

CASE REPORT

Neurogenous hyperplasia in the oesophagus

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Abstract

Leiomyoma and gastrointestinal stromal tumours take first place among mesenchymal tumours of the oesophagus, where tumours of peripheral nerve origin are rarely seen. Schwann and enterochromaffin cell proliferation occur in neurogenous hyperplasia, an entity observed in the appendix which has not been reported in the oesophagus in the medical literature. Oesophagogastroscopy of a 58-year-old woman showed linear erosions and nodularity at the gastroesophageal junction. The microscopic examination of biopsies taken from this area revealed proliferation of spindle cells with oval-round nuclei forming focal fascicular arrangement in the lamina propria. These cells stained positive for synaptophysin and S100-protein, while immunohistochemistry for smooth muscle actin and CD117 were negative. The case was diagnosed as neurogenous hyperplasia with these findings. Control endoscopic biopsies showed no evidence of neurogenous hyperplasia. Neurogenous hyperplasia can be considered as a distinct entity which might also be observed in the oesophagus as in the appendix.

Key words: Neurogenous hyperplasia, oesophagitis, Barrett's oesophagus

INTRODUCTION

Tumours originating from the peripheral nervous system are rarely seen in the oesophagus. Only a few oesophageal schwannomas have been reported in the medical literature.¹⁻⁴ Fibrous obliteration (appendiceal neuroma, neurogenous hyperplasia, neurogenic appendicopathy), is a known entity in the appendix, and has also been reported in the anus.⁵ It is characterised by proliferation of spindle cells in the connective and fatty tissue which exhibit S100-protein and neuron specific enolase (NSE) positivity immunohistochemically.^{6,7} To our knowledge neurogenous hyperplasia of the oesophagus has not been reported in the medical literature to date. The present case shows that this phenomenon can also be observed in the oesophagus.

CASE REPORT

A 58-year-old woman complaining of stomach pain, heartburn and bloating, was admitted to Mersin University Hospital. Epigastric and left lower quadrant tenderness was elicited on physical examination. Oesophagogastroduodenoscopy

(EGD) showed linear erosions in the lower end of the oesophagus and finger-like projections of gastric mucosa towards the oesophageal lumen. Mucosal irregularities with a micronodular appearance was observed within this area. Endoscopic biopsies were taken with the clinical diagnosis of Barrett's oesophagus and oesophagitis.

Pathology

Microscopical examination of the biopsies demonstrated short fascicles of spindle-shaped cells with eosinophilic cytoplasm and oval-round nucleus located beneath oesophageal epithelium (Figure 1). The total size of the lesion was 5 mm microscopically. A lymphoid infiltrate among the spindle cells was observed. The spindle cells stained positively with S100-protein and synaptophysin (Figure 2) whereas smooth muscle actin and CD117 were negative by immunohistochemistry. Intestinal metaplasia was not detected in the epithelium. The case was diagnosed as neurogenous hyperplasia with these findings.

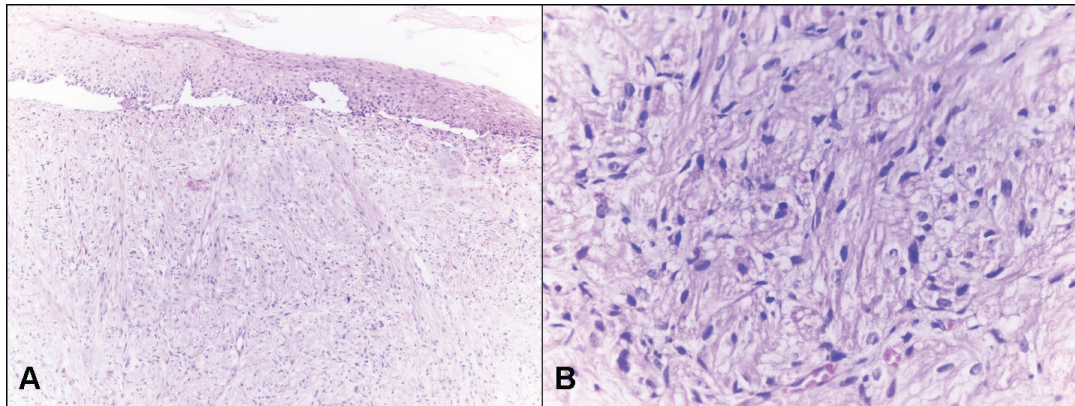


FIG. 1: A: Spindle-shaped fascicles beneath the epithelium (H&E, x100), B: Cells with spindle, undulating cytoplasm (H&E, x400)

Follow up

The patient was discharged with medical treatment recommendations. Six months later the control EGD showed an erosion at the gastroesophageal junction. The biopsies taken from this area showed intestinal metaplasia which stained positively with PAS/Alcian blue 2.5 combination. There was no evidence of neurogenous hyperplasia.

