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Original contribution

Clinicopathologic study of calcifying fibrous tumor of the gastrointestinal tract: a case series☆

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Summary Calcifying fibrous tumor (CFT) is a rare benign mesenchymal lesion known to arise at multiple body sites that may clinically mimic other more aggressive lesions in the gastrointestinal (GI) tract. In this study we describe the clinicopathologic findings of 28 GI tract CFTs. Tumors predominantly arose in middle-aged adults with a slight female predominance. The most commonly involved sites were small bowel and colon, followed by stomach and appendix. Tumors ranged from 0.3 to 9.3 cm (median 1.4 cm), and submucosa was the most commonly involved layer. All tumors were well circumscribed and unencapsulated. Microscopically, tumors were hypocellular and composed of spindle cells with abundant, haphazardly arranged hyalinized collagen. No necrosis and less than one mitosis per 10 HPF were identified in all cases. Calcification was present in most (81%) of the cases. All cases had lymphoplasmacytic inflammatory infiltrates either scattered throughout the lesion with occasional perivascular conglomeration or in the form of lymphoid aggregates. A lymphoplasmacytic cuff was usually present (81%). Immunostains showed variable CD34 immunoreactivity and variable numbers of IgG4-positive plasma cells. The lesional cells were negative for DOG-1, ALK-1, S100, C-kit, Sox10, Melan A, HMB45, desmin, CK7, and CK20, and showed cytoplasmic staining for β-catenin. Follow-up information was available in 5 cases with no recurrences reported to date (mean follow-up, 3 years). CFT is a rare benign tumor that can occur in part of the GI tract and should be distinguished from other mesenchymal tumors due to its low risk of recurrence.

1. Introduction

Calcifying fibrous tumor (CFT) is a rare benign mesenchymal lesion, first described by Rosenthal and Abdul-Karim in 1988 as a pediatric soft tissue lesion [1]. Later in 1993 the term *calcifying fibrous pseudotumor* was introduced to describe the same entity [2]. Since then, this lesion has been documented at a variety of anatomic sites including serosal surfaces, solid and tubular organs as well as soft tissue. Most CFTs of the gastrointestinal (GI) tract have been the subject of case reports, mainly involving the stomach and small intestine [3-7]. Though these tumors are typically identified incidentally, patients can present with abdominal pain, ulceration, intussusception or obstructive symptoms [3]. Rare familial cases have been reported [8]. The

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age of presentation varies from pediatric to late adulthood with no sex predilection [3].

Soft tissue CFT usually presents as a well-circumscribed, unencapsulated, spherical or lobulated mass. Histologically, these tumors show abundant hyalinized collagen with scattered calcification and inflammatory cell infiltration [9,10]. Bland spindle cells with ovoid, vesicular nuclei and eosinophilic to amphophilic cytoplasm are embedded within the collagenous stroma. CFT show immunolabeling with CD34 as well as rare cells immunoreactive with smooth muscle actin and desmin. S-100 and ALK-1 show consistent negativity [9]. The presence of IgG4-positive plasma cells in these tumors has raised the possibility that they might be another variant in the spectrum of IgG4-related sclerosing disease [11,12]. However, this putative relationship with IgG4-related sclerosing disease or inflammatory myofibroblastic tumor remains unsubstantiated [9,12-16].

CFT is considered a distinctive benign mesenchymal neoplasm with a low risk of recurrence, approximately 20% (3 out of 15) in one study [9]. The largest series of GI CFTs consists of 7 gastric examples [14]. To our knowledge, no study has yet systematically described clinicopathologic features of these lesions in the remainder of the gastrointestinal tract, and that is the aim of the present study.

2. Materials and methods

A search of the Pathology Data System (PDS) of the Johns Hopkins Hospital during the period of 1984 to 2016 identified 27 CFTs of the GI tract. One additional case was contributed by a colleague at George Washington University Hospital. Gross description, pathology reports, and available hematoxylin and eosin–stained sections slides (available in 16 cases) were reviewed. All Johns Hopkins cases had been reviewed by one of the authors (E.A.M. or L.V.) and demographic information could be culled for all cases. The following histopathologic findings were recorded: collagenous matrix patterns, characteristics of the spindle cells, types of calcification, nature of the inflammatory component, presence of germinal centers, encapsulation, and presence of necrosis. Number of mitoses per 10 high-power fields was also recorded. The available immunoshistochemical stains were also reviewed. Clinical information and follow-up data were obtained through the medical chart or the referring pathologists or clinicians. The Johns Hopkins Medicine institutional review board approved this study (02–04-29-08e).

3. Results

3.1. Clinical findings

There was a slight female predominance (N = 18, 64.2%) and mean patient age was 49.2 years (range 18 to 83 years). The most commonly involved sites were small bowel (N = 13, 46%) and large intestine (N = 8, 29%), followed by stomach (N = 5, 18%) and appendix (N = 2, 7%). The most frequent location in the large intestine was the rectum (N = 4). Tumors ranged from 0.3 to 9.3 cm (median 1.4 cm). The submucosa was the most commonly involved layer (N = 12, 43%) followed by the mesentery (N = 11, 39%) and serosa (N = 5, 18%). None of the cases showed mucosal involvement. Most CFTs were identified incidentally during endoscopic examination or unrelated surgical procedures (Table). One case presented with intussusception and, in three cases the large or small bowel CFT caused obstruction and volvulus leading to ischemia and necrosis. Follow-up information, ranging from 3 months to 5 years (mean follow-up of 3 years) was available in 5 cases. All patients were treated with local resection alone. No recurrence has been reported to date in any of the cases.

3.2. Pathologic features

All of the GI tract CFTs were well-circumscribed, unencapsulated masses with a homogenous gray-tan to pink-purple rubbery or fibrotic cut surface. One case presented with multifocal lesions involving the stomach submucosa, peripancreatic, and splenic hilum lymph nodes.

Hematoxylin and eosin–stained slides were available in 16 cases. Microscopically, tumors were well-circumscribed, unencapsulated, hypocellular spindle cell proliferations with abundant hyalinized collagen mostly arranged haphazardly (94%) and rarely in a whorled pattern (6%) (Fig. 1). The spindle cells displayed bland, ovoid, vesicular nuclei, inconspicuous nucleoli, and eosinophilic cytoplasm (Fig. 2). No necrosis and less than 1 mitoses per 10 HPF were identified in all cases. Calcification was present in most cases and was dystrophic (N = 5, 31%), psammomatous (N = 2, 12%), or mixed (N = 6, 38%) (Fig. 2). No calcification was found in 3 cases (19%), but the morphology was otherwise typical. All cases had associated lymphoplasmacytic inflammatory infiltrates (Fig. 3). The lymphoplasmacytic infiltrate was mostly in the form of lymphoid aggregates with or without germinal centers (Fig. 3) (N = 13, 81%) and rarely scattered throughout the lesion or conglomerating around the blood vessels (Fig. 4) (N = 3, 19%). A partial lymphoplasmacytic cuff with or without germinal centers was present in most cases (N = 13, 81%) (Fig. 4). None of our cases showed peripheral entrapment of small nerves or adipocytes.

Immunostains had been performed on 12 cases, 10 of which were available for review. The tumors showed variable immunoreactivity for CD34 ranging from negative (67%) to focally positive (33%). Scattered IgG4-positive plasma cells were seen in 3 cases that were stained. The lesional cells were universally negative for DOG-1, ALK-1, S100, C-kit, Sox10, Melan A, HMB45, desmin, CK7, and CK20. β-catenin showed cytoplasmic staining.