Myofibroblastic tumor of the esophagus – a case report of long-term follow-up and literature review

Myofibroblastický nádor jícnu – kazuistika, dlouhodobý follow-up a přehled literatury

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Summary

Background: Inflammatory myofibroblastic tumor (IMT) is a rare mesenchymal neoplasm with intermediate malignant potential. Although most often seen in the lungs, it can occur at multiple anatomical locations, including the gastrointestinal tract. An esophageal lesion is extremely rare, however. IMTs present most commonly in children and young adults. The main therapeutic approach is surgical resection. ***Case report:*** We report on the follow-up of a case in a 13-year-old boy with IMT in the esophagus. He underwent surgical resection in 2013 and is free of disease to date. ***Conclusion:*** Surgical resection is the most preferred therapy. If the resection is complete, the risk of recurrence is low. Nevertheless, every patient should be carefully followed up after the resection.

Key words

inflammatory pseudotumor – esophageal carcinoma – myofibroblastic tumor – plasma cell granuloma – endoscopy – surgery

Souhrn

Východiska: Zánětlivý myofibroblastický nádor jícnu je vzácná mezenchymální neoplazie středně maligního potenciálu. Přestože se nejčastěji vyskytuje v plicích, může se objevit v mnoha jiných anatomických lokalizacích vč. gastrointestinálního traktu, avšak postižení jícnu je velmi vzácné. Myofibroblastický nádor jícnu se nejčastěji manifestuje u dětí a mladých dospělých. Základním terapeutickým postupem je chirurgická resekce. ***Kazuistika:*** V této kazuistice prezentujeme případ 13letého chlapce s myofibroblastickým nádorem jícnu, který podstoupil chirurgickou resekci v roce 2013 a od té doby je v trvalé remisi. ***Závěr:*** Chirurgická léčba je nejvíce upřednostňovanou metodou léčby. V případě kompletní resekce je riziko recidivy nízké. Nicméně každého pacienta po resekci je třeba pečlivě dispenzarizovat.

Klíčová slova

zánětlivý pseudotumor – karcinom jícnu – myofibroblastický tumor – granulom z plazmatických buněk – endoskopie – chirurgie

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Introduction

Inflammatory myofibroblastic tumor (IMT) is a rare neoplasm that can occur in various anatomical locations but appears most commonly in the lungs and mesentery or omentum [1,2]. Although these lesions have been found in nearly every anatomical location, there are only a few documented cases of esophageal localization [3]. Microscopically, IMT consists of inflammatory cells and spindle-shaped cells that are either fibroblasts or myofibroblasts [4]. IMT is equally distributed across genders [1,2] and can occur at any age; however, it presents most commonly in children and young adults [5]. Although IMTs are generally benign, they are classified as intermediate tumors because of the rare possibility of recurrence [6,7].

Distinguishing features of IMT (15–30% of cases) include the presence of inflammatory syndrome consisting of fever, weight loss, nausea, anemia, thrombocytosis, polyclonal hyperglobulinemia, and elevated erythrocyte sedimentation rate that has been attributed to cytokine stimulation [8]. Various pathogenetic backgrounds have been proposed as initiating factors, such as reactive infections and autoimmune or neoplastic processes, but the etiology of most cases remains unknown [9]. The most commonly reported curative therapy of IMT is surgical resection [4,10].

A case report of this patient was published in 2015 [11], and we now present data from a long-term follow-up.

