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Case Report

Esophageal Plexiform Fibromyxoma: An Extremely Rare Localization

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Abstract

Plexiform fibromyxoma (PFM) is a rare gastrointestinal tumor, primarily found in the stomach. Esophageal PFM is exceptionally rare. We describe a case of a mid-20s woman with respiratory and swallowing difficulties, revealing a 105x65 mm upper thoracic esophageal submucosal tumor during endoscopy. Biopsy lacked histological evidence of gastrointestinal stromal tumors (GISTs). Post-tumor removal histopathology showed a spindle tumor with plexiform architecture and myxoid-vascular stroma. Immunohistochemistry revealed vimentin and alpha-smooth muscle actin expression, while desmin, c-kit, DOG1, and CD34 were absent, confirming PFM. No recurrence or metastasis appeared during a 6-month follow-up. This case underscores the extreme rarity of esophageal PFM, emphasizing the need for precise diagnostic tools to navigate challenging differential diagnosis.

Keywords: Esophagus, Plexiform fibromyxoma, Gastrointestinal stromal tumor, Histology, Immunohistochemistry.

INTRODUCTION

Gastrointestinal stromal tumor (GIST) is the most common gastric mesenchymal tumor affecting the public health worldwide [1]. Typically, more than 90% of the GIST cases showed expression of CD117 and DOG-1 [2], while more than 80% of the cases expressed CD34 [3]. Plexiform fibromyxoma (PF), also known as plexiform angiomyxoidmyofibroblastic tumor, is a rare benign mesenchymal neoplasm of the stomach. It was first described in 2007 [4], and officially designated by the World Health Organization in 2010 [5]. Most PF is arisen from the antrum and pyloric region, forming a lobulated intramural/submucosal mass. In clinical settings, PF is often misdiagnosed as GIST due to similar clinical manifestations. It has been described in other GI tract segments such as duodenum, jejunum, gallbladder and mediastinum. Esophageal presentation is extremely rare, and it has been described in the literature only four times [6- 22]. In this study, we reported a case with PF the esophagus firstly reported in Africa, with the clinical characteristics, histopathologic and immunophenotypical features, as well as the discussion on the misleading differential diagnosis.

CASE PRESENTATION

A 25-year-old woman who presented with chest pain, dyspnea and dysphagia. Laboratory findings were normal. Computed tomography (CT) revealed a well-defined posterior mediastinal mass arising from the esophagus, pushing against the heart and pulmonary vessels. Endoscopic examination demonstrated a solid mass within the submucosa and muscularis propria of the upper thoracic esophagus, measuring approximately 105 × 65 mm in. The biopsied sample did not provide a definitive histological diagnosis of gastrointestinal stromal tumor (GIST). The patient underwent thoracotomy followed by surgical local excision to remove the tumor.

Under gross examination, we identified a para-esophageal mass measuring 9x6.5x6 cm, displaying a multinodular, gray-white aspect with myxoid and cystic areas, mainly involving the submucosa, muscularis propria, and subserosal adipose tissues. An intact esophageal mucosal layer enveloped it (Figure1).

