Myelofibrosis presenting as chronic cholecystitis

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Abstract

A 61 year old man presented with abdominal pain typical of chronic cholecystitis of one month's duration. Pallor was noted on examination and investigation uncovered myelofibrosis and a small gallstone. Cholecystectomy relieved the pain and pathological examination of the gall bladder showed widespread myeloid metaplasia. This is the first reported case of myelofibrosis presenting as chronic cholecystitis.

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Keywords: Myelofibrosis, myeloid metaplasia, gall bladder, chronic cholecystitis, pain.

Myelofibrosis is normally a chronic haematological disorder of the elderly characterised by anaemia, weight loss, anorexia, and fever. Fibrosis, abnormal haemopoiesis and increased megakaryocytes are seen in the bone marrow. Extramedullary haemopoiesis causing hepatosplenomegaly is common and tumours composed of abnormal myeloid tissue may arise. The latter are frequently located in the retroperitoneum, pelvis, mesentery, and pleura and rarely in lymph nodes and skin.¹ We report a rare case of myelofibrosis producing myeloid metaplasia of the gall bladder and presenting with features of chronic cholecystitis.

Case report

A 61 year old man presented with a one month history of upper abdominal pain. The pain occurred approximately three times a week and lasted from 30 minutes to two hours. It was associated with nausea and flatulence, and precipitated by fatty foods. On examination, he was pale and had mild epigastric tenderness. There were no abdominal masses and neither the liver nor spleen was palpable. Ultrasound examination revealed a small gallstone in the gall bladder. Endoscopy of the upper gastrointestinal tract, liver and bone biochemistry and serum amylase were normal. Full blood count showed a haemoglobin concentration of 9.4 g/dl, platelet count of $95 \times 10^{12}/l$, and a white cell count of $1.7 \times 10^9/l$. The blood film was normal. A bone marrow aspirate was scanty, but contained increased megakaryocytes and myelofibrosis was diagnosed on examination of a bone marrow trephine biopsy specimen. The bone marrow was hypocellular and fibrotic with immature erythroid and myeloid precursors, clusters of dysplastic megakaryocytes, and increased reticulin fibres.

The patient's abdominal pain persisted and, five months later, he underwent laparoscopic

cholecystectomy. At surgery, the gall bladder was thickened and adherent, and contained a single mixed gallstone measuring 0.5 cm. The spleen was greatly enlarged. One month after surgery, the patient had no abdominal pain but required regular blood transfusions. After two months, he developed acute myeloid leukaemia, severe ascites and thrombosis of the left internal jugular vein. The ascitic fluid contained neutrophils, immature myeloid and erythroid cells, blast-like cells, megakaryocytes, lymphocytes, and mesothelial cells. The patient deteriorated rapidly and died four months after surgery. There was no necropsy.

Pathology

An opened gall bladder, measuring $7 \times 2.5 \times 1.5$ cm, was submitted for pathological examination and fixed in 10% buffered formalin. A few adhesions were present and the mucosal surface was unremarkable. The gall bladder wall was diffusely thickened and grey, measuring 0.4 to 0.6 cm in depth. Histological examination of the neck, body and fundus revealed extensive myeloid metaplasia. This completely replaced the normal lamina propria and adventitia, and extended between smooth muscle bundles in the muscularis. Epithelium and smooth muscle were spared. The infiltrate was composed mainly of immature myeloid and erythroid cells, with dysplastic megakaryocytes, often forming small clusters (fig 1). The fibrous stroma was rich in reticulin fibres. The appearances were similar to those in the bone marrow trephine biopsy specimen. Immunostaining for CD68 (Dako, High Wycombe, UK; 1:50) and factor VIII (Dako; 1:50) confirmed the presence of immature myeloid cells and megakaryocytes, respectively. Immunostaining for CAM 5.2 (Becton Dickinson, San Jose, California, USA; 1:1), vimentin (Dako; 1:100),

Figure 1 Megakaryocytes in the adventitia immunostained by factor VIII. (Immunoperoxidase, $\times 40$.)

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desmin (Dako; 1:100), and S100 protein (Dako; 1:500) was negative. Leucocyte common antigen (Dako; 1:50) stained a few lymphocytes within the abnormal myeloid tissue.

Discussion

The patient had upper abdominal pain characteristic of chronic cholecystitis which responded to cholecystectomy. This implies the pain was originating from the gall bladder; no other source of pain was identified. Myeloid metaplasia or the small gallstone, or both, may have caused the pain. Myeloid metaplasia may have been the sole cause of pain as many gallstones are asymptomatic² and there were no histological features of chronic cholecystitis. The gall bladder is rarely biopsied in patients with myelofibrosis and asymptomatic myeloid metaplasia could occur commonly. Thickening of the gall bladder wall can be seen in acute and chronic leukaemia.³

The histological diagnosis was relatively straightforward because of the history of myelofibrosis. Without this knowledge, the presence of a pleomorphic infiltrate containing atypical giant cells may have produced an incorrect diagnosis of malignancy. One distinctive feature was that only fibrous tissue was infiltrated and the epithelium and smooth muscle were spared. Also, there was little mitotic activity. Immunohistochemical stains confirmed

the correct diagnosis and excluded other possibilities.

As far as we know, there is only one other reported case of myeloid metaplasia of the gall bladder.⁴ This occurred in a 71 year old woman with myelofibrosis for 14 weeks, who presented with clinical features of acute cholecystitis. Cholecystectomy was performed and two weeks later she developed acute leukaemia and a pleural effusion containing myeloid cells. She died six weeks after surgery. Unlike this case, "cholecystitis" followed the diagnosis of myelofibrosis, gallstones were not present and there was an acute presentation. In both cases symptomatic involvement of the gall bladder was quickly followed by leukaemic transformation, serous effusions and death. There were similar pathological changes in both gall bladders.

In summary, this is the first reported case of myelofibrosis presenting with features of chronic cholecystitis.

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Review of clinical activity by microbiologists

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Abstract

A data form was devised and used to collect information on clinical cases involving a microbiologist. From the results a relational database management system was created. Of a total of 280 interventions, 137 (49%) were proactive, and in 118 (86%) of these cases the advice given was accepted. The majority of the patients in these cases showed subsequent improvement. Of all the interventions, the given advice was acted upon in 235 (84%), in 22 (8%) it was not and for the remainder this information was not available. This study was a simple method of gaining information on the clinical involvement of the microbiology department of a large city hospital. It provides a reference point from which further research and audit can be based.

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It is difficult to separate the various components of a medical microbiologist's activities. One "diary exercise"¹ of a single-handed microbiologist in a district general hospital suggested that approximately one third of the time was spent on each of infection control, clinical activity and laboratory management. Activity in infection control is known to be cost effective² but it is harder to show benefit of outcome in clinical activity. This study was designed to determine to what extent microbiologists are involved in the management of clinical cases, and additionally whether their actions actually influence patient outcome.

Methods

A data form (fig 1) was devised and information gathered over a 10 week period. The microbiology department provides a service to its own hospital of approximately 1000 beds, several smaller outlying hospitals, and local general practitioners (GPs). The GP workload is