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Case Reports

FOUR CASES OF APPENDICEAL NEUROMA MIMICKING ACUTE APPENDICITIS

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Abstract. *Herein we report four cases of appendiceal neuroma found during a short (one month) monitoring period in patients with severe pain in the lower right abdominal quadrant that underwent appendectomies. Tissue samples were routinely processed to obtain histological sections that were stained with hematoxylin and eosin (H&E) and further with anti-S100 protein antibody. Characteristics of appendiceal neuroma were noted in these cases and they included the absence of mucosal and lymphoid tissue of the appendices, stroma with spindle-shaped cells that were positively stained with anti-S100 protein antibody. This clinical entity is important due to a possible misdiagnosis with acute appendicitis or exacerbation of inflammatory bowel disease and great attention should be paid during the clinical evaluation of similar symptoms.*

Key words: *appendiceal neuroma, misdiagnosis, lumen obliteration, immunohistochemistry, S100 protein*

Introduction

Acute appendicitis is the most frequent appendiceal disease and abdominal surgical condition [1]. The differential diagnosis of appendicitis is often a clinical challenge because appendicitis can mimic several abdominal conditions and should be conducted in several directions in order to determine the cause; however, sometimes it can be challenging even with the modern radiological equipment at hand.

Among others, the fibrous obliteration (appendiceal neuroma (AN)/neuronal hyperplasia) should be taken into consideration when the diagnosis of acute appendicitis is considered. The WHO classification of appendiceal tumors puts the fibrous obliteration in the group of miscellaneous tumors of the appendix [2] with the estimated incidence around 30% [3].

This paper aims to present four cases of appendiceal neuroma diagnosed in a period of one month and to give a survey of the literature on the same topic.

Case Reports

All four cases were first admitted to the Department of Abdominal Surgery, for severe pain in the lower right abdominal quadrant, where the operations were performed after radiological and laboratorial surveys were made. None of the patients had a history of inflammatory bowel disease (IBD). The clinical diagnoses of the mentioned patients were acute phlegmonous appendicitis.

Case No. 1

The removed appendix, from a 23-year-old male, was 5.5 cm long with 2–3 mm thick walls, blurred serosa and hyperemic blood vessels. There was no gross tumor mass present.

Case No. 2

The removed appendix, from a 61-year-old female, was 8 cm long with 1–2 mm thick walls; a macroscopically visible obliterated lumen and an abundant periappendicular fatty tissue were visible. There was no gross tumor mass present.

Case No. 3

The removed appendix, from a 38-year-old male, was 5.5 cm long with 2 mm thick walls, hyperemic blood vessels and a reduced periappendicular fatty tissue. There was no gross tumor mass present.

Case No. 4

The removed appendix, from a 60-year-old female, was 9 cm long, and had 3 mm thick walls; the lumen was mostly obliterated, whereas the entrance and distal part were wider. There was no gross tumor mass present.

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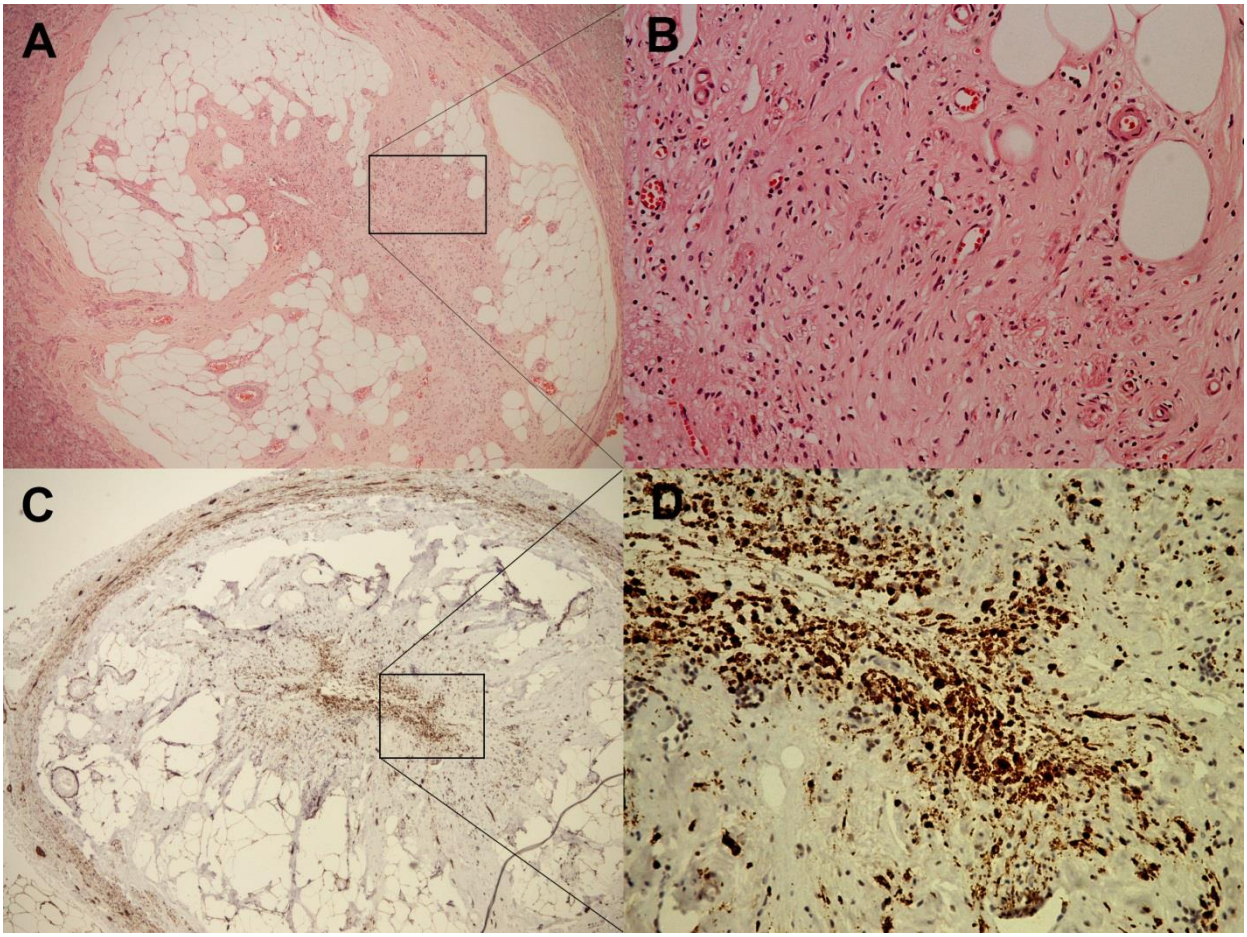

