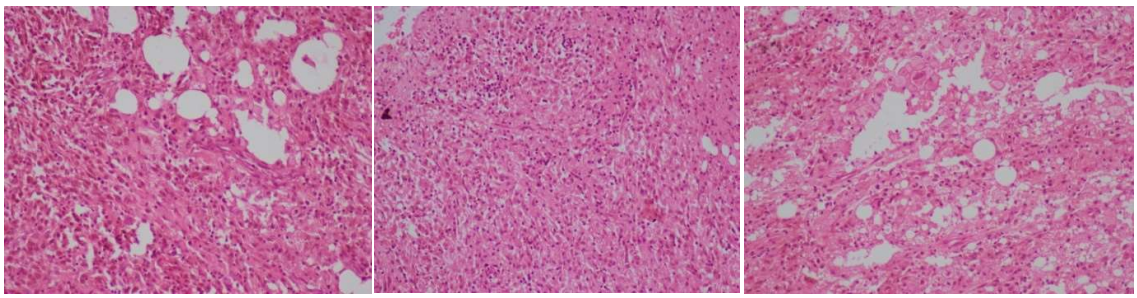
In view of suspected malignancy of gall bladder and non reduction in bilirubin levels despite ERCP and CBD stenting, the patient was taken up for Exploration, with a plan for Radical cholecystectomy.

At surgery, the intra-op findings were, the fundus of gall bladder was necrosed and attached to transverse colon. The remaining portion of GB wall was thickened and the serosa was surrounded by dense fibrous adhesions. Dissection between GB serosa and hepatic parenchyma was difficult leading to partial cholecystectomy. A large gall stone, approx 1.5 X 1.5 cm removed. Thick walled CBD was noted. CBD exploration was done and coiled stent in CBD was removed and a T-tube was inserted in CBD and fixed.

Post operatively, the patient recovered well with gradual reduction of bilirubin to 6.0 mg/dl in one week and to 4.0 mg/dl after two weeks.

Post operative CA-19-9 levels were reduced to 66.98 IU / ml after two weeks.

Histologically, gall bladder specimen showed, Xanthogranulomatous foci which were composed of abundant lipid laden histiocytes, lymphocytes, plasma cells, neutrophils, and fibroblasts, suggestive of Xanthogranulomatous cholecystitis (Figures – 7, 8, 9).



Figures – 7, 8, 9 - Microphotographs showing, Xanthogranulomatous foci which are composed of abundant lipid laden histiocytes, lymphocytes, plasma cells, neutrophils, and fibroblasts, suggestive of Xanthogranulomatous cholecystitis (Stain- Haematoxylin and Eosin, Magnification - X 200).

Postoperative T- tube cholangiogram reported as - bilobar IHBR adequately opacified. Duodenum bulb and small bowel loops were adequately opacified. Prominent CBD with T tube in situ.

The patient was discharged after three weeks from date of surgery, with T tube in situ, without any major complications. Subsequently, T tube removal was done without any events. At follow up after two months patient was doing well with significant reduction in jaundice.

III. DISCUSSION:-

Xanthogranulomatous cholecystitis (XGC) is an uncommon variant of chronic cholecystitis characterized by focal or diffuse severe inflammatory destruction of the gall bladder which may simulate malignancy radiologically and pathologically[8]. The incidence of XGC is variable and has been described among series of cholecystectomies to range between 0.7% - 10% [9].

Patients can present with features of acute cholecystitis (22%), chronic cholecystitis (88%), pain (95%), obstructive jaundice (22%), cholangitis (2%) and palpable mass (5%). On examination, a palpable mass or positive Murphy's sign can be localised. However, these clinical features are not specific for XGC and often no clinical difference between patients with XGC and carcinoma gall bladder can be found [9].

The xanthogranulomatous inflammation of the gallbladder can be very severe and can spill over to the neighboring structures like liver, bowel and stomach resulting in dense adhesions, perforation, abscess formation, fistulous communication with adjacent bowel [9].

Many studies have been performed investigating whether there are imaging findings that might permit differentiation of XGC from cancer, like diffuse gall bladder wall thickening, intramural "nodules" related to macrophage deposition, an intact gall bladder mucosa, and calculi [8, 11]. Preoperative diagnosis of XGC is often difficult, and an intra-operative frozen section examination may be required in selected cases to distinguish it from malignancy.

On Ultrasonography, presence of hypoechoic nodules or bands in the thickened wall can occasionally be seen, the presence of which is considered a characteristic finding of XGC. Hypoechoic nodules on sonography have been observed in 15% and 73% cases by Parra et al and Kim et al respectively. Hypoechoic band has been observed in around 19% cases of XGC. Xanthogranulomatous nodules behave as well-defined hypoechoic areas on sonography. Hypoechoic bands might be caused by a more generalized involvement of the mucosa. Complications like perforation, abscess and hepatic infiltration can also be seen on sonography[9].