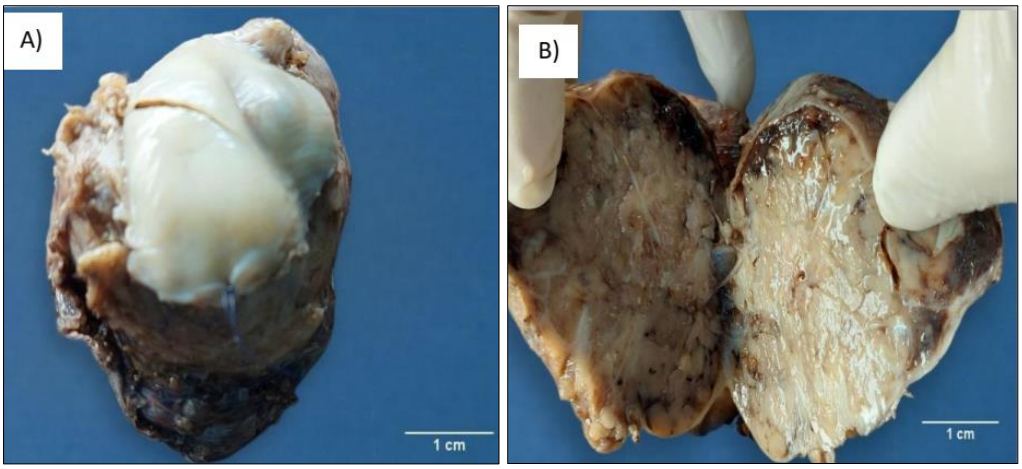

Figure 1: grossing images: (A) the resected specimen with an intact esophageal mucosa covering the tumor, B) the cross-section show a white-grayish, multinodular appearance of the tumor

For the histopathologic findings, we observed a multi-nodular, plexiform growth pattern tumor involving submucosa, muscularis propria, and subserosal adipose tissue. The nodules were comprised of bland-looking spindle cells characterized by eosinophilic cytoplasm and elongated ovoid nuclei with finely distributed chromatin. These cells were dispersed within a loose myxoid background, which contained numerous delicate, thin-walled blood vessels. This spindle-shaped cell tumor significant nuclear atypia, mitotic activity, or necrosis (Figure2).