Case report

We report the case of IMT in a 13-year-old boy, who presented with a 2-month history of dysphagia. There were no other symptoms or weight loss. There was no evidence of any consumption of chemicals or foreign bodies. In the patient's personal anamnesis, there was only a case of pneumonia, which he had suffered from when he was 18 months old. No comorbidities were found. His father had suffered from a melanoma of the right upper limb, which remains in remission after surgical resection. The results of a physical examination of the patient were unremarkable; laboratory data showed no abnormalities except mild anemia and marginal leukopenia. A barium meal examination of the upper digestive tract revealed a filiform stenosis above level Th4/5, 14 mm in length, with prestenotic dilatation (Fig. 1A). A CT scan detected a lesion of size 25 × 20 × 15 mm in the posterior mediastinum, coming from the wall of the esophagus (Fig. 1B). In the endoscopic ultrasound, an intramural lesion of the esophageal wall was identified. It involved approximately two-thirds the circumference of the esophageal lumen. There were no signs of infiltration in the surroundings of the esophagus. The patient also underwent gastroscopy, which revealed esophageal stenosis 20 cm from the incisors that was impassable for the endoscope. A biopsy did not show any malignant changes. Therefore, a thoracotomy was carried out, taking a second biopsy from the esophagus. The histological analysis of this perioperative biopsy confirmed IMT. In 2013, the patient was prepared for a radical surgical resection of the thoracic part of the esophagus, which was replaced by a part of the stomach. An intrathoracic esophagogastric anastomosis was performed. A perioperative view of the tumor can be seen in Fig. 2. During the operation a nutritional jejunostomy was inserted. Postoperatively, the patient developed a catheter sepsis and

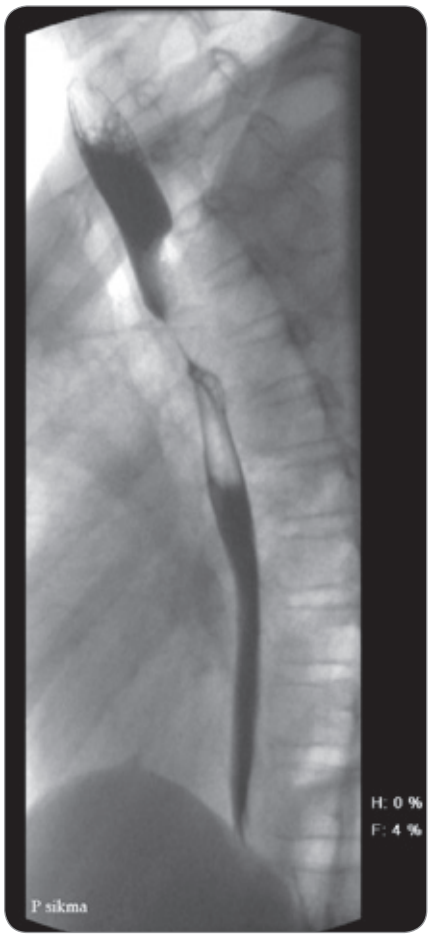

Fig. 1A. Oblique projection skiagram, passage through the esophagus, orally administrated barium contrast agent.
Image shows a sharply contoured tight stenosis of the esophagus at the interface of the oral and middle thirds of the esophagus, dorsal impression, prolonged passage.

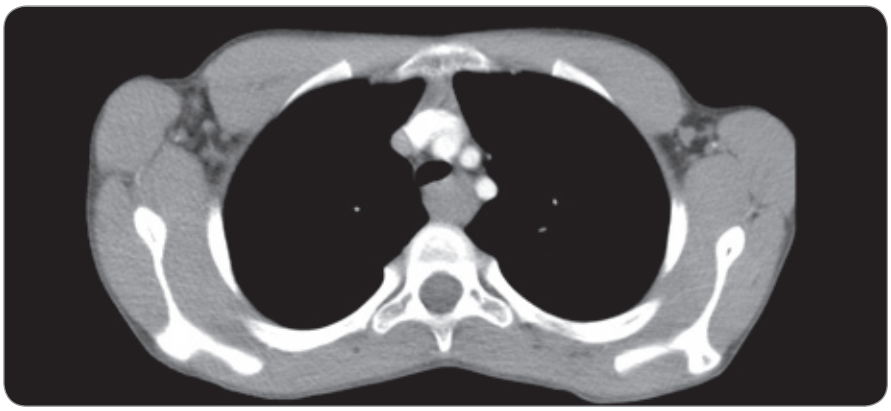

Fig. 1A. Axial CT scan at the level of the left brachiocephalic vein after intravenous application of iodine contrast agent.
Hypodense expansion of the posterior mediastinum, slightly compressing the trachea, displacing the esophagus ventrolaterally to the left, visible after the administration of a contrast agent isodensic with the chest muscles. It is not possible to differentiate the boundary of the expansion from the esophageal wall (intramural lesions).