DISCUSSION

Leiomyomas are among the most common submucosal tumours of the gastrointestinal tract, particularly in the oesophagus and stomach. However, recent immunohistochemical studies show that a portion of these spindle cell tumours are gastrointestinal stromal tumours.^{3,8} Neurogenic tumours originate more commonly from the mediastinum than the oesophagus. These lesions occur mainly in the muscularis propria of the oesophagus and grow into the

lumen. Previous studies showed that oesophageal schwannoma arises from the oesophageal neural plexus, and results in dysphagia due to the narrowing of the lumen.¹ To date, only a few cases have been reported in the literature.¹⁻⁴ In all the reported cases there was a mass originating from the wall of oesophagus which protruded to the lumen causing symptoms in some of the patients. However, in our case only mucosal irregularity and micronodular appearance was detected and there was no finding of a mass lesion. The microscopical examination revealed spindle and undulating cell populations in the submucosa which showed staining with S100-protein and synaptophysin leading to the conclusion that these cells were hyperplastic schwannian cells. With these findings schwannomma, neurofibroma and neurogenous hyperplasia were included in the differential diagnosis. Lack of a well-defined encapsulated mass lesion and characteristic hypercellular and hypocellular areas (Antoni A and Antoni B

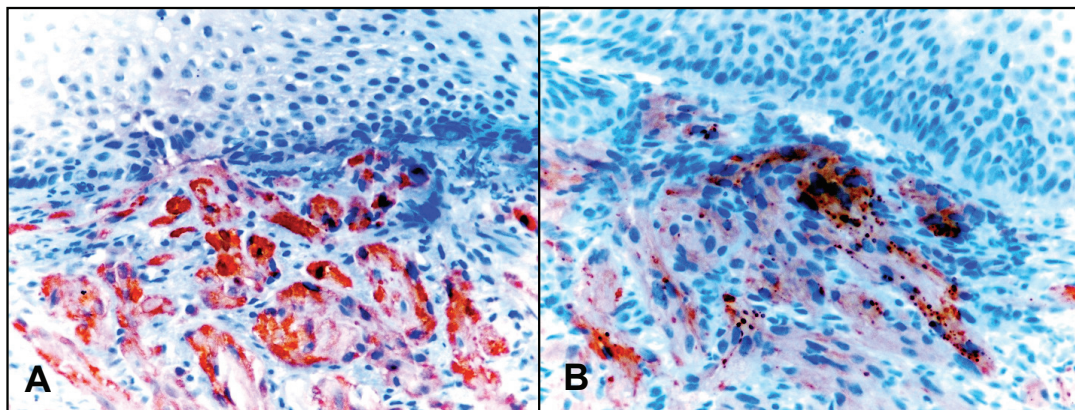


FIG. 2: Positive immunoreactivity of fascicles for (A) S100-protein (x 400), (B) Synaptophysin (x400)

patterns), presence of more than one type of cell (schwann cells, neuroendocrine cells) have been helpful in excluding schwannoma. In addition, the absence of a mass lesion and existence of neuroendocrine cells within the lesion which stained positively for synaptophysin helped to rule out neurofibroma. The mucosal irregularity recognized in the EGD which consisted of schwann cells, fibroblasts, neuroendocrine cells and a small number of inflammatory cells was considered as neurogenous hyperplasia. Although endoscopic appearance was consistent with Barrett's oesophagus, this was not confirmed histologically in the first biopsy. However Barrett's oesophagus was verified histologically in the second biopsy. This can be attributed to sampling error.

The term "fibrous obliteration" (of the appendix) which is still used today, can be regarded as an interpretation of the lesion rather than a diagnostic entity.⁹ Today the terms appendiceal neuroma, neurogenous hyperplasia, neurogenic appendicopathy are used as synonyms. It is a common entity which has an increasing incidence with older age. This entity represents an almost unknown pathology which clinically cannot be differentiated from acute appendicitis. The diagnosis can only be established histologically. Nerve proliferation and an increased number of endocrine cells are typical for neurogenous hyperplasia.¹⁰ Initially, it was believed that the obliteration was due to fibrosis, hence fibrous obliteration and obliterated appendix were used as synonyms. However, the presence of a neural component has been suggested increasingly. Neural tissue hyperplasia resulting from the irritation of stromal argyrophilic cells due to recurrent episodes of subclinical inflammation of appendix is the most common theory.^{11,12} The irritation of stromal neuroendocrine cells, which are members of neurointestinal system, in different ways causes proliferation of these cells as well as nerve bundles. It has been reported that a large number of nerve fibres showed Substance P immunoreactivity whereas the stromal cells contained 5-hydroxytryptamine and somatostatin as well.¹³ Older lesions predominantly or entirely consisting of fibrous tissue are believed to be the final step in this process. It was shown that the argyrophilic cells decrease in number when large bundles of nerve cells occur, hence neuroendocrine cells are lost in neurogenous hyperplasia.¹¹ As has been proposed in the appendix, neurogenous hyperplasia may develop

secondary to recurrent episodes of minimal inflammation in the oesophagus. Detection of Barrett's oesophagus and presence of chronic inflammatory cells in the control biopsy of the present case may probably be accepted as a finding that supports the presence of chronic irritation. However, this discussion on its pathogenesis can only be speculative due to the absence of similar cases in the literature.

In conclusion, neurogenous hyperplasia is an entity that has been diagnosed in many organs particularly in the appendix due to chronic irritation. Its occurrence in the oesophagus should be kept in mind as the oesophagus can also be exposed to chronic irritation such as in gastroesophageal reflux disease.

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