

Case Report

High fever as an initial symptom of primary gastric inflammatory myofibroblastic tumor in an adult woman

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Abstract: Inflammatory myofibroblastic tumor, also known as inflammatory pseudotumor, plasma cell granuloma or inflammatory myofibroblastoma, is characterized histopathologically by myofibroblastic spindle cells with inflammatory cell infiltrates composed of plasma cells, lymphocytes and eosinophils. Inflammatory myofibroblastic tumor is typically seen in children or young adults and is most commonly localized to the lungs, but it can occur anywhere in the body. To date, however, only a few cases involving the stomach have been reported. Herein, we present a case of gastric inflammatory myofibroblastic tumor in an adult woman with an initial symptom of high fever.

Keywords: Inflammatory myofibroblastic tumor, stomach, inflammatory pseudotumor, high fever, surgery

Introduction

Inflammatory myofibroblastic tumor (IMT) is an uncommon mesenchymal neoplasm occurring mainly in children and young adults. IMT was first described in the lung, but has since been observed in a wide variety of extrapulmonary sites such as the liver, urinary bladder, mesentery, retroperitoneum, omentum and central nervous system [1]. IMT is rarely seen in the stomach, especially in adults [2]. Here we report a case of primary gastric IMT in an adult woman with high fever as the initial symptom. The clinical and histopathological features of this rare lesion are described with a review of the literature.

Case presentation

A 61-year-old female was admitted to the emergency department suffering from a high fever of 39.8°C. She had been experiencing intermittent epigastric pain and abdominal distention over a period of 5 days before fever developed, but had no other presenting symptoms such as cough, nausea, vomiting, hematochezia, reflux, asthma or shivering. In addition, she had no history of alteration in bowel habits. Her past medical history was unremarkable, with the exception of hypertension for the past 10 years.

Clinical examination did not reveal any palpable abdominal mass and there were no signs of

tenderness. Routine blood tests revealed microcytic hypochromic anemia with a hemoglobin level of 10.8 g/dl and a hematocrit of 34.3%. Repeated blood cultures came up negative for the presence of bacteria or fungus. Radiologically, chest X-rays were normal, but contrast-enhanced abdominal computed tomography (CT) showed a 3.0 × 3.0 cm low-density mass located on the lesser curvature of the stomach, near the angular incisure, and with several enlarged lymph nodes around it (**Figure 1**). Flexible upper digestive endoscopy identified a small, superficial mucosal lesion in the gastric antrum, and endoscopic ultrasound (EUS) showed a round hypoechoic mass, 3.0 × 3.0 cm in diameter, originating from the muscularis propria layer (**Figure 2**). Endoscopic biopsy revealed inflamed gastric mucosa. Upon admission, the patient was initially administered intravenous piperacillin and tazobactam for 3 days, followed by 3 days of intravenous meropenem, but her temperature continued to fluctuate between 39°C and 39.8°C. The patient's temperature finally returned to normal after being treated with dexamethasone and indomethacin.

Based on the findings described above, a diagnosis of gastric sarcoma was suspected, and surgical excision was recommended due to the presence of a gastric mass with unclear tumor histology. The patient therefore underwent



Figure 1. Abdomen CT scan. CT scan shows a 3.0 × 3.0 cm low-density mass, marked with the arrow, located on the lesser curvature near the angular incision.