was treated with antibiotics. Afterwards, he tolerated a regular diet and the nutritional jejunostomy was removed. A final histology confirmed the diagnosis of IMT (Fig. 3A–C). In the postoperative course, the stenosis formed in the anastomosis and the patient repeatedly underwent several series of esophageal dilations with good results. As part of an oncology consultation, the patient has been followed up annually with upper GIT endoscopy. After a follow-up period of 8 years, he is symptom-free and there has been no endoscopic evidence of recurrence (Fig. 4 includes endoscopic images from 2020).

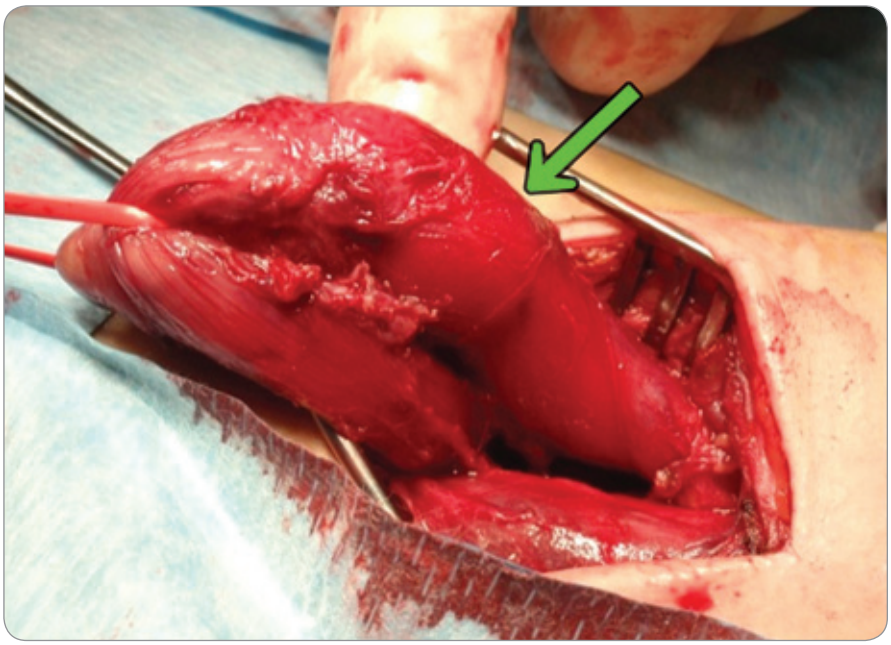

Fig. 2. Peroperative view. The esophageal tumor is indicated by an arrow.

Discussion

IMT is a very rare neoplasm and mostly occurs in the soft tissue of children and young adults, with the lungs as the most commonly affected site, though it has been recognized in many anatomical localizations, such as in the peritoneum, colon, liver, bladder, breast, and nasal cavity [12]. Histologically, IMT includes myofibroblastic and fibroblastic spindle cells with variable inflammatory infiltration by lymphocytes, plasma cells, eosinophils, and histiocytes [13,14].

Differential diagnoses of IMTs include other submucosal lesions, such as leiomyoma and gastrointestinal stromal tumors and other benign non-neoplastic tumorous lesions, including inflammatory fibroid polyps, fibrovascular polyps, and inflammatory polyps, as these lesions are composed of fibroblastic cells and inflammatory cells, the same as IMT. The differentiation of these lesions from IMT is therefore rather difficult [15–17].

IMT exhibits variable biological behavior ranging from frequently benign lesions to more aggressive variants. It remains a topic of discussion whether IMT should be considered a tumor or inflammation, and also whether it is normally benign or malignant. Local recurrence is possible, although it rarely metastasizes [12].

Approximately 50% of IMTs are positive for anaplastic lymphoma kinase (ALK) expression as confirmed by immunohistochemistry. ALK-negative IMTs may be more aggressive, with higher frequency of metastasis compared to ALK-positive IMTs [18]. For patients with ALK-positive IMT with unresectable tumors or with advanced stage IMT, ALK inhibition can be an effective therapy [19].