Contrast enhanced computed tomography (CECT) scan, shows thickened gall bladder wall, hypodense band and homogeneous contrast enhancement of the mucosa. A continuous mucosal lining on CECT indicates that the mucosal surface overlying the lesion is intact and the lesion is intramural pointing towards a diagnosis of XGC.

Gallbladder carcinoma, however, shows absence or extensive disruption of the mucosal lining. Gallbladder wall thickening can range from 4.0 to 18.5 mm and is usually diffuse in nature [9].

A retrospective study by Goshima S et al[8], proposed five CT findings to differentiate both these entities which includes :

1) Diffuse gall bladder wall thickening;
2) Continuous mucosal line;
3) Intramural hypo-attenuated nodules;
4) Absence of macroscopic hepatic invasion; and
5) Absence of intra-hepatic bile duct dilatation.

They also reported intra-hepatic bile duct dilatation in 27.8% and extra-hepatic bile duct dilatation in 11.1% of patients with XGC, while these rates were 76.5% and 17.6% in patients with gallbladder tumors, respectively [8].

Dilatation of the biliary tract was observed in seven patients (8.9%) in another study [10].

Krishnani et al reported a significant association between gall bladder carcinoma and XGC (19.6% of cases). Although the exact mechanism underlying the association between the two conditions remains unclear, both are considered to be secondary to the chronic inflammatory process caused by cholelithiasis and / or cholecystitis [11].

The use of MRI in diagnosing XGC is limited. Chemical shift MRI helps classifying intramural nodules in the gall bladder wall [12]. Kang et al have concluded that the addition of DWI [Diffusion Weighted MRI] to conventional MRI improves discrimination between XGC and the wall thickening type of gallbladder cancer[13].

Sawada et al have described positive uptake of XGC on Fluorine -18 fluoro-deoxy-glucose positron emission tomography (^{18}F- FDG PET) scan, which again adds to the confusion. They have described the expression of GLUT-1 and GLUT-3 receptors in XGC to be the causative factor behind the false positive PET scan[14].

XGC may be clinically confused with carcinoma gall bladder due to the presence of inflammatory processes in neighboring organs and the release of serum Carbohydrate Antigen 19-9 (CA 19-9) levels[15, 16]. Cholestatic pathologies involved in the etiology of XGC are also thought to indicate elevated CA 19-9 levels. Although CA 19-9 value may increase in XGC patients, this may be due to the role of obstructive pathologies in the etiology. The increased presence of tumor markers such as CEA and CA 19-9 should raise suspicion of gallbladder cancer. Tumor markers are not very helpful in differentiating XGC from gallbladder carcinomas but may help in post operative follow-up. High serum CA 19.9 elevation may occur both in carcinoma and XGC.

However, CA 19.9 normalizes early after surgery for XGC whereas it remains high for a longer duration in gall bladder cancer [11].

Even though EUS-guided FNAC is a feasible and safe method for obtaining samples, its role in the diagnostic workup of gall bladder lesions remains undefined. While a positive FNAC confirms the diagnosis of GB cancer, a negative sample does not shed much light. The overall sampling adequacy is reported to be 86%. The accuracy of EUS FNAC for detecting malignancy and for the final diagnosis is approximately 93% and 80%, respectively. Sampling errors in the form of samples from non-representative areas along with a confounding factor of coexistence of XGC and GB cancer limit the widespread applicability of EUS-FNAC in XGC [17].

Intra-operative frozen section examination is another very valuable tool for differentiating XGC from malignancy and guiding optimum surgery when the xanthogranulomatous inflammation is confined to gallbladder and invasion of adjacent organs is not present. If Hematoxylin and Eosin frozen section examination is combined with immune-histochemistry it becomes much easier to differentiate XGC from gallbladder cancer peroperatively[18].

The best management of XGC is cholecystectomy and excision of Xanthogranulomatous tissue. When inflammation is localized to gall bladder the patients should be considered for laparoscopic cholecystectomy after an adequate patient selection, preoperative FNAC and an intra-operative frozen-section examination to rule out co-existing malignancy.

Cholecystectomy is the first choice for XGC, either complete or partial. Dissection should not proceed by force and the excision range should not be blindly extended in order to avoid injuries to the extra-hepatic bile duct and neighboring organs. Special attention should be paid to cases where internal fistula or Mirizzi syndrome is found and biliary injuries should be avoided.

Analysis of data from outside of China shows that in 65% of XGC cases, complete cholecystectomy was difficult and 35% of them underwent partial cholecystectomy[19].