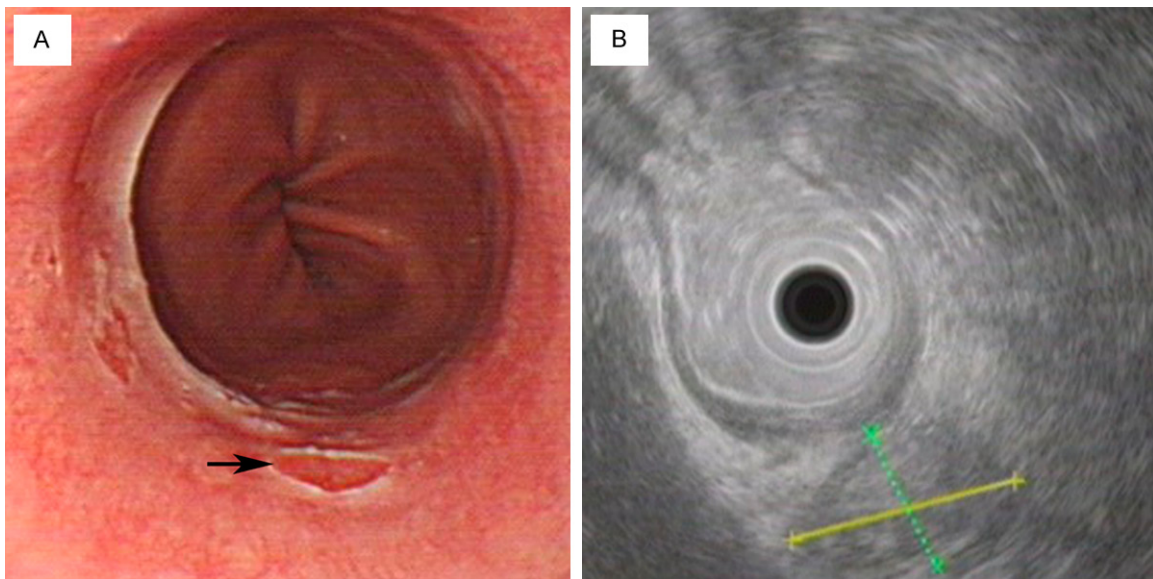


Figure 2. Flexible upper GI endoscopy. A small, superficial mucosal lesion marked with the arrow in the gastric antrum is demonstrated (A). EUS shows a round hypoechoic mass, 3.0 × 3.0 cm in diameter, originating from the muscularis propria layer (B).

exploratory laparotomy 10 days after admission, during which the tumor's location in the lesser curvature near the angular incisure was confirmed, where it was found to have infiltrated the entire thickness of the gastric wall. Several enlarged lymph nodes were observed near the tumor, but no signs of adjacent organ invasion or metastasis were detected. A radical surgical procedure was performed including a distal gastrectomy with D2 lymph node dissection and Billroth I reconstruction. Histopathological examination of the tumor revealed spindle cells with inflammatory infiltrate of neutrophils, eosinophils, lymphocytes and plasma cells. Immunohistochemical analysis showed that the tumor cells were positive for vimentin and smooth muscle actin (SMA), but negative for cytokeratin (CK), CD117, CD21, CD23,

CD35, IgG4 and anaplastic lymphoma kinase (ALK) (**Figure 3**). The immunological and morphological findings were found to be consistent with the diagnosis of IMT in the present case. The postoperative course was uneventful, and the patient appears to be doing well over 3 months of follow-up.

Discussion

IMT has been characterized as a histologically distinctive lesion with unpredictable behavior. While there was previous debate as to whether IMT is a tumor or inflammation, it is now recognized as a neoplasm of intermediate biological potential, with frequent recurrences and only occasional metastasis [3]. The etiopathogenesis of IMT remains unclear. Various mechanisms of tumor development have been postu-

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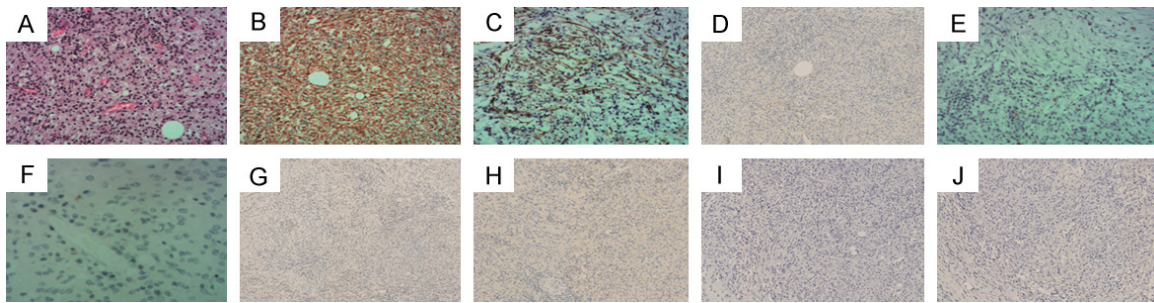