The exact etiology of IMT is still unknown; however, commonly reported etiologies include the Epstein–Barr virus, human herpes virus 8 infection, trauma, reflux, and overexpression of interleukin 6 [2,13].

IMT is very rare in the esophagus and to date there are few such cases reported in the English-language literature. Although it is seen mostly in children and young adults, the disease can occur at any age. The most frequent symptoms of esophageal IMTs are dysphagia, substernal pain, and inflammatory features related to cytokine release, such as fever, weight loss, and elevated acute phase reactants [20].

The basic treatment strategy is radical surgery, which also helps to confirm the diagnosis by histopathological examination and immunohistochemistry. In the case of esophageal location, this mostly means esophagectomy, and gastric transposition is the preferred type of esophageal replacement. After resection, if radicality was not achieved, a higher rate of recurrence is expected. Enucleation or endoscopic excision are also reported [11,21]. Goldin et al [22] and Santa Cruz et al [23] have described surgical resection as their first choice of treatment. Although surgery is the most common therapy for IMT, there remains a risk of complications. Seco et al have reported the case of a 19-year-old woman with esophageal IMT who underwent a partial esophagectomy and upon whom a reoperation was later performed due to dehiscence of the anastomosis. Eleven days later, she died of sepsis [21].

In case of inoperable tumor, radiotherapy or chemotherapy should be considered. Patients with ALK-positive unresectable IMTs have an effective treatment option in targeted molecular therapy [11,24]. Crizotinib is a small-molecule tyrosine-kinase inhibitor of ALK, ROS1 and another proto-oncogene receptor tyrosine kinase, MET. Lovly et al reported a patient with ALK-negative IMT in the mediastinum who was treated with the ALK inhibitor crizotinib. This was a 6-year-old boy with a 1-year history of coughing and fatigue having an IMT in the mediastinum that was unresectable due to its intimate association with the pulmonary vein, aorta, and esophagus. After the treatment with crizotinib, there was a decrease in the size of his tumor mass. Since molecular tumor

