

## Fever of Unknown Origin as a Presentation of Gastric Inflammatory Myofibroblastic Tumor in a Two-Year-Old Boy

Gastric inflammatory myofibroblastic tumor (IMT) is an extremely rare lesion with mimicking malignant features and accompanied with various clinical manifestations. Here we present a 2-yr-old boy who had a gastric IMT with a huge extra-gastric mass, which closely resembled a neuroblastoma on imaging studies. He experienced intermittent fever and poor appetite for 6 weeks. Fever remained up to 38°C even on the operation day. He underwent partial gastrectomy and distal pancreatectomy with splenectomy including the tumor. The preoperative fever disappeared and did not recur in the postoperative course.

Key Words : Fever of Unknown Origin; Inflammation; Stomach Neoplasms

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### INTRODUCTION

Inflammatory myofibroblastic tumor (IMT) is a clinical and pathological disease entity (1), which is an inflammatory lesion with unknown etiology and usually originates from the lung, but can also arise in any sites in the body (2). IMT is used to denote a histologically similar group of tumors, characterized by a spindle cell proliferation with a fibroinflammatory appearance that has been reported under a variety of additional descriptive terms, such as atypical fibromyxoid nodule, inflammatory fibroid polyp, inflammatory pseudotumor, plasma cell granuloma, and pseudosarcomatous myofibroblastic proliferation (2, 3). We report a case of a 2-yr-old boy who presented with fever of unknown origin and was diagnosed with a gastric IMT. The clinical and histopathological features of this rare lesion are described with a review of the previously reported cases.

### CASE REPORT

A 2-yr-old boy was referred to our emergency room because of fever of unknown origin. According to his mother, he experienced intermittent fever of up to 39°C, preceded by shivering and followed by profuse sweating, together with poor appetite for 6 weeks. The fever was alleviated by non-steroidal

anti-inflammatory drugs such as ibuprofen and acetaminophen. However, his body temperature gradually increased again several hours later. The tuberculin skin test showed weakly positive for *Mycobacterium tuberculosis* in another pediatric clinic he was first admitted to. The body temperature remained within normal range following antituberculous medications including INH (isonicotinic acid hydrazid), rifampicin, and pyrazinamide, however, fever developed 2 weeks later. He had no past history of serious illnesses, operations, or hospitalizations.

On admission to our hospital, his anthropometry was between the 50th and 75th percentile. No abnormalities were detected on physical examination except a fullness in the upper abdomen in deep palpation. Laboratory evaluation revealed microcytic hypochromic anemia (hemoglobin, 10.5 g/dL; hematocrit, 33.3%; mean corpuscular volume, 68.8 fL), normal white blood cell count, eosinophilia (10%) and thrombocytosis (695,000/ $\mu$ L). The erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were elevated at 116 mm/hr and 279 mg/L, respectively. Electrolytes, urinalyses, and liver and renal function tests were normal. Widal-Wright and Weil-Felix reactions, and serum markers for hepatitis B and C and of human immunodeficiency viruses were all negative. Urinary vanillylmandelic acid (VMA) and homovanillic acid (HVA) levels were normal. A culture of gastric juice yielded a growth of *Streptococcus viridans*, but all other bacteri-

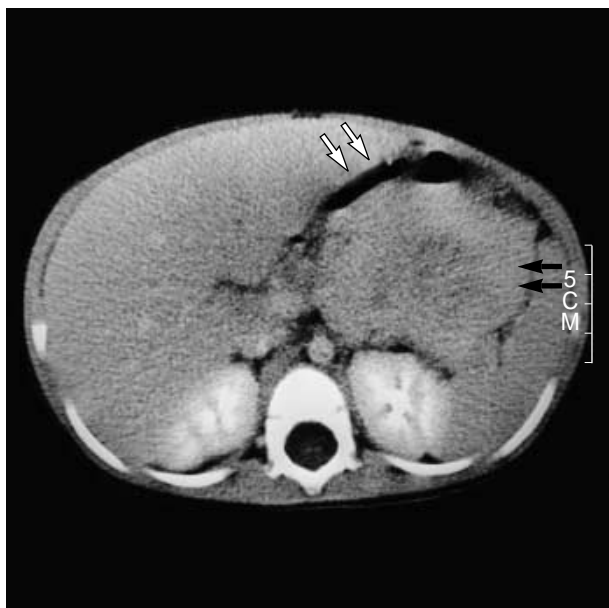


Fig. 1. Transverse contrast-enhanced CT image of the upper abdomen reveals a large solid mass with inhomogeneous enhancement (black solid arrows), displacing the stomach (open arrows) anteriorly. The mass locates between the stomach and pancreas.

ologic studies with throat swab, blood and urine specimens were negative even for *Mycobacterium tuberculosis*. No pathogens including parasites were recovered from stool.