Figure 3. Microscopy of gastric IMT. Image shows spindle cells with inflammatory cell infiltration (A). Immunohistochemistry reveals the presence of vimentin (B) and smooth muscle actin (SMA) (C); whereas negative for ALK (D), CD117 (E), CK (F), CD21 (G), CD23 (H), CD35 (I) and IgG4 (J) (HE staining $\times 10$).

lated, including exaggerated inflammatory response to infections and rearrangement of the ALK gene [4, 5]. As stated previously, it occurs mainly in children and young adults, and the lungs are the most commonly affected site. Primary gastric IMTs in adults are very rare. To date, only 16 adult patients with gastric IMT have been reported based on the available literature, with a male to female ratio of 1 to 4 [6, 7]. Clinical and pathological findings from a review of 16 cases of gastric IMT in adults that has been reported are summarized in **Table 1**.

Gastric IMT typically present with abdominal pain, hematemesis, melena and a palpable abdominal mass. Weight loss, fever and hypochromic anemia may also be associated with gastric IMT. To our knowledge, however, the present case is the first report of primary gastric IMT in adults with high fever of almost 40°C as the initial and main symptom.

Radiologically, there is no specific feature to the IMT [16]. Pre-surgical EUS and CT may help to determine the extragastric invasion. Due to the tumor's submucosal location, endoscopic biopsies frequently reveal only normal gastric mucosa. Surgical exploration with complete resection is therefore the most efficient treatment method and can meanwhile obtain an accurate histological diagnosis. The histological appearance of gastric IMT is characterized by proliferation of spindle-shaped myofibroblastic cells and a lymphoplasmacytic infiltrate distributed among the tumor cells. Immunohistologically, IMT cells are usually positive for vimentin, SMA, desmin, but negative for CD117 and S-100. There are a few tumors or lesions in the stomach such as inflammatory fibroid polyp (IFP), gastrointestinal stromal

tumor (GIST), leiomyoma and follicular dendritic cell sarcoma (FDCS) that must be distinguished from IMT. Usually, IFP, GIST and smooth muscle tumors do not display the systemic symptoms as seen in IMT patients. The definitive diagnosis should be verified by a histopathological study. IFP is a benign tumor-like lesion which rarely invades the muscularis. The tumor cells in IFP also present an onion skin-like pattern around blood vessels and glands which is absent in IMT. Immunohistochemically, IFP mostly presents positive for CD34 but negative for SMA [17]. In the present case, IFP was therefore ruled out by the transmural location, lack of onion skinning on histology and immunopositivity for SMA. GIST microscopically shows only scattered inflammatory cells, and immunohistochemically nearly always presents positive for CD117 and DOG1 which was opposite for IMT [18]. Although leiomyoma can show myxoid change and occasional eosinophilic infiltrates with immunohistochemically positive for SMA, leiomyomas do not demonstrate marked lymphoplasmacytic infiltrates and sparsely arranged spindle cells, moreover, leiomyomas often show numerous scattered CD117 positive mast cells, which helped in differentiating it from IMT [7]. Follicular dendritic cell sarcoma is a malignant neoplasm derived from follicular dendritic cell that possess and present antigens to B cells in the follicular centers of lymphoid organs. They often occur in lymph nodes, although they can also arise at extranodal sites. Histologically, the characteristics of FDCS are whorl, storiform and fascicular arrangements of oval to spindle tumor cells with indistinct cell borders. Immunohistochemically, the most sensitive and specific markers for FDCS are positive for CD21, CD23 and CD35 but negative for CK which may be

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Table 1. Review of patient characteristics of previously reported gastric IMT

