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Rare disease

Gallbladder malakoplakia in type 2 diabetes mellitus: a rare entity

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Summary

Gallbladder malakoplakia in type 2 diabetes mellitus is a rare condition. Differentiating malakoplakia, which is a more aggressive disease condition with possible genetic abnormality from a more benign but closely related condition such as xanthogranulomatous cholecystitis, is of prognostic importance in postoperative patient management and follow-up.

BACKGROUND

Gallbladder (GB) malakoplakia is a rarely seen condition. Although it is morphologically closely related to xanthogranulomatous cholecystitis, postoperative disease process differs significantly between the two. Malakoplakia is a disease condition with more aggressive behaviour, which requires further specific antibiotic chemotherapeutic administration and ascorbic acid in order to prevent development of postoperative complications such as disease recurrence and fistulising lesion.

CASE PRESENTATION

A 45-year-old woman, a known patient of type 2 diabetes mellitus, presented with a history of dull aching pain in the right hypochondrium for 2 months associated with loss of appetite and weight. Abdominal examination showed vague palpable non-tender mass in the right hypochondrium with no other palpable mass. She did not have any significant history relating to the present problems such as pain, jaundice or postprandial discomfort. She had two living young sons and her menstrual history was normal. There was no significant family history that relates to present symptomatology except that her mother also has type 2 diabetes mellitus, which is under control with no complications.

INVESTIGATIONS

She had haemoglobin of 11.4 g/dl with normal leucocytic counts. Liver and renal function tests were within normal range except for mildly increased serum alkaline phosphatase (127 U/l). Fasting blood sugar level and haemoglobin A1C was 149 mg/dl and 12.5%, respectively. Ultrasonography of the abdomen showed hypoechoic areas adjacent to GB fossa in the liver and with liver span of 16 cm, GB wall was thicken, cavity contained a 2-cm-sized stone. Contrast-enhanced CT of the abdomen showed circumferential mural thickening of GB with fat stranding infiltrating into hepatic flexure of the colon and an intramural hypodensity.

DIFFERENTIAL DIAGNOSIS

- GB mass possibly carcinoma GB.

TREATMENT

Clinically a possibility of GB carcinoma was considered. She was subjected to exploratory laparotomy with extended cholecystectomy and en-bloc segmental colectomy. Her immediate postoperative period was non-eventful. She was given broad-spectrum antibiotics.

Grossly, the specimen was composed of 7 cm long GB and wedge of the liver measuring 6×6×5 cm^3 and colon measuring 10 cm in length. GB was grossly enlarged and dilated cavity containing a mixed stone measuring 2 cm in diameter (figure 1). Mucosa was diffusely congested with large ulcers. The thickened wall was firmly adherent to the transverse colon. Many peridochal lymph nodes measuring ~1.5 cm size were identified. Microscopy showed diffuse mucosal ulceration with transmural fibrosis and heavy mixed inflammatory cell infiltration comprising of histiocytes, lymphocytes, plasma cells, eosinophils and neutrophils (figure 2). Foreign body giant cells, epithelioid cell histiocytes, cholesterol clefts and bile pigment could also be identified. Inflammation was seen infiltrating liver

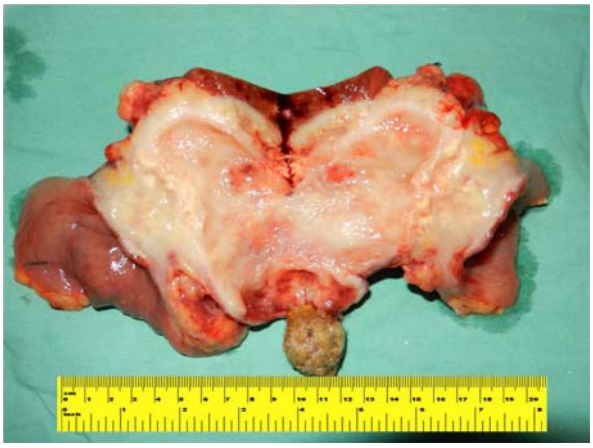

Figure 1 Cut-open specimen of the gall bladder (GB) showing grossly dilated GB with congested mucosa, thicken and fibrotic wall and a cholesterol stone within the lumen.

