Case Report

RECTAL AND APPENDICEAL INFLAMMATORY MYOFIBROBLASTIC TUMORS

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Inflammatory myofibroblastic tumors are neoplasms characterized by spindle cell proliferation and a fiboinflammatory vascular stroma. Herein, we presented the successful treatment of a rectal inflammatory myofibroblastic tumor in an 11-year-old boy who presented with diarrhea and abdominal pain of 1½ months duration and an appendiceal inflammatory myofibroblastic tumor in a 29-year-old man presented with recurrent abdominal pain of two months duration with associated tenderness and rebound tenderness in the right lower abdomen. Histologically, our cases had inflammatory myofibroblastic tumors very similar to that of other sites; the spindle cells were positive for vimentin and muscle-specific actin.

Introduction

Inflammatory myofibroblastic tumors (IMTs) are challenging lesions with respect to classification, differential diagnosis, and biologic potentials. Recently, considered of having neoplastic nature, they are characterized by pseudosarcomatous proliferation of spindle cells in an inflammatory fibrous stroma.1 – 3 The terms currently used by WHO to describe this lesion are inflammatory fibrosarcoma and IMT.2, 4, 5 IMTs are very rare and the most frequently involved organs are lung and mesentery; rectum, and appendix are rarely involved.2,6,7 Herein, we described the clinical presentation, differential diagnosis, treatment options, and the outcome of two patients with IMT.

Case Reports

Case 1

An 11-year-old boy was referred to Mofid Children’s Hospital because of foul smelling bloody diarrhea, fecal incontinence, and mid-abdominal pain of 1½ months duration. He also complained of fatigue and had a 4-kg weight loss. On physical examination, a posteriorly located firm, nontender, and nonmobile rectal mass protruding into the lumen was present at 3 – 4 cm from anal verge, involving 50% of the rectum. He also had microcytic hypochromic anemia with a hemoglobin of 7.5 g/dL, MCV of 53.5 fl, MCH of 23.5 pg, platelet count of 606×10³/µL, an erythrocyte sedimentation rate of 60 mm after one hr, and a positive C-reactive protein test. Other laboratory studies were within normal range.

Abdominal ultrasonography and computerized tomography (CT) scan revealed compacted fecal material and a well-defined solid rectal mass with focal calcification (Figure 1). On laparotomy the rectal mass was well-defined, though not encapsulated. With clinical impression of rectal leiomyoma/fibroma, the mass was completely removed along with attached 5 × 2 cm of intestinal wall (thickness 0.5 cm). No residual tumor was left behind grossly. No other tumor was detected in the rest of gastrointestinal tract during surgery. The postoperative course was uneventful and a 3-year follow-up showed no recurrence.

Case 2

A 29-year-old man was admitted to Imam
Hossein General Hospital with on-and-off abdominal pain of one month duration with increased severity over the past six days.

His pain was localized in the hypogastric and right lower quadrant regions. He also complained of dysuria. The patient denied having anorexia, nausea, vomiting, or changes in the bowel habit.

On physical examination, vital signs were within normal limits. He had abdominal tenderness and rebound tenderness in the right lower quadrant. Abdominal ultrasonography and CT scan with contrast revealed a 10.5 × 2.5 cm heterogeneous paracolic mass in the right lower quadrant. No peritoneal free fluid was present. All laboratory data including complete blood count and blood and urine biochemistry were within normal range. The patient underwent laparotomy. The appendix was hard and enlarged, grossly appearing as a tumor. No intraabdominal fluid or omental attachment was present; however, omentum was also thickened measuring 13 × 7 cm in area and 3 cm in thickness, which was removed. Right hemicolectomy and ileo-transverse colon anastomosis were performed. The postoperative course was uneventful. No recurrence is reported after 11 months of follow-up.