In cases of XGC with extensive infiltration of adjacent organs, a radical resection of the mass is the only reasonable option because of the possibility of carcinoma associated with XGC.

Although XGC is a benign change of the GB with a low mortality rate, patients with XGC usually have a longer hospital stay than those with cholecystitis who undergo cholecystectomy and more postoperative complications, including leakage of bile, bile peritonitis, GB bleeding, hepatic abscess, infection of the incisional wound, and cholangitis stenosis. This is largely related to difficulty in stripping the GB, the mode of operation, and the physical condition of the patient [19].

XGC shows a yellow-brown lesion, well-demarcated foci of mural thickening with or without surface ulceration. Gallstones are present in most cases. The infiltrate can be focal, multinodular or diffuse. The overlying mucosa may show partial denudation or ulceration. Xanthogranulomatous foci are composed of abundant lipid laden histiocytes, lymphocytes, plasma cells, neutrophils, and fibroblasts. The xanthogranulomatous foci can infiltrate adjacent organs[20]. In literature, an association of bile duct carcinoma and XGC has also been reported. [11,21]. Macroscopically, it may be confused with bile duct carcinomas because it can be palpated as a hard mass on the bile duct. As all these findings may suggest malignancy originating from the bile duct, intra-operative frozen examination may be required for differential diagnosis[22].

Up to 25% of XGC can be diagnosed incorrectly, leading to inappropriate treatment such as inadequate surgery [9].

IV. CONCLUSION :-

To conclude, preoperative identification of XGC is important for proper surgical management of the patients. Although clinical features and radiological investigations may help, probably the only way to clearly differentiate XGC from malignancy is by intra-operative frozen section examination and immunohistochemistry on frozen sections.

In our case, the radiological investigations were suggestive of gall bladder mass probably malignant. Also, increased presence of tumor markers such as CA 19-9 –preoperatively, further raised suspicion of gallbladder cancer. Complete cholecystectomy was difficult in our case, so our patient underwent partial cholecystectomy. However, the recovery was good without any post operative complications. Also, level of Bilirubin and Tumor markers such as CA 19-9 was reduced significantly at post operative period.

Importance of XGC lies in the fact that it is a potential cause of confusion with gallbladder carcinoma on clinical and radiological evaluation and also, malignancy may co-exist with XGC in the same case [6, 23].

REFERENCES :-

[1]. P B S Kansakar, G Rodrigues, S A Khan. Xanthogranulomatous Cholecystitis: A Clinicopathological Study From A Tertiary Care Health Institution. Kathmandu University Medical Journal 2008;, 6.4, (24), 472-475.

[2]. Yang T, Zhang BH, Zhang J, Zhang YJ, Jiang XQ, Wu MC. Surgical Treatment Of Xanthogranulomatous Cholecystitis : Experience In 33 Cases. Hepatobiliary Pancreat Dis Int 2007; 6:504-8.

[3]. Sharma D, Babu R, Sood G, Kapoor G, Solanki RS, Thomas S. Xanthogranulomatous Cholecystitis Masquerading As Malignancy With Liver Metastasis. ANZ J Surg 2009 ; 79 : 946 -7.

[4]. McCoy JJ, Vila R, Petrossian G, McCall RA, Reddy KS. Xanthogranulomatous Cholecystitis. Report Of Two Cases. J S C Med Assoc. 1976;72:78-79. [PubMed]

[5]. Christensen AH, Ishak KG. Benign Tumors And Pseudotumors Of The Gallbladder. Report Of 180 Cases. Arch Pathol. 1970 ; 90 : 423 - 432. [PubMed]

[6]. Amazon K, Rywlin AM. Ceroid Granulomas Of The Gallbladder. Am J Clin Pathol. 1980 ; 73 : 123 - 127. [PubMed]

[7]. Lucas Souto Nacif, Amelia Judith Hessheimer, Sonia Rodríguez Gómez, Carla Montironi, Constantino Fondevila. Infiltrative Xanthogranulomatous Cholecystitis Mimicking Aggressive Gallbladder Carcinoma: A Diagnostic And Therapeutic Dilemma. World J Gastroenterol 2017; 23 (48) : 8671-8678. doi PMID: 29358875.

[8]. Goshima S, Chang S, Wang JH, Kanematsu M, Bae KT, Federle MP. Xanthogranulomatous Cholecystitis: Diagnostic Performance Of CT To Differentiate From Gallbladder Cancer. Eur J Radiol 2010;74:e79-83.

[9]. Vaibhav Singh , S Rajesh , Chhagan Bihari, Saloni Desai , Sudheer Pargewar , Ankur Arora. Xanthogranulomatous Cholecystitis: What Every Radiologist Should Know. World J Radiol 2016; 8(2)183-91.

[10]. Ahmet Gokhan Saritas , Mehmet Onur Gul, Zafer Teke , Abdullah Ulku , Ahmet Rencuzogullari , Ishak Aydin, Atilgan Tolga Akcam. Xanthogranulomatous cholecystitis: a rare gallbladder pathology from a single-center perspective. Annals of Surgical Treatment and Research Ann Surg Treat Res 2020; 99 (4) : 230-237

[11]. Krishnani N, Dhingra S, Kapoor S, Pandey R. Cytopathologic Diagnosis Of Xanthogranulomatous Cholecystitis And Coexistent Lesions. A Prospective Study Of 31 Cases. Acta Cytol 2007; 51:37 – 41.

[12]. Feng Zhao , Pu-Xuan Lu, Sen-Xiang Yan, Gao-Feng Wang, Jing Yuan, Shi-Zheng Zhang, Yi-Xiang J Wang. CT And MR Features Of Xanthogranulomatous Cholecystitis: An Analysis Of Consecutive 49 Cases. Eur J Radiol 2013 ; 82 : 1391 -7.

[13]. Kang TW, Kim SH, Park HJ, Lim S, Jang KM, Choi D, Lee SJ. Differentiating Xanthogranulomatous Cholecystitis From Wall Thickening Type Of Gallbladder Cancer: Added Value Of Diffusion Weighted MRI. Clin Radiol 2013; 68: 992-1001.

[14]. Sawada S, Shimada Y, Sekine S, Shibuya K, Yoshioka I, Matsui K, Okumura T, Yoshida T, Nagata T, Uotani H, Tsukada K. Expression Of GLUT-1 And GLUT-3 In Xanthogranulomatous Cholecystitis Induced A Positive Result On 18F-FDG PET: Report Of A Case. Int Surg 2013; 98: 372-378.

[15]. J Yoshida , K Chijiiwa, H Shimura, K Yamaguchi, N Kinukawa, H Honda, M Tanaka. Xanthogranulomatous Cholecystitis Versus Gallbladder Cancer: Clinical Differentiating Factors. Am Surg. 1997; 63 (4) : 367 –371.

[16]. Y Adachi , Y Iso, M Moriyama, T Kasai, H Hashimoto. Increased Serum CA 19-9 In Patients With Xanthogranulomatous Cholecystitis.Hepatogastroenterology.1998; 45 (19) : 77 – 80.

[17]. Ashwin Rammohan, Sathya D. Cherukuri, Jeswanth Sathyanesan, Ravichandran Palaniappan, and Manoharan Govindan. Xanthogranulomatous Cholecystitis Masquerading as Gallbladder Cancer: Can It Be Diagnosed Preoperatively? Gastroenterology Research and Practice 2014, Article ID 253645, 5 pages http://dx.doi.org/10.1155/2014/253645 Hindawi Publishing Corporation .

[18]. U Kämmerer , M Kapp, A M Gassel, T Richter, C Tank, J Dietl, P Ruck. A New Rapid Immunohistochemical Staining Technique Using The Envision Antibody Complex. J Histochem Cytochem 2001 ; 49 : 623 - 30.

[19]. Guzman-Valdivia G. Xanthogranulomatous Cholecystitis In Laparoscopic Surgery. J Gastrointest Surg 2005 ; 9(4): 494-497.

[20]. Archana Rastogi, Deepak Kumar Singh, Puja Sakhuja, Ranjana Gondal. Florid Xanthogranulomatous Cholecystitis Masquerading As Invasive Gallbladder Cancer Leading To Extensive Surgical Resection. Indian Journal of Pathology and Microbiology. 2010 ; 53 (1) : 144-7.

[21]. Hyo Sup Lee , Kwang Ro Joo, Do Ha Kim, Neung Hwa Park, Yoong Ki Jeong, Jae Hee Suh, Chang Woo Nam. A Case Of Simultaneous Xanthogranulomatous Cholecystitis and Carcinoma of The Gall bladder. Korean J Intern Med. 2003. 18 : 53–56.

[22]. Ling-Fu Zhang , Chun-Sheng Hou, Jian-Yu Liu, Dian-Rong Xiu, Zhi Xu, Li-Xin Wang, Xiao-Feng Ling. Strategies For Diagnosis of Xanthogranulomatous Cholecystitis Masquerading As Gallbladder Cancer. Chinese Medical Journal 2012; 125, (1) , 109–113.

[23]. Natori S, Takimoto A, Endoh K, Ishikawa T, Yamaguchi S, Fjii Y, Takahashi T, Takeda K, Watarai S, Nakano A, et al. A Case Of Xanthogranulomatous Cholecystitis Difficult To Be Differentiated From Gallbladder Cancer. Tann To Sui. 1997;18:593–596.