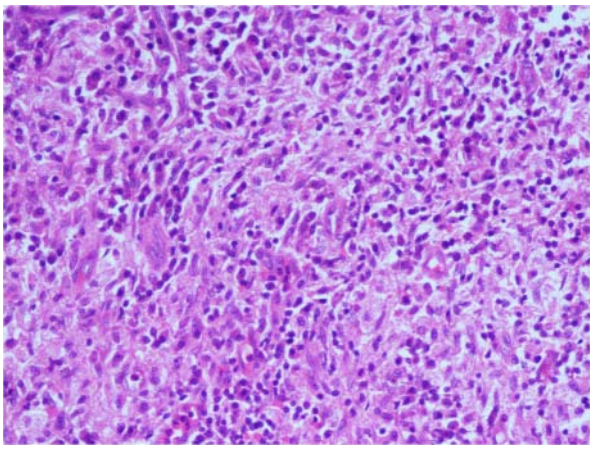

Figure 2 Medium-power photomicrograph showing sheets of macrophages intermixed with other types of inflammatory cells and scattered myofibroblastic cells (H&E, ×250).

capsule and colonic wall with preserved colonic mucosa. There were many PAS (periodic acid Schiff) positive round to oval globular structures within and outside histiocytes (figure 3), which showed positive staining for iron pigment and calcium on Perl's and von Kossa stainings (figure 4). Sections of the lymph nodes showed reactive changes in the form of sinus histiocytosis and lymphoid follicular hyperplasia. The final histological diagnosis was malakoplakia of the GB. The patient was treated with additional medicines such as trimethoprim-sulfamethoxazole, bethanechol and ascorbic acids.

OUTCOME AND FOLLOW-UP

Follow-up at 6 month postoperative, the patient is symptom free and her diabetes is under control.

DISCUSSION

Malakoplakia is a rare chronic granulomatous inflammatory disorder first described in 1902 by Michaelis and Gutman.[1] The name (Greek, *malakos* means soft and *plakos* means plaque) is derived from the characteristic gross appearance of the soft yellow-brown plaques or nodules.

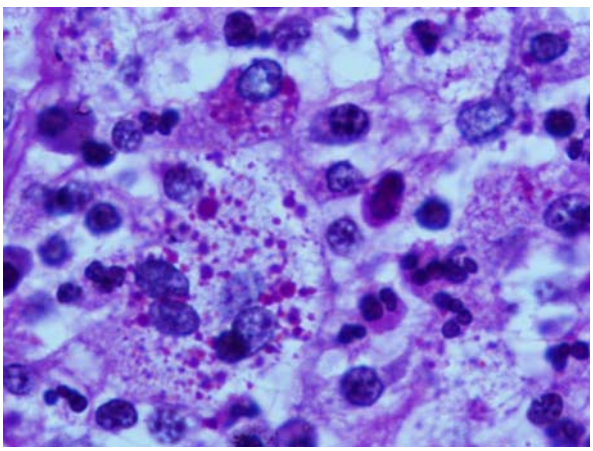

Figure 3 High-power photomicrograph to highlight the round to oval intracytoplasmic periodic acid Schiff-positive granules (PAS, ×500).

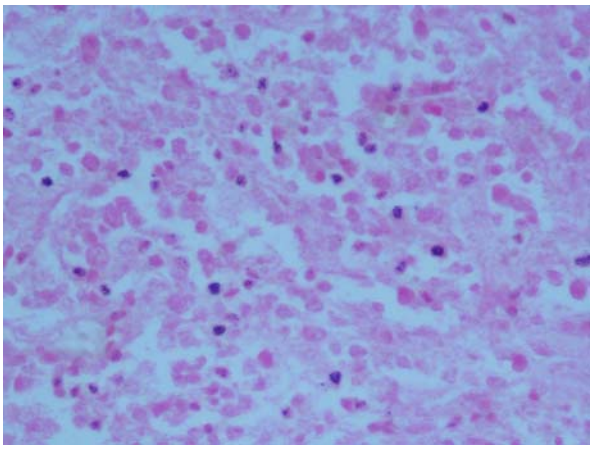

Figure 4 High-power photomicrograph to show the blackish round to oval von Kossa-positive calcified spherules (von Kossa, ×500).

Histologically, it is characterised by the presence of sheets of histiocytes with granular cytoplasm (von Hansemann cells) admixed with intracellular and extracellular basophilic round to oval inclusions known as Michaelis-Gutmann bodies in a background of mixed inflammatory cell infiltration. Urinary tract is the most common site followed by gastrointestinal tract. Importance of identifying this condition is due to high disease recurrence with fistulisation.[2] It has been observed with various immune compromised states and defective macrophage function exhibiting defective phagolysosomal activity.[3 4] The hypothetical aetiology for the defective macrophage function is the result of decreased intracellular cyclic guanosine monophosphate (cGMP) level interfering with microtubular function and lysosomal activity resulting in incomplete elimination of bacteria.[3] Accumulated partially digested bacteria within the macrophages lead on to deposition of calcium and iron on residual bacterial glycolipid resulting in the formation of basophilic round to oval intracytoplasmic and extracytoplasmic structures known as Michaelis-Gutmann bodies, which is considered pathognomic for malakoplakia. Till date, there are only eight case reports of GB malakoplakia and none of them had association with the known risk factors.[5–10]

