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CASE REPORT

Small bowel perforation secondary to intestinal tuberculosis in patient with chronic idiopathic myelofibrosis

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Idiopathic myelofibrosis is a myeloproliferative disorder in which blood cell development is abnormal. It causes scarring and fibrotic changes in the bone marrow. Also known as primary myelofibrosis (PMF), this condition is usually chronic and progressive. The exact causative factor is not clear but scientists found that the condition is typically characterized by the mutations in Janus Kinase 2(JAK2) gene. Clinical features of PMF include progressive anemia, symptomatic splenomegaly, and other constitutional symptoms. PMF is associated with a poor prognosis and a marked reduction in life expectancy, with median survival ranging from 3.5 to 6 years. There have been reports on the coexistence of PMF with other granulomatous diseases such as tuberculosis. It was reported that the incidence of tuberculosis is much higher in patients having PMF compared to the normal population. PMF is commonly treated with JAK2 inhibitor (Ruxolitinib) and prednisolone. Several case reports have shown that PMF treatment may lead to opportunistic infections, such as tuberculosis. We would like to report a case of small bowel tuberculosis flare-up by patients of chronic idiopathic myelofibrosis that leads to bowel perforations.

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Introduction

Idiopathic myelofibrosis is a clonal hematopoietic stem cell disorder due to a mutation in the signaling regulator gene JAK2. The condition is widely treated with Ruxolitinib which is a JAK2 inhibitor along with prednisolone. The only curative treatment available till now is allogeneic haematopoietic stem cell transplant.[1] Ruxolitinib with prednisolone despite promising has been linked with the risk of opportunistic infections and reactivation of tuberculosis.[2]We herein report a patient with chronic idiopathic myelofibrosis who developed small bowel perforations secondary to the flare-up of gut tuberculosis.

Case report

A 57-year-old Malay ethnicity male which was diagnosed with primary myelofibrosis since 2014 and under regular haematology follow up was referred to the general surgery department for acute onset of generalized abdominal pain. The patient has an underlying history of Pulmonary Tuberculosis (TB) and has completed treatment about ten years ago. He claimed that he was on anti TB drugs for about six months and was tested negative after completion of the therapy. The rest of the family members were screened negative otherwise. The patient gave a history of loss of weight and appetite with persistent lethargy and poor oral intake for the past two months. He has been receiving treatment from the haematology department ever since he was diagnosed with PMF. His JAK2 status was negative while the peripheral blood film showed borderline bicytopaenia with leucoerythroblastic picture and occasional suspicious mononuclear cells. Bone marrow trephine biopsy confirmed the diagnosis of myelofibrosis (in cellular phase). The patient arrived at the emergency department with signs of hypotension and prompt resuscitation measures were taken while arrangement for an urgent chest and abdominal x-rays were ongoing. The initial chest x-ray showed air under the diaphragm and the patient was rushed to the operating room with the diagnosis of perforated gastric ulcer (Figure 1). Upon entering the abdomen noted that there were copious collections with small bowel adhesions especially at the ileum (Figure 2). A segment of the small bowel (ileum) was noted to have multiple perforations (three perforations each measuring 2-4mm in diameter) with content leakage. Segmental bowel resection (about 10cm in length), double-barrel stoma with peritoneal lavage was performed. The peritoneal collections were sampled for culture and sensitivity and acid-fast staining. Resected bowel segment HPE came out as perforated granulomatous ileitis secondary to mycobacterium infection (figure 3 and 4). Peritoneal fluid acid-fast staining showed negative for Mycobacterium while the culture and sensitivity showed mixed growth. The patient was subsequently started on anti-TB medications and was put under direct supervision therapy. With our latest follow up, the patient was doing well with no further complications since the operation.