During hospitalization, the patient underwent ultrasonography (US) of the upper abdomen that showed a hypoechoic lobulated mass lesion with irregular margin in the area of pancreas, measuring approximately  $5 \times 7$  cm. This was confirmed by abdominal computed tomography (CT) scan, which localized the tumor to the left suprarenal and suprapancreatic region (Fig. 1). The mass displaced the left kidney, pancreas, spleen, and stomach. The radiologist diagnosed the tumor as adrenal neuroblastoma. Percutaneous sono-guided fine needle aspiration cytology of the mass showed a few clustering and scattered spindle cells and some atypical cells with a high N/C (nuclear/cytoplasmic) ratio in scanty cellular smear. Fever remained up to  $38^{\circ}\text{C}$  even on the operation day.

At laparotomy, an irregularly margined, round and rubbery mass appeared to arise from the posterior gastric wall along the greater curvature of the fundus and extend into the lesser and greater sac; the mass was tightly adherent to the pancreas along with splenic artery and hilar vessels of the spleen. The mass was separated from the left adrenal gland but could not be dissected from the pancreas and splenic hilum without bleeding or injuries. For this reason, we performed partial gastrectomy and distal pancreatectomy with splenectomy including the tumor.

Gross examination of the primary tumor revealed an ill-defined, smooth, glistening mass adherent to the anterior surface of the pancreas and the hilum of the spleen with an



Fig. 2. A large well-circumscribed solid and fibrous tumor is measured  $7.5 \times 7$  cm. It is well demarcated from the normal pancreas and spleen.

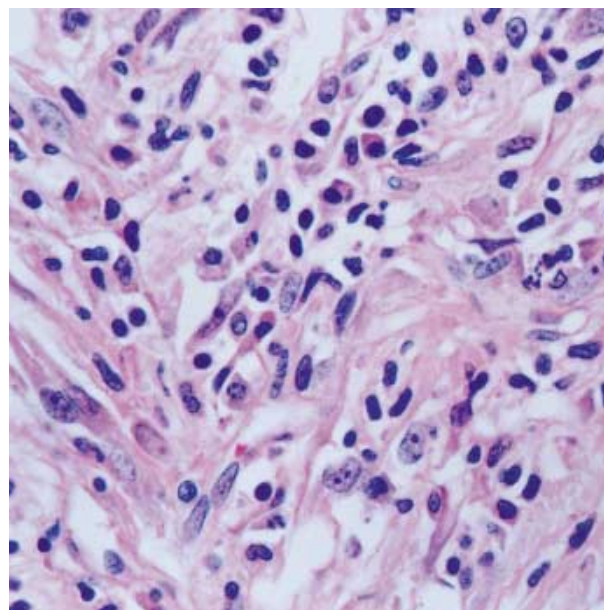


Fig. 3. The tumor cells are characterized by proliferation of spindle-shaped atypical myofibroblastic cells and chronic inflammatory cells including plasma cells and lymphocytes (H&E,  $\times 400$ ).

infiltration into the adjacent gastric wall. The excised tumor measured  $9 \times 7 \times 6$  cm and weighed 270 g. Cut surfaces of the primary tumor showed a whitish gray lobulated mass, measuring  $7.5 \times 7$  cm. The mass was well demarcated from the normal pancreatic parenchyma and the splenic capsules (Fig. 2). Histologically, the tumor was characterized by fibro-

sis and proliferation of spindle cells. The tumor was principally composed of spindle or plump cells that had round or elongated nuclei, prominent nucleoli with hypercellularity, and mild nuclear atypism. Polymorphous inflammatory infiltration of plasma cells, histiocytes, and lymphocytes with fibroblasts was also noted (Fig. 3). The pattern of growth was infiltrative, with the whole thickness of the gastric wall

being infiltrated by the proliferating spindle cells. Immunohistochemically, the atypical tumor cells showed positive immunoreactivity for vimentin and smooth muscle actin protein, while stainings for desmin, myoglobin, and S-100 protein were negative.

