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Calcifying fibrous tumor of the esophagus in a myasthenia gravis patient

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Abstract

Calcifying fibrous tumor is a probably non-malignant lesion which was classically described as soft tissue mass of children and young adults. It is now believed that it could be seen in wide range of ages and in variety of anatomic sites. According to the literature, only one case of calcifying fibrous tumor has been reported in esophagus. Herein we report a case of calcifying fibrous tumor in the esophagus of a 23-year-old lady, known case of myasthenia gravis, presenting with dysphagia.

We also discuss clinical significance of correct diagnosis and probable immunologic pathogenesis.

Keywords: Calcifying Fibrous Tumor, Esophagus, Myasthenia.

Introduction

Calcifying fibrous pseudotumor was first described by Fetsch et al[(1)] in1993 and was renamed as calcifying fibrous tumor (CFT) by WHO in 2002.[(2)]

CFTs are classified as non-malignant lesions that can occur virtually anywhere and are defined by triad of dense fibrosis, inflammation and psammomatous/ dystrophic calcification.[(3)] Despite benign nature, CFT may mimic other neoplastic lesions intra-operatively. Although various forms of these lesions have been described in genital organs, oral cavity, respiratory system, lower gastrointestinal tract and even the heart, occurrence of these lesions in the esophagus has been rarely reported.[(4)] Herein we present a case of CFT involving the esophagus in a 23-year-old lady with previous history of myasthenia gravis.

Case Presentation

A 23-year-old lady, known case of myasthenia gravis for nine months referred to our center for thymectomy. The diagnosis of myasthenia gravis was already based on presence of clinical symptoms including ptosis, diplopia, dysphagia, hoarseness and weakness as well as high level of acetylcholine receptor antibody in serum sample. Chest X-ray was unremarkable with no evidence of space-occupying lesion. Consequently she underwent corticosteroid therapy and was candidate for thymectomy for better control of disease. During operation the surgeon discovered a bulged area in cervical esophagus, deviating trachea to left. Besides thymectomy, esophageal mass was excised with clinical impression of either leiomyoma or gastrointestinal stromal tumor (GIST). Macroscopically the esophageal lesion had well-defined border with elastic to firm consistency, pale-tan homogeneous cut surface measuring 5 cm in greatest dimension. On microscopic examination, hyalinized collagen fibers with scattered lympho-plasmacytic infiltration and dystrophic/psammomatous calcifications were noted. Immunohistochemistry (IHC) study was negative for ALK and focal weak positive for CD34. Histomorpholoy and IHC findings were consistent with CFT.

As previously mentioned, thymectomy was also performed. Thymus tissue weighed 6g and was unremarkable in gross and microscopic examination.

She underwent corticosteroid therapy and up to now, after 21 month follow up, there is no evidence of recurrence or post-operative complication.

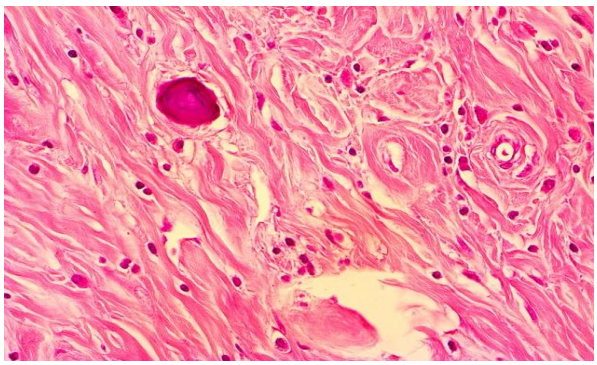

Fig. 1: Dense hyalinized collagenous tissue and scattered lymphocytic infiltration and psammomatous calcifications (×400)

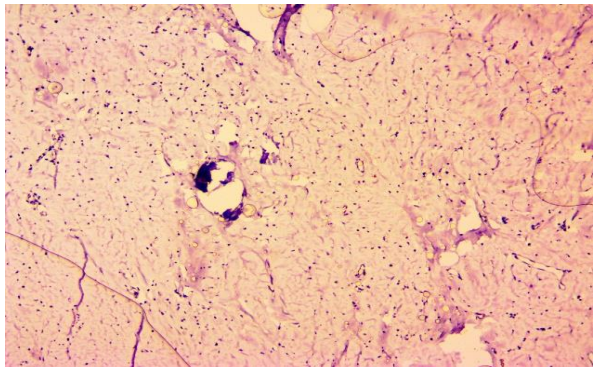

Fig. 2: Negative ALK immunoreactivity

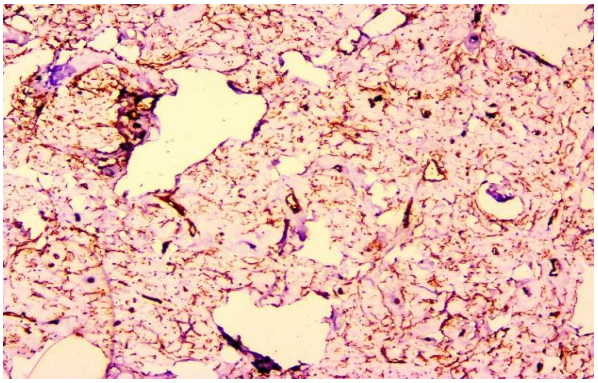

Fig. 3: Focal CD34 immunoreactivity in stromal cells. Vessels are also highlighted

Discussion

While CFT was first described in soft tissue of children, it could be seen in wide range of age and variety of anatomic sites. Distribution of age ranges from 1 to 65 years but is more common in adolescents and young adults. In gastrointestinal tract, involvement of stomach and small intestine was more reported in literature and according to our knowledge esophageal involvement was reported only once.[3,4] The etiology and course of disease are not well known.[5] Clinical manifestations and imaging findings are non-specific, making histopathology the only definite method for diagnosis. Grossly CFTs are well-delineated, somewhat lobulated, and solid or firm and their size are usually around 3-5cm.[6] On microscopic examination, hypocellular hyalinized fibro-connective tissue combined with lympho-plasma cell infiltration and psammomatous/ dystrophic calcifications are noted.