Figure 1 CXR showed presence of pneumoperitoneum

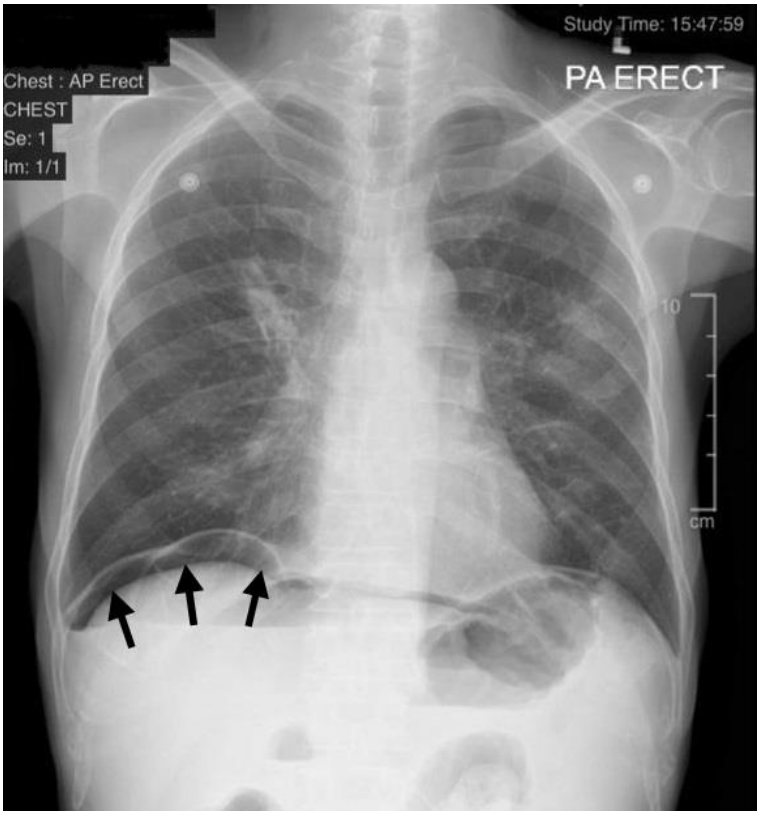


Figure 2 Laparatomy findings of small bowel adhesions

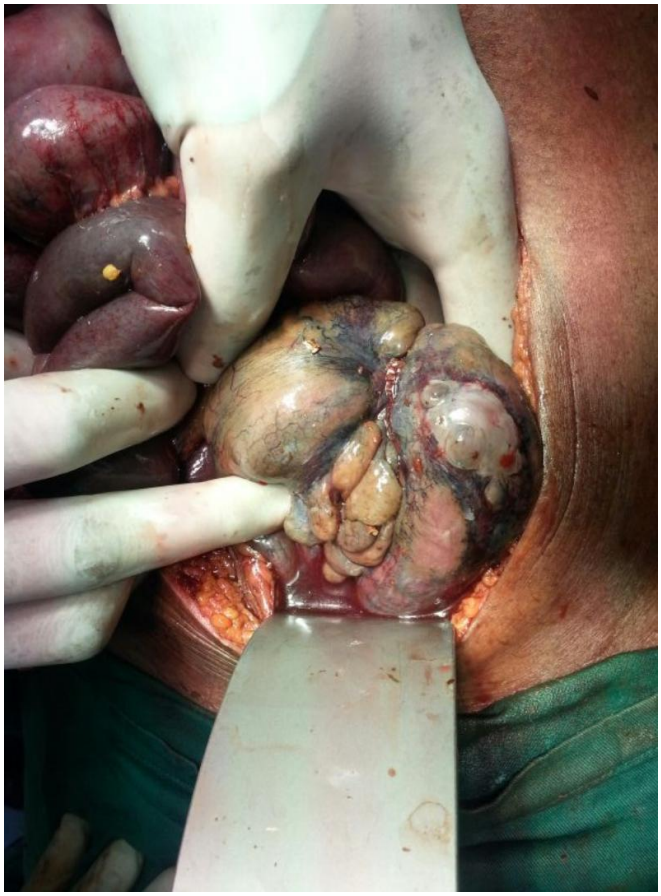


Figure 3 (Hematoxylin and eosin, 40x magnification) showing granuloma formation composed of epithelioid cells (arrowhead) with oval to elongated nuclei and abundant eosinophilic cytoplasm, surrounded by mature lymphocytes and histiocytes collection. Langerhans cells are also seen (circle) and central caseous necrosis (arrow).