The preoperative fever disappeared and did not recur in the postoperative course. The patient was discharged with-

**Table 1.** Clinical and pathological findings of gastric inflammatory myofibroblastic tumor in children

Reference	Age/sex	Presentation	Duration	Laboratory workup	Preoperative diagnosis	Operation	Pathology	Follow-up Recurrence
Cho <i>et al.</i> present report, Korea	2 yr Male	Fever, Poor appetite	6 weeks	MH anemia*, Elevated ESR <sup>†</sup> , Thrombocytosis, Eosinophilia	Neuroblastoma	Partial gastrectomy, Distal pancreatectomy, Splenectomy	Fundus, Extragastric, 7.5 × 7 cm	3 months No
Estêvão-Costa <i>et al.</i> (8) 1998, Portugal	10 yr Female	Abdominal pain, UGI bleeding <sup>‡</sup> , Poor appetite	2 months	MH anemia*, Elevated ESR <sup>†</sup>	Leiomyosarcoma	Partial gastrectomy	Prepyloric, Ulcerated, Extragastric, 3 cm	3 yr No
Kim <i>et al.</i> (9) 1996, U.S.A.	5 yr Female	Vomiting, Weakness	?	No abnormal findings	Mass	Subtotal esophagogastrectomy, Wedge resection of liver	Low esophagus & stomach	1 month Yes Liver
Riedle <i>et al.</i> (4) 1996, U.S.A.	4 months Female	UGI bleeding <sup>‡</sup> , GE reflux <sup>§</sup>	2 weeks	MH anemia*, Elevated ESR <sup>†</sup> , Thrombocytosis	?	Partial gastrectomy, Splenectomy	Ulcerated, Extragastric, 4 cm	3 yr No
Murphy <i>et al.</i> (10) 1994, Canada	6 yr Male	Weakness	?	MH anemia*	?	Partial gastrectomy, Pyloroplasty	Endogastric, 6 × 7 cm	16 months Yes Stomach
Marr and Hsu (11) 1992, U.S.A.	5 yr Male	Weakness, Pallor, Growth retardation	?	MH anemia*, Elevated ESR <sup>†</sup>	IMT <sup>  </sup>	Partial gastrectomy	Ulcerated, Endogastric,	?
Meis and Enzinger (12) 1991, U.S.A.	2 yr Female	?	?	?	?	?	Stomach	14 yr No
Meis and Enzinger (12) 1991, U.S.A.	3 yr Male	?	?	?	?	?	Stomach, 11 cm	4 yr No
Lin and Hsueh (13) 1990, Taiwan	2 yr Female	Fever, Weight loss, Abdominal mass, Ascites	3 months	MH anemia*	Non-Hodgkin's lymphoma	Partial gastrectomy	Pylorus, Ulcerated, Extragastric, 4 cm	3 yr No
Tang <i>et al.</i> (14) 1990, U.S.A.	5 yr Female	Abdominal pain, Weakness, Vomiting	2 days	MH anemia*, Elevated ESR <sup>†</sup>	?	Partial gastrectomy	Fundus & body, 10 × 10 cm	3 yr No
Maves <i>et al.</i> (15) 1989, U.S.A.	5 yr Female	UGI bleeding <sup>‡</sup>	?	MH anemia*, Hypergamma-globulinemia	Mass	Resection	Fundus, 6 × 8 cm	4 yr No
Maves <i>et al.</i> (15) 1989, U.S.A.	18 months Female	Fever, Abdominal mass, Weight loss	6 months	MH anemia*, Thrombocytosis	Perforation and mass	Resection	Greater curvature	11 months No
Shroeder <i>et al.</i> (16) 1987, U.S.A.	5 yr Female	Abdominal pain, Weakness, Vomiting	1 week	MH anemia*	Mass	Subtotal gastrectomy	Fundus	?