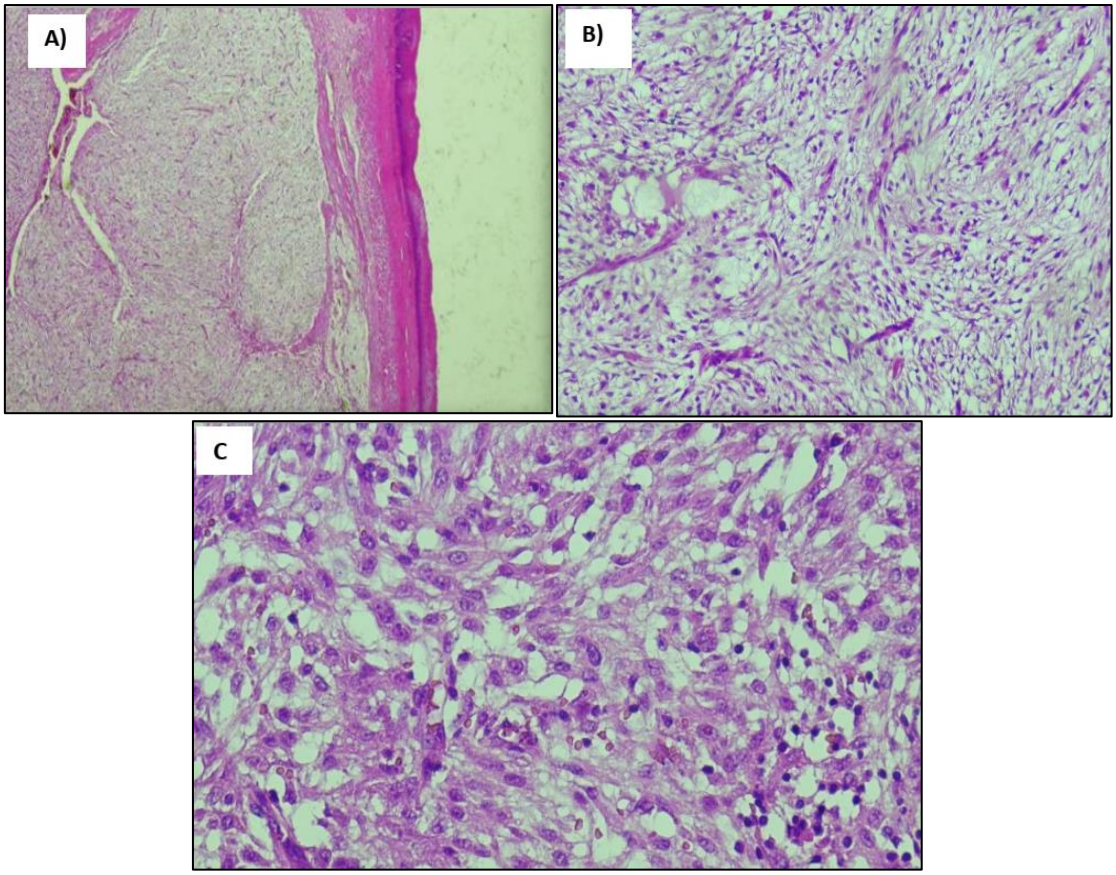

Figure 2: A) H&E stain microscopic images with ×5 magnification showing a submucosal multinodular tumor with plexiform growth pattern overlying an intact esophageal mucosa: B) H&E stain with ×20 magnification, showing proliferation of bland myofibroblastic cells and arborizing capillaries in a loose myxoid stroma and plexiform pattern *area. C) H&E stain with ×40 magnification, showing proliferation of bland myofibroblastic cells with minimal nuclear atypia and no mitosis.*

Immunohistochemically, the spindle cells were diffusely immunoreactive for SMA (Fig. 2D) and vimentin (Fig. 2F) and negative for CD117 (c-kit), Dog 1, CD34, CD31, ERG, PS100, Desmin, H-Caldesmon, STAT6, ALK, Cytokeratin AE1/AE3, EMA, Melan A, HMB45, SOX 10, HHV8, HHF35, β-Catenin, and CD10 antibodies. The patient was followed up for 6 months with no recurrence and metastasis. The prognosis was satisfactory (Figure 3, Figure 4).

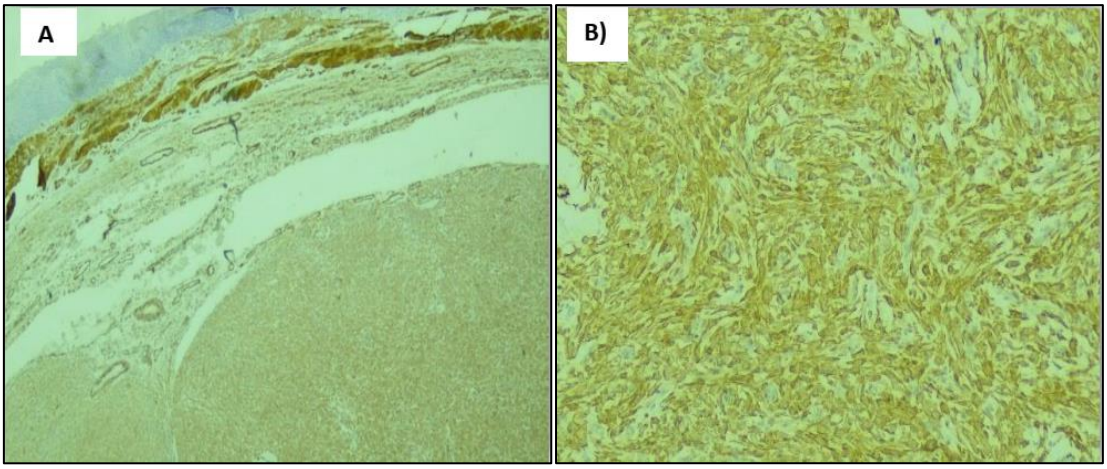

Figure 3: Immunohistochemical staining: A) positive staining for SMA with ×5 magnification, B) positive staining for SMA with ×20 magnification.