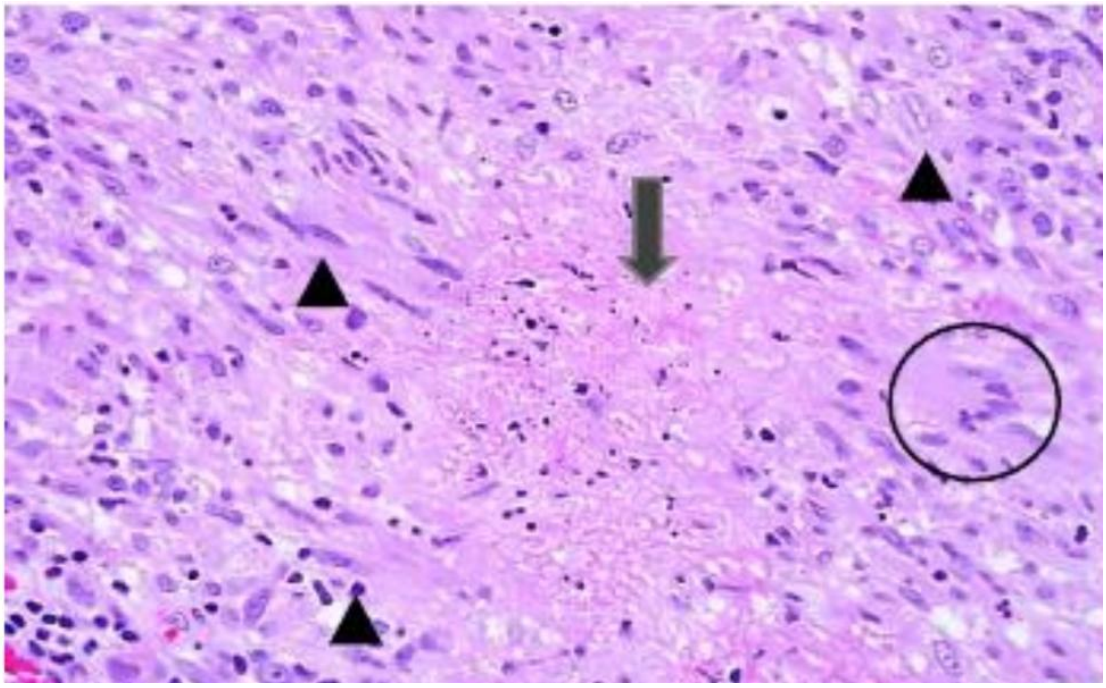
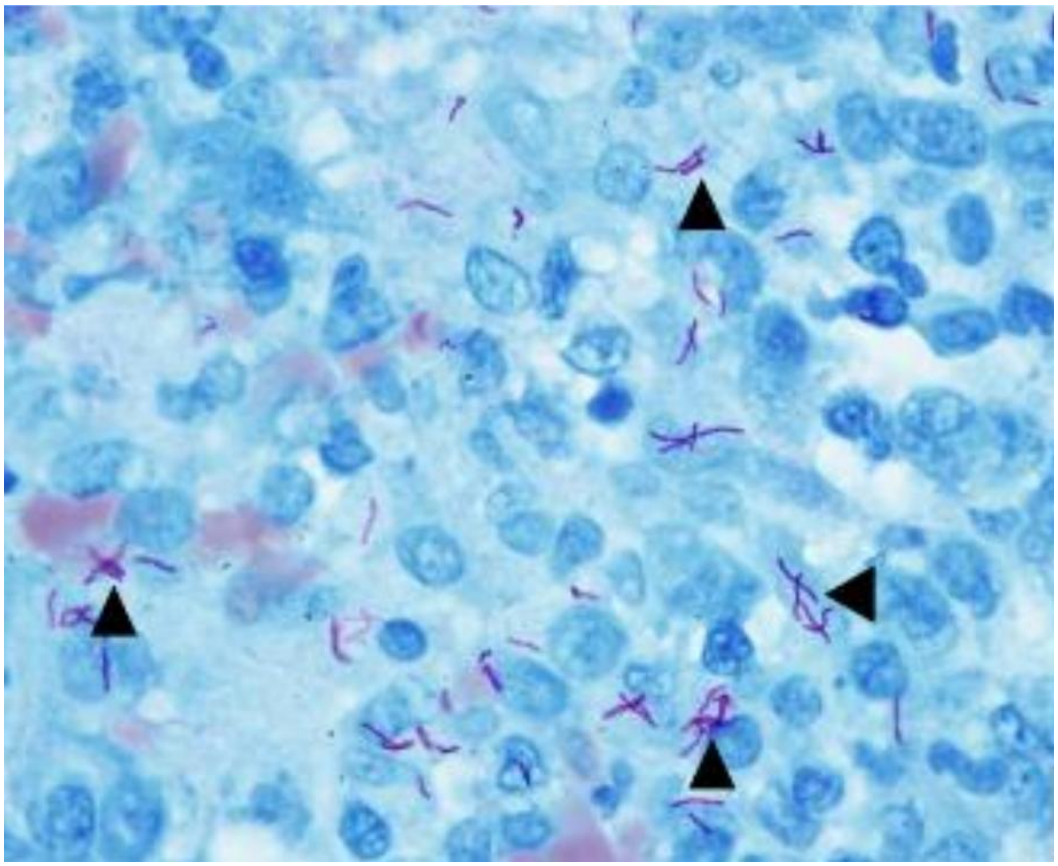