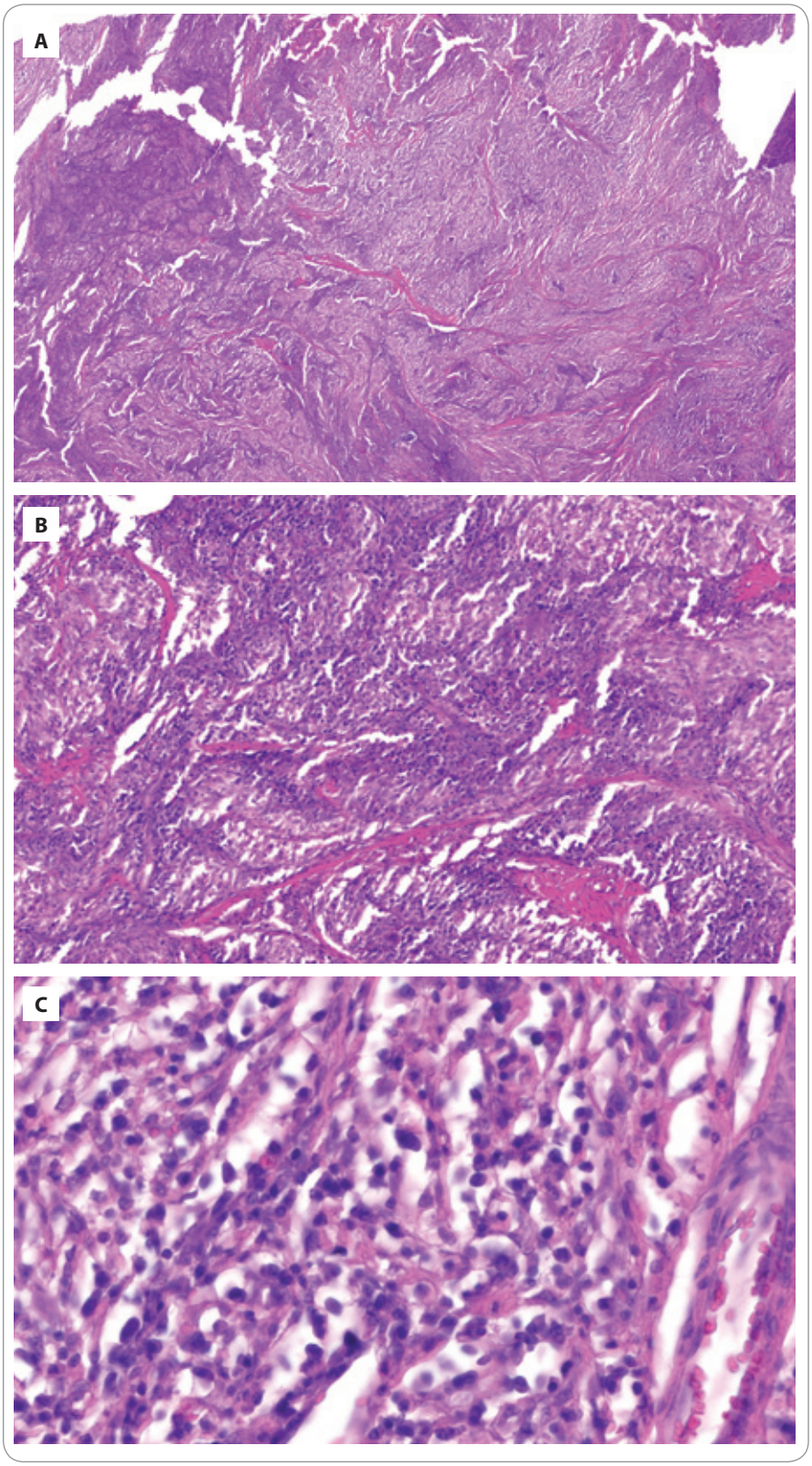

Fig. 3. Histopathology.
Hematoxylin and eosin stain of the esophageal tumor showing features consistent with inflammatory myofibroblastic tumor. Spindle cells with a fascicular pattern and nuclear atypia are seen in the background of mixed inflammation with variable myxoid stroma. A) Hematoxylin and eosin, 10×; B) hematoxylin and eosin, 50×; C) hematoxylin and eosin, 200×.

profiling revealed a ROS1 fusion in this case, there was a dramatic response to the treatment with the ROS1 inhibitor. Therefore, crizotinib is also used for the treatment of ALK-negative IMT with ROS1 fusion [18,25].

In 2021, Zhang et al reported a retrospective analysis of 23 child patients with pulmonary IMT, all of whom had undergone surgical treatment with a 5-year overall survival rate of 100%. Two patients developed local recurrence and reoperations were performed (both of them exhibited ALK-negative tumors). All patients survived until the end of the study. According to the authors of this study, consideration could be given to the concept of reducing the risk of surgical morbidity in large, difficult, multifocal ALK-positive tumors by the treatment with an ALK inhibitor prior to definitive surgical resection [26].

In 2020, Song et al presented another retrospective study of 17 patients (aged 16–56 years). The most commonly identified locations were the bronchi and the lungs, but there were also occurrences in the gastrointestinal and urogenital tracts. Sixteen of these patients underwent tumor resection, and one patient died due to tumor progression. During the follow-up period, two patients relapsed and both of them underwent surgery again. At the end of the study, they were still alive. One patient was lost from the follow-up, 13 of them were ultimately reported as cured [27].