In short review done by Brent K in 2014, forty three cases of CFTs were reported in gastrointestinal tract.[3] Shou-Wu Lee et al reported an esophageal CFT in a 54-year-old woman with intermittent dysphagia. The latter was the only reported case in literature.[4] Van Dorpe reported a 17-year-old lady with multiple peritoneal CFTs and synchronous inflammatory myofibroblastic tumor(IMT) in which some nodules showed both histological features. They suggested relationship between these two entities and proposed CFT as late sclerosing stage of IMT at least in some cases.[7]

Hill KA et al also investigated relationship between these two entities and compared histomorphologic and immunohistochemical characteristics. They demonstrated all CFT cases were diffusely positive for factor XIIIa and negative for smooth muscle actin, muscle specific actin, and CD34. All IMTs demonstrated diffuse positivity for actin, variable positivity for CD34, and focal positivity for Factor XIIIa. They concluded that there is no certain distinct histologic, immunohistochemical, and electron microscopic features between IMTs and CFT.[11]

Sigel JE et al assessed deep soft tissue CFTs by using ALK immunohistochemical study and suggested that CFT is a different clinicopathologic entity than representing a "burned out" IMT.[12]

Jen-Chieh Lee and colleagues reported a 43-year-old woman, carrier of HBV, who had co-existing splenic angiomatoid nodular transformation (SANT) and multiple CFTs in omentum. They proposed both SANT and CFT are thought to be variants of IMT. However morphologic and immunohistochemical findings showed still some differences between them.[13]

Nascimento AF et al studied 15 cases of CFT in 1950-2001 and analyzed microscopic features and relationship between this lesion and IMT. They concluded all CFTs had well circumscribed border but were not encapsulated, showing extensive stromal hyalinization with a haphazard, vaguely fascicular arrangement of collagen fibers. Intermingled bland-looking spindle cells and admixed inflammatory cells especially plasma cells and lymphocytes were also noted. Two of 15 cases showed increased number of eosinophils and occasional mast cells and some of them showed occasionally lymphoid follicles with germinal centers. All cases revealed psammomatous or dystrophic calcification and numerous blood vessels. No necrosis observed and mitotic count was inconspicuous. None of them showed area of hypercellularity, like IMT. In IHC study, all cases were negative for ALK and S100 and some of them were positive for SMA and CD34. Solitary fibrous tumor, leiomyoma and desmoid fibroma were supposed as differential diagnoses. Ultimately they found no convincing morphologic or immunophenotyping justification to support an association between CFT and IMT.[8]

In our case the neoplastic cells showed negative immunoreactions for ALK marker in IHC staining that is discordant with IMTs which are expected to be ALK positive.

Masaharu Fukunaga, et al reported a subcutaneous lesion in a 20-year-old Japanese lady with microscopic features identical to CFT. In IHC study cells were diffusely positive for vimentin and α-smooth muscle actin and negative for desmin, muscle specific actin, factor-VIII related antigen, S-100 protein, neurofilament, cytokeratin CAM5.2, CD34, and CD31. By flowcytometry the tumor had diploid DNA content. After all evaluations the diagnosis of CFT was made.[9]

Nanette B. Pincard et al presented three cases of CFT in the pleura and proposed fibrous tumor of pleura, calcified pleural plaques, chronic fibrous pleuritis, calcified and hyalinized granulomas must be considered as differentials.[10]

Karl T.K. Chen suggested genetic susceptibility for CFT because of occurrence of multiple peritoneal calcifying fibrous tumor in two sisters and also 2 children of one of sisters.[14]

M. Zárnečnik et al reported a lesion morphologically identical to calcifying fibrous tumor in thigh of young lady after trauma that supports the concept of the reactive nature of CFT.[15]

The diagnosis of CFT in esophagus may be mistaken in surgical assessment with more common lesions such as esophageal diverticulum, smooth muscle tumor, gastrointestinal stromal tumor or solitary fibrous tumor. An adequate diagnosis can be achieved by histological evaluation of resected specimen and for excluding other differential diagnosis; ancillary studies such as IHC may be contributory.

Although few recurrences of CFT are on record, probability of malignant behavior and potential for metastasis has not been reported yet.[3,4]

In our case, as second report of esophageal CFT in the literature, synchronous occurrence of the lesion and myasthenia gravis could suggest a probable causative association between these two clinical conditions and propose an immunological pathogenesis for CFT.

Conclusion

In conclusion, with respect to surgical treatment and favorable outcome, both clinicians and pathologists should be aware of CFT as a differential diagnosis when considering other mesenchymal lesions in the GI tract.

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