Pathologic findings

Case 1: The resected fragment was an 8 × 6 × 4 cm firm, nonencapsulated ovoid tan mass attached to a 5 × 2 cm segment of intestinal wall. Cut surface was solid, trabeculated, and white-tan with focal calcification (Figure 2). Microscopically, a spindle cell proliferation involving the submucosa with focal invasion to the mucosa (Figure 3) and ulceration were noted. The spindle cells were arranged in interlacing fascicles in a vascular fibrous stroma infiltrated by mixed inflammatory, predominantly mononuclear cells. The spindle cells showed moderate pleomorphism. Mitosis was infrequent and there was no necrosis. Focal calcification, collagen deposition, and myxoid changes of stroma were also noted. The tumor was immunostained for muscle-specific actin, desmin, vimentin, cytokeratin, and S-100 protein using Avidin-Biotin technique (Table 1). The spindle cells were strongly positive for actin and vimentin and focally for S-100 protein.
Case 2: The specimen consisted of 10.5 cm of terminal ileum attached to 7.5 cm of cecum, ascending colon, and an enlarged hard appendix measuring 9 cm in length and 4.5 cm in maximal diameter. A separate thickened hard omentum 13 × 7 cm in area and two hard round nodules of sigmoid colon measuring 3 and 1.5 cm were also received.

External surface of the appendix was smooth and tan. Cut surfaces were homogeneous tan and hard. Lumen of the appendix was obliterated (Figure 4). Microscopic examination showed extensive spindle cell proliferation involving serosa, periappendiceal fat, and muscle layers of the appendix with mixed inflammatory cells and lymphoid follicle formation (Figure 5). The spindle cells were bland looking in most areas with collagen deposition but showed pleomorphism in other regions. Mitotic figures were rare. The spindle cells showed immunoreactivity for vimentin and desmin and focally for muscle-specific actin. The omentum and nodules on sigmoid colon were also involved by the spindle cell proliferation. The ileum and large bowel revealed nonspecific chronic inflammation.

Discussion

We report a rectal IMT in an 11-year-old boy who presented with diarrhea and systemic symptoms, as well as an appendiceal IMT in a 29-year-old man presented with abdominal pain and pathologic features similar to those described in the literature. The most common site of IMT is the lung, which affects various age groups ranging from 1 to 77 years with a peak at mid-adulthood. It has also been reported in a variety of extrapulmonary sites, affecting younger patients (mean age of 9.7 years) with a peak at the first and second decades of life.

The extrapulmonary IMTs are rare, larger in size, multinodular, less circumscribed, and tend to be aggressive.2, 4, 8 – 14 The most common site, involved by IMT in gastrointestinal tract is small intestine;15 rectal2 and appendiceal6, 7 IMTs are rarely reported.

The onset may be rapid or insidious and there is a slight female preponderance.1, 2 In 15 – 30% of cases, it may be accompanied by fever, growth failure, weight loss, hypochromic anemia, thrombocytosis, polyclonal hypergobulinemia, and elevated sedimentation rate. Interleukin-6 (IL-6), interleukin-1β, and cyclin D1 production by the IMTs are the apparent cytokine mediators of those clinical and laboratory abnormalities, which may persist for months before the IMT is diagnosed and improve within days or a few weeks after removal of the tumor.1 – 4, 9, 10, 12 – 14, 16 One of our patients had four of the above presentations.

The microscopic pattern is polymorphous composed of a myxoid, vascular, and inflammatory proliferation; compact spindle cells arranged in haphazard fashion (with or without pleomorphism); occasional mitotic figures; and dense plate-like collagen with or without calcification.2, 5, 9, 11, 12, 15,17 Immunohistochemically, most spindle cells show strong diffuse reactivity with antibody against vimentin, muscle-specific actin, but no or slight staining with desmin and cytokeratin.7, 12, 13 Recently-introduced anaplastic lymphoma kinase (ALK)-1 expression by most IMTs and not by other spindle cell tumors appear to be a more specific marker.3, 18 – 20

The clinical course is usually benign in the majority of cases, and even local recurrence is rare.2, 5, 9, 11, 16, 18, 21 There are few well-documented patients with distant metastasis, and most of these had metastasis at presentation or developed metas-

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**Table 1. Immunohistochemical reagents.**

<table>
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<tr>
<th>Reagent</th>
<th>Retrieval</th>
<th>Buffer</th>
<th>Dilution</th>
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<tr>
<td>Muscle-specific actin</td>
<td>—</td>
<td>—</td>
<td>1/200</td>
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<tr>
<td>Desmin</td>
<td>Autoclave</td>
<td>Tris