Figure 4 (Ziehl- Neelsen staining 100x magnification) Numerous scattered magenta coloured, beaded acid fast bacilli (AFB, arrowhead) is seen in between the cells



Discussion

Primary Myelofibrosis is a myeloproliferative monoclonal disorder characterized by extensive bone marrow fibrosis. Till the present day, treatment for PMF is using Ruxolitinib, a JAK 2 inhibitor along with other newer drugs.[3-4] Curative treatment is by using allogeneic haematopoietic stem cell transplant with a five-year survival rate.[5] Nonetheless, treatment for PMF has been linked with the risk of weakening host immunity and opportunistic infections.[6] Tuberculosis is a granulomatous infection with the hallmark of caseating necrosis that can be found in both pulmonary and extra pulmonary regions. The case that we encountered showed that patients with PMF on treatment have a high probability to get a flare-up of tuberculosis be it pulmonary or extra pulmonary. Despite being JAK2 negative, the patient has been prescribed with long term steroids since 2014 by the haematology unit. He was offered with allogenic stem cell bone marrow transplant which the patient refused. Asymptomatic patients usually do not need treatment. Treatment is subjected to patients to improve their quality of life and to manage the ongoing complications. We would like to establish a link between PMF and TB and the potential flare-up of tuberculosis that might occur in such patients.[7] Interestingly extra pulmonary tuberculosis flare-up in PMF has never been reported before. The coexistence of PMF and TB has been documented decades ago.[8] Besides myeloproliferative disease itself, the treatment may potentiate granulomatous infection in the host. As per this case, the patient has a history of pulmonary TB some ten years ago. It is well known that mycobacterium may remain dormant for many years in the host before reactivation.[9] We would also like to highlight the importance of strengthening the host immunity once been diagnosed with myeloproliferative disease. As per today, the only curative treatment available is allogeneic stem cell bone marrow transplant.[10] The patient in this case succumbed to the complications of extra pulmonary tuberculosis flare up secondary to the myeloproliferative disease and its treatment. It is a challenge to the treating physician as well as to the patient diagnosed with myeloproliferative disease to endure the uncertainty of the course of the disease. With the reported case above, we should be vigilant in dealing with patients with myeloproliferative disease and the complications of the current treatment modalities and definitely to be aware of tuberculosis flare up both pulmonary and extra-pulmonary.

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