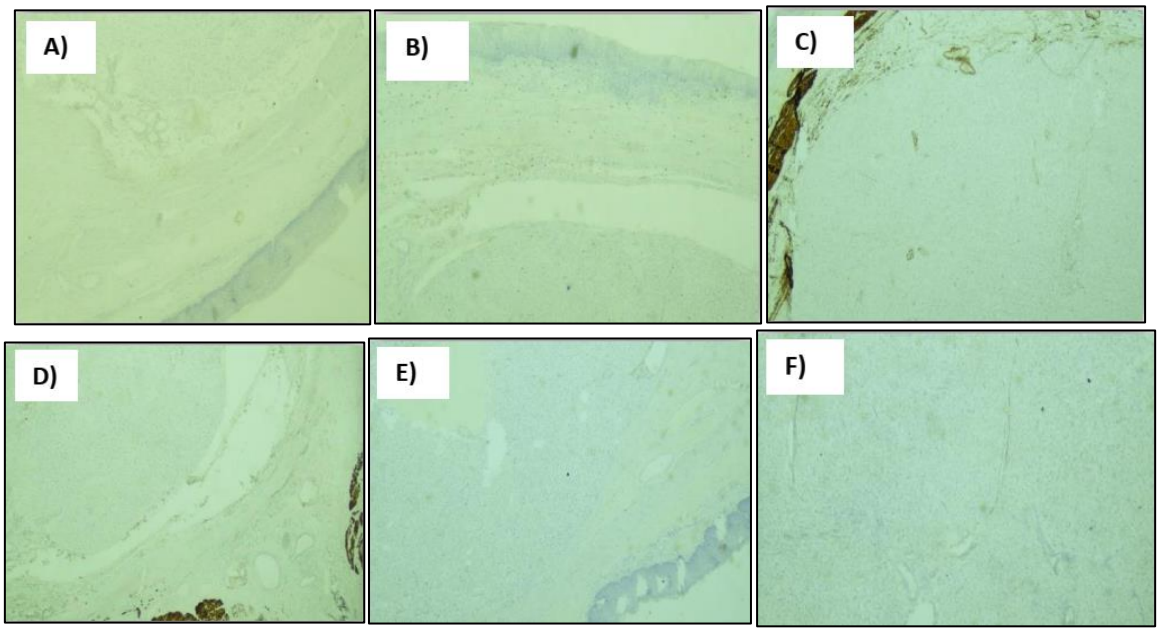

Figure 4: Immunohistochemical staining: negative l staining for A) DOG1, B) CD117, C) Desmine, D) H caldesmone, E) β catenine, F) ALK.

DISCUSSION

Due to its rarity, not many cases of PF have been described in the literature. In particular, an esophageal presentation is extremely rare. An esophageal localization of PF neoplasm has never been reported in morocco and Africa, although two cases of gastrointestinal PFs have been reported in South Africa and Tanzania, both localized in the stomach [1].

Initially considered a gastrointestinal mesenchymal tumor, PF has been documented beyond the gastrointestinal tract. Among 120 reported cases, most tumors were found in the gastric antrum (79.2%), followed by the gastric body (8.3%), unspecified stomach locations (4.2%), gastric fundus (3.3%), duodenum (1.7%), jejunum (1.7%), gallbladder (0.8%), and mediastinum (0.8%). Tumors often extend into the duodenal bulbs, potentially causing obstruction. Despite its gastric predominance, PF occurs both in and outside the stomach, with 114 gastric tumors and 6 extragastric tumors reported [7].

The clinical manifestations ranged from asymptomatic to nonspecific gastrointestinal (GI)

symptoms and hemorrhagic gastrointestinal presentations. The most common symptom was abdominal pain. Other clinical presentations included bloating, abdominal discomfort, bleeding, anemia, melena and weight loss. Different manifestations may arise when PF occurred with other diseases or resided in other sites [8]. For our case, the patient showed only a chest pain, shortness of breath, and an occasional dysphagia.

Due to the submucosal localization of the tumor, Endoscopic ultrasound (EUS) and fine needle aspiration biopsy (FNA) are considered the diagnostic gold standards, even if primary resection is usually the first choice [9].

The final diagnosis of PF still relies on histological and immunohistochemical examination of the lesion. Histologically, the typical characteristics of PF include spindle-shaped bland tumor cells arranged characteristically in a plexiform or multinodular pattern, separated by myxoid stroma and rich blood vessels, rare cytological atypia, and mitosis. Immunohistochemistry indicates that PF is diffusively positive for vimentin, muscle-specific actin (MSA), and smooth muscle actin (SMA). The tumor cells may be variably positive for desmin, CD10, and caldesmon. Other markers such as CD117, DOG-1, S100, CD34, β-catenin, anaplastic lymphoma kinase (ALK), and cytokeratin are negative [10].