In 2020, Casanova et al reported a prospective study of 60 patients with IMT (all of them were < 25 years old). Patients were prospectively registered for The European Pediatric Soft Tissue Sarcoma Study Group database from September 2005 to December 2016 in 9 different countries. They were staged according to the Intergroup Rhabdomyosarcoma Study grouping system, depending on the amount and extent of residual tumor after initial surgery (group I – complete R0 resection, group II – R1 resection with microscopic residual disease or regional lymph nodal spread, group III – R2 resection with macroscopic residual disease or biopsy alone, group IV – metastases at onset). In group I, 31 patients underwent complete R0 resection (4 of them devel-

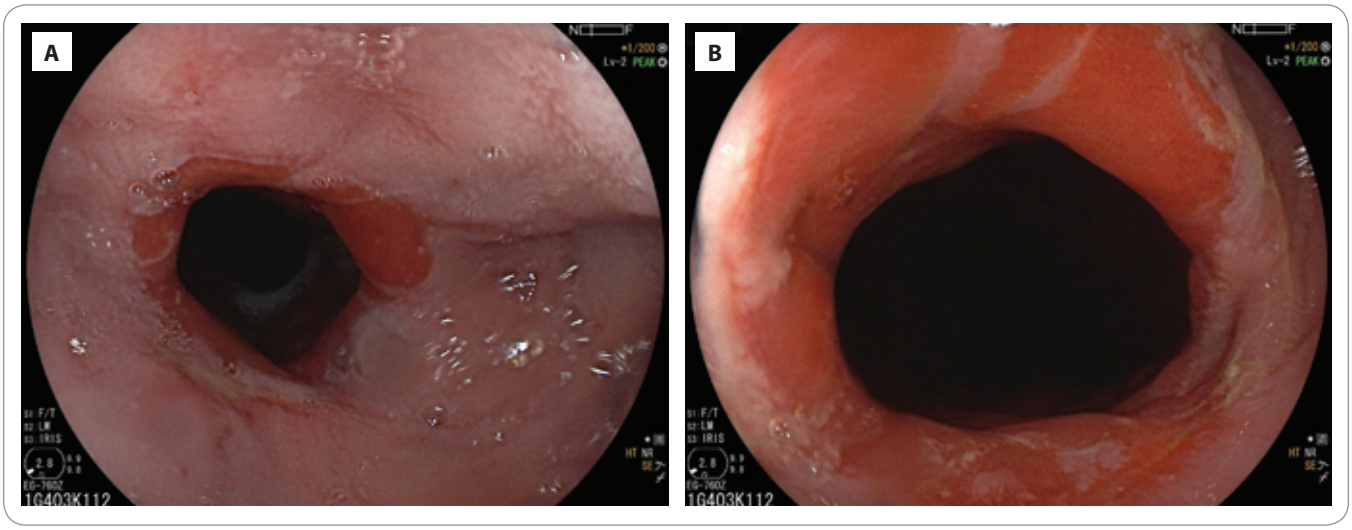

Fig. 4. Endoscopy.
Endoscopic view of esophagogastric anastomoses. No sign of disease recurrence.

oped a local relapse). In group II, 9 patients underwent resection (2 of them had nodal involvement), two patients with tumors relapsed. In Group III, 19 patients had macroscopic residual disease after R2 surgery. Out of them, 19 received various systemic treatment and one patient did not receive any therapy. One of the treated patients with ALK-negative lung IMT died of this disease 15 months after its diagnosis. In group IV, there was only one patient who was given chemotherapy with remission of the lesions. At the end of the study, all patients were alive, except the one patient from group III, who died. The study demonstrated a good overall prognosis for IMT, even for initially unresecable disease [28].

IMT rarely metastasizes, and it has a very low risk of recurrence. Lu et al reported the exceptional case of a 14-year-old boy with high-volume pelvic abdominal IMT and early tumor recurrence. It was the first reported case of IMT in the pelvic extraperitoneal perivesical space and the largest reported IMT (30 cm) among pediatric patients until that date. Although the tumor was completely resected, there was a recurrence just 20 days after the surgery. The patient refused further treatment and died 6 months later [29].

Conclusion

The occurrence of IMT in the esophagus is extremely rare, and only a few cases have been reported in the literature. Surgical resection is the most preferred type of therapy. If a tumor is completely resected, the risk of recurrence is very low. Nevertheless, every patient should be carefully followed up after the resection. In case of inoperable advanced disease, targeted molecular therapy could be effective. However, chemotherapy is still a valid option for the advanced stage.

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