	Author	Age/ sex	Presenting symptoms	Tumor location	Tumor size	Treatment	ALK status	Follow-up
1	Kojimahara et al. 1993 [8]	19/F	Vomiting, Weight loss	C to LC	9 cm	TG	NA	Asymptomatic at 2.5 years
2	Al-Taie et al. 2002 [9]	45/F	Abdominal pain	Body	6 cm	PG	NA	Not available
3	Kim et al. 2004 [10]	26/M	Palpable lump, anemia	C to body	8 cm	TG	NA	7 cm mass in rectovesical pouch at 5 weeks
4	Leon et al. 2006 [2]	50/F	Vomiting, Weight loss	PW	7 cm	SG	NA	Asymptomatic at 2 years
5	Park et al. 2008 [11]	55/F	Abdominal pain	GC	8.5 cm	Gastric wedge resection	Negative	No recurrence
6	Shah et al. 2008 [4]	80/F	Epigastric discomfort, anemia	Prepyloric region	1.5 cm	Excision	NA	Asymptomatic
7	Albayrak et al. 2010 [12]	56/F	Hematemesis, melena, vomiting	C	11 cm	PG	Negative	Asymptomatic at 8 months s
8	Shi et al. 2010 [13]	36/M	Abdominal pain and mass	Antrum, LC	4.5 cm	PG	Positive	NED at 5 years
9	Shi et al. 2010 [13]	42/M	Abdominal pain and mass, upper GI hemorrhage	Upper Body, GC	8 cm	PG	Positive	NED at 2 years
10	Shi et al. 2010 [13]	40/M	Abdominal mass	Upper Body, AW	6.3 cm	PG	Positive	NED at 3.3 years
11	Shi et al. 2010 [13]	45/M	Abdominal mass and pain	Angle	5.5 cm	PG	Positive	NED at 2.6 years
12	Shi et al. 2010 [13]	40/F	Abdominal pain and mass	Lower Body, PW	5.8 cm	PG	Positive	NED at 4 years
13	Jain et al. 2012 [7]	35/F	Abdominal pain, vomiting, anemia	GC	11 cm	Wide excision	Negative	Asymptomatic at 7 months
14	Ribeiro et al. 2012 [14]	37/F	Epigastric pain, Weight loss	Lower body	9.0 cm	SG	Positive	Not available
15	Bjelovic et al. 2013 [6]	43/F	Abdominal pain, nausea	Distal stomach	6 cm	DG	Positive	2 years
16	Arslan et al. 2013 [15]	65/F	Dyspepsia, Intermittent Epigastric pain	antrum	11 cm	Gastric wedge resection	Positive	NED at 3 months
17	Present case	61/F	High fever	LC	3.0 cm	DG	Negative	NED at 3 months

Abbreviations: C, cardia; F, female; M, male; LC, lesser curvature of the stomach; GC, greater curvature of the stomach; AW, anterior wall of the stomach; PW, posterior wall of the stomach; PG, partial gastrectomy; DG, distal gastrectomy; SG, subtotal gastrectomy; TG, total gastrectomy; NED, no evidence of disease; NA, not available.

used to discriminate FDCS from IMT [19, 20]. IgG4-related inflammatory pseudotumor (IPT) and IMT share the similar morphological features as proliferation of spindle cells along with fibrosis and an inflammatory infiltrate comprising of lymphocytes and plasma cells. However, the spindle cell proliferation is more obvious in IMT whereas lymphoplasmacytic infiltrate is more notable in IPT. Immunohistochemically, IPT often shows marked positive for IgG4 but negative for ALK. Although the present case showed immunonegative for ALK, the marked proliferation of spindle cells and immunopositive for vimentin and SMA but immunonegative for IgG4 are helped in differentiating these morphologically similar but biologically different lesions [21, 22].

Recently, ALK reactivity was found important in the diagnosis of IMT and associated with local recurrence thus suggesting that ALK reactivity may be a favorable prognostic indicator in IMT [3]. Approximately 60% of IMTs contain ALK proteins which can be detected by immunohistochemistry and form a specific marker if positive [5]. ALK-negative tumors are more seen in older patients and likely to present atypical histological features which was considered to be associated with metastases [3, 7]. However, other study did not confirm such an association [23]. Of the 17 cases of adult gastric IMT, ALK immunohistochemistry was performed in 12 cases, and 4 cases (including our case) were negative for ALK. The status of ALK expression in all of 17 cases of gastric IMT in adult was seen in **Table 1**.

The rate of recurrence for gastric IMTs is estimated to somewhere between 15% and 37% [24]. Factors that affect recurrence include tumor size, incomplete resection, presence of multinodular masses and age. The first-line treatment for IMT is surgical resection. Some patients may also respond to treatment with dexamethasone and indomethacin.

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Disclosure of conflict of interest

None.

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