Concerning molecular biology, MALAT1-GLI1 fusion and other genetic markers, such as a deletion or mutation in PTCH1 and FANCC, have been reported in a few cases; however, the importance of these gene abnormalities as diagnostic molecular markers has not yet been established [11, 12].

The main considerations in the differential diagnosis of myxoid mesenchymal tumors in the gastrointestinal tract include GIST, leiomyoma, leiomyosarcoma, schwannoma, desmoid tumor, solitary fibrous tumor, inflammatory fibroid polyp, inflammatory myofibroblastic tumor, plexiform neurofibroma, low-grade fibromyxoid sarcoma, myxoma, and for women, myxoid low-grade endometrial stromal sarcoma [4- 17]. The lack of immunoreactivity for c-kit and DOG 1 argues against a GIST in our case. Myxoid leiomyomas and leiomyosarcomas typically demonstrate more cytoplasmic eosinophilia, evidence of smooth muscle differentiation of the tumor, and absence of the multinodular, lobulated architecture seen with PF. Although this tumor tested positive for SMA, the absence of other smooth and skeletal muscle markers such as H-Caldesmon and MSA (HHF35) contradicted the diagnosis of leiomyoma. Our tumor lacked nuclear palisading or the Antoni A and Antoni B areas seen with schwannomas; also, they were negative for S-100 protein. Desmoid tumor demonstrates spindle cells arranged in long sweeping fascicles with dense collagen deposition with B catenin positivity, not seen in our cases. Solitary fibrous tumor can exhibit myxomatous change but usually displays alternating areas of hypercellularity and hypocellularity with dense keloid like collagen and staghorn vessels; it is also typically CD34 positive. Inflammatory fibroid polyp can occur in a submucosal location but tends to exhibit condensation of spindle cells around blood vessels and prominent eosinophils. Finally, the lack of a prominent mixed inflammatory component and ALK reactivity distinguishes our cases from inflammatory myofibroblastic tumor.

Appropriate immunohistochemical studies and, if warranted, molecular testing should resolve the differential in all cases, although distinction from a myxoid low-grade endometrial stromal sarcoma might prove challenging, as some cases of PF have shown positivity for CD10 and progesterone receptor.In our case, there was no exoteric hemorrhage and the hysteroscopy was totally normal.

From the viewpoint of molecular markers, gastroblastoma and malignant epithelioid tumors with GLI1 rearrangement are also included in the differential diagnosis of PFM because these tumors may harbor MALAT1-GLI1 fusion. Gastroblastoma is a rare biphasic tumor consisting of both spindle and epithelial components [12- 20]. The IHC profiles of gastroblastoma are different from those of PFM; the epithelial cells are positive for some keratins (AE1/AE3, CK7, and CK18), but negative for CK5/6, CK20, and EMA, while the spindle cells are positive for vimentin and CD10, and both components are negative for c-kit, SMA, desmin, and S-100 [19, 20].

PF are usually considered benign conditions, even if vascular, lymphatic and mucosal invasion have been described. Neoplasia with similar histologic features (GIST, smooth muscle tumors) have instead a malignant potential [1- 21]. For this reason, an accurate differential diagnosis is essential [1- 9].

CONCLUSION

Here, we report a rare case of esophageal PF with typical histomorphology and immunochemical aspects. Digestive PFs have a non-specific clinical appearance in terms of signs and symptoms. Due to there intramural position, upper gastrointestinal endoscopy has a restricted function and radiological characteristics frequently overlap. Endoscopic ultrasonography requires specialized knowledge in order to allow for tumor visualization and biopsy. A definitive diagnosis necessitates histological and immunohistochemical analysis, which is not commonly performed in developing countries. Additionally, because plexiform fibromyxoma is a rare tumor with only a few cases

reported in this region, it can be easily overlooked or misdiagnosed. This poses a significant challenge for gastroenterologists, pathologists, and surgeons when they encounter patients with this condition and need to differentiate it from other gastric intramural tumors, especially GIST.

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