Fig. 1 Neuroma of the appendix. (A) The obliterated lumen of the appendix; the mucosal and lymphoid tissues are replaced with fatty, collagenous and myxoid stroma (H&E, ×40). (B) The proliferation of spindle-shaped cells that formed an eosinophilic bundle together with nerve fibers and occasional eosinophils (H&E, ×200). (C) and (D) Spindle-shaped cells positive for the S100 protein (S100 protein, ×40 and ×200, respectively).

The entire appendix was processed further to obtain three transversal microscopic sections, from the entrance, middle and distal parts. The slides were routinely stained with H&E and further with an anti-S100 protein antibody (Ready to use; Dako, Glostrup, Denmark). An examination of the slides revealed that the mucosal and lymphoid tissues of the appendices were completely absent and replaced with collagenous, fatty and myxoid stroma (Fig. 1A and B). The cells within the stroma were spindle-shaped (in different ratios) with occasional mast cells, eosinophils and lymphocytes. The additional staining (anti-S100 protein) revealed that the spindle-shaped cells immunoexpress this protein (Fig. 1C and D) which led us to the final diagnosis of AN in all four cases.

Discussion

During a one month period a total of 37 consecutive cases (48% female and 52% male) of appendectomies were submitted to pathological examination with the median patient age of 35.5. All patients were clinically diagnosed with acute appendicitis (*Appendicitis acuta*), whereas some of the diagnoses (n=15) were phlegmonous or gangrenous acute appendicitis. The final pathological diagnosis of these cases included: acute appendicitis of differing genesis (n=28; 75%), chronic appendicitis (n=4; 11%), AN (n=4; 11%) and lymphoreticular hyperplasia (n=1; 3%).

Appendiceal neuroma was first described in 1928 and represents the hyperplastic proliferation of unmyelinated nerves and Schwann cells [4]. When the lumen of the appendix is obliterated and other characteristics are present, diagnosis is straightforward; however, AN can affect the mucosa and submucosa without an obliteration of the appendix lumen and this is more challenging to diagnose [2]. The triggers for these neuroendocrine-cell-proliferation-related changes are thought to be repeated subclinical attacks of appendiceal inflammation [5].

The data describing the incidence of this entity varies and one cannot be sure about the exact percentage. In one study, out of 8699 patients who underwent appendectomy, only 5 AN were observed out of a total 101 appendiceal tumors [6]. According to a recent publication, the incidence of AN in a 12-year period is 3.7% [7]. Our one month monitoring period revealed the incidence of 11% which is most certainly less than the suggested 30% [3].

The association of AN with clinical symptoms, such as abdominal pain, is unclear. Although AN can sometimes mimic the acute/chronic appendicitis, the diagnosis of this entity can be found only after pathological examinations [6,8].

Alongside acute appendicitis, AN could be misdiagnosed in patients with IBD. The appendices of most patients with IBD, that were surgically removed, displayed chronic inflammation due to Crohn's disease or ulcerative colitis [9]. In the literature, there are some extreme examples, such as when the right lower quadrant abdominal pain, in a patient with IBD, was misinterpreted as Crohn's disease of the distal ileum for 20 years. Only after exploratory laparotomy, an appendectomy was performed and a pathological examination revealed AN [10]. Although AN is rare in children (one can say that it is the disease of adults), a study that involved 41 cases of children with IBD that underwent appendectomy revealed the presence of AN (among other rare diagnoses) in 20% of cases [9]. As in IBD, AN also has no known causes and the overlaps between these two entities are probably only coincidental.

The diagnosis of patients with possible appendicitis/ IBD, both clinical and pathological, should be reached cautiously and one should not forget that appendiceal neuroma (AN) exists, although it is a relatively rare entity, and that as such it deserves more attention from those making the diagnosis.

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