The question mark (?) signifies that there was no relevant description in the literature reviewed; \*MH anemia: microcytic hypochromic anemia; <sup>†</sup>ESR: erythrocyte sedimentation rate; <sup>‡</sup>UGI bleeding: upper gastrointestinal bleeding; <sup>§</sup>GE reflux: gastroesophageal reflux; <sup>||</sup>IMT: inflammatory myofibroblastic tumor.

out complication after vaccination for *Streptococcus pneumoniae* and *Hemophilus influenzae* type b. The patient was clinically well without evidence of recurrence during the 3 months after the operation.

## DISCUSSION

Inflammatory myofibroblastic tumor is a rare benign solid tumor with an obscure etiology (4, 5). Despite an apparently benign morphological nature, some cases of IMT have been reported to have a malignant clinical course, such as a locally aggressive growth and a tendency to recur after a complete resection (5). It is usually difficult to confirm the accurate diagnosis before operation (6, 7). Gastric IMT is also a very rare tumor during childhood. To our knowledge based on the available relevant literature, the present case is the first gastric IMT throughout all ages in Korea.

Clinical and pathological findings from a review of 13 cases of gastric IMT in children that has been reported under a variety of additional descriptive terms are summarized in Table 1 (4, 8-16). Most cases were of less than 6-yr-old children (92.3%) and females (69.2%). The clinical presentations were variable such as weakness, fever, abdominal pain, upper gastrointestinal bleeding, abdominal mass, weight loss, vomiting, poor appetite, gastroesophageal reflux, pallor, growth retardation, and ascites, either single or in combination. Especially, three cases with fever as a main presentation showed long durations of symptoms from 6 weeks to 6 months. In our case, the cause of fever was not identified until the patient underwent abdominal ultrasonography. Most cases (90.9%) showed microcytic hypochromic anemia refractory to iron therapy. Other laboratory features were an elevated ESR, thrombocytosis, eosinophilia, or hypergammaglobulinemia. In most cases (87.5%), the diagnosis of IMT could not be confirmed in preoperative workup. Despite the preoperative diagnostic workups including ultrasonography, CT, endoscopy, or percutaneous fine needle aspiration biopsy, it was difficult to make an accurate preoperative diagnosis in this tumor. Some tumors had extragastric extension to adhere or infiltrate to the adjacent organs including the spleen, pancreas, and the liver. In our case, we could not discriminate the margin of tumor from the pancreas during the operation, although the histopathology of tumor specimen revealed that the tumor did not invade the pancreas or spleen. We performed partial gastrectomy and distal pancreatectomy with splenectomy including the tumor. Primary resection of the tumor was the first treatment of choice in all cases reviewed and was generally successful except in 2 cases.

The pathological diagnosis of IMT is based on the gross and microscopic features. IMT is confirmed by the finding of a stroma with mature spindle cells, often arranged in whorls with fibrous bands. Mixed throughout the lesion is an inflammatory infiltration consisting predominantly of plasma cells

but often lymphocytes, histiocytes, and occasionally a small component of acute inflammatory cells (17). Immunohistologically, the spindle cells are reactive against antibodies to vimentin, smooth muscle actin, and muscle-specific protein in a majority of cases (2) as well as in ours.

Most extrapulmonary IMT including gastric IMT are successfully managed by surgical resection without development of recurrence (3). Although the recurrence rate is seemingly higher in the retroperitoneum, mesentery, and upper airway (3), the prognosis of gastric IMT is usually good, as the outcomes of the cases reviewed showed only 2 recurrences (9, 10) out of 11 cases after surgery. The tendency for local recurrence appears to be related to the initial site of the tumor in the extrapulmonary IMT. Abdominal and sinonasal tumors appear prone to recurrent and locally aggressive behavior (3). For this reason, several authors recommended a complete surgical resection of the lesion as the first treatment of choice for IMT (3, 7, 9, 18).

In conclusion, gastric IMT is an extremely rare lesion with mimicking malignant features and accompanied with various clinical manifestations. However, gastric IMT is a benign lesion and surgically curable. Therefore, in order to avoid unnecessary aggressive therapy, gastric IMT should be considered as the possible cause for a gastric mass in children accompanied with the various clinical manifestations and all patients require a careful long-term follow-up because of the risk of recurrence.

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