Development of malakoplakia in chronic cholecystitis could be in the background of otherwise a typical xanthogranulomatous cholecystitis, which is thought to result due to unsuccessful phagocytosis of the bile material.[5 6 10] Another important implicated hypothesis is a defective immune regulatory system resulting in an impairment of mononuclear phagocytosis and lysosomal hydrolytic functions observed in alcohol abuse, malnutrition, postorgan transplant, intake of certain drugs such as steroids or cytotoxic agents, malignancy and chronic diseases such as diabetes mellitus, autoimmune disease and sarcoidosis.[2 7] The index patient is a known type 2 diabetes mellitus and diabetes per se is a condition that associates with compromised macrophage function including phagocytotic activity.[11] Although malakoplakia is considered as a benign pathological process that requires local excision but it has been observed that many of these cases have aggressive disease process including high disease recurrence with fistulisation and partial or failure to respond to antibiotics.[11–13] More

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specific therapy with antibiotics that concentrate in macrophages such as quinolone, trimethoprim-sulfamethoxazole, is associated with a high cure rate. Bethanechol, a choline agonist, has been used in combination with antibiotics and surgery with the concept that Bethanechol may correct the decreased cGMP levels that are believed to interfere with complete bacterial killing.[13] Ascorbic acid has been in used to increase the cGMP and cyclic AMP levels in monocytes, which may represent an effective strategy for therapy, though it is under trial.[4]

To conclude, the importance of identifying more aggressive GB malakoplakia from self-limited xanthogranulomatous cholecystitis lies in the basic difference in postoperative management and follow-up protocol. Moreover, the malakoplakia patient will require a totally different chemotherapeutic regime for an effective disease outcome.

Learning points

- Gall bladder (GB) malakoplakia needs to be differentiated from more commonly seen and benign condition such as xanthogranulomatous cholecystitis.
- Initiating factor for GB malakoplakia may not be the usual kind of bacteria, but it could be undigested bile acids in a genetically predisposed individual.
- Chronic debilitating condition such as type 2 diabetes mellitus may be an important underlying aetiology for macrophage dysfunction.
- Postoperative management requires the specific therapy with a mandatory close follow-up.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Dasgupta P,** Womack C, Turner AG, *et al*. Malacoplakia: von Hansemann's disease. *BJU Int* 1999;**84**:464–9.
2. **Yousef GM,** Naghibi B. Malakoplakia outside the urinary tract. *Arch Pathol Lab Med* 2007;**131**:297–300.
3. **van Crevel R,** Curfs J, van der Ven AJ, *et al*. Functional and morphological monocyte abnormalities in a patient with malakoplakia. *Am J Med* 1998;**105**:74–7.
4. **Biggar WD,** Keating A, Bear RA. Malakoplakia: evidence for an acquired disease secondary to immunosuppression. *Transplantation* 1981;**31**:109–12.
5. **Hanada M,** Tujimura T, Kimura M. Cholecystic granulomas in gallstone disease. *Acta Pathol Jpn* 1981;**81**:221–31.
6. **Charpentier P,** Prade M, Bognel C, *et al*. Malacoplakia of the gallbladder. *Hum Pathol* 1983;**14**:827–8.
7. **Hide G,** Desai S, Bloxham CA. Malakoplakia of the gall-bladder: imaging and histological features. *Clin Radiol* 2001;**56**:326–8.
8. **Agnarsdottir M,** Willen R, El Hag IA. Three cases of malacoplakia of gallbladder. *Ups J Med Sci* 2004;**109**:255–9.
9. **Sengupta S,** Bucchanan M, Danne P. Malakoplakia of the gall-bladder. *Ind J Surg* 2005;**67**:156–8.
10. **Di Tommaso L,** Arizzi C, Roncalli M. Malacoplakia of the gallbladder. *Histopathol* 2005;**46**:474–5.
11. **Maruyama K,** Asai J, Ii M, *et al*. Decreased macrophage number and activation lead to reduced lymphatic vessel formation and contribute to impaired diabetic wound healing. *Am J Pathol* 2007;**170**:1178–91.
12. **Muguti GI,** Gwavava NJ. Malakoplakia of the small intestine as a cause of enterocutaneous fistula. *Cent Afr J Med* 1991;**37**:333–6.
13. **Webb M,** Pincott JR, Marshall WC, *et al*. Hypogammaglobulinaemia and malakoplakia: response to bethanechol. *Eur J Pediatr* 1986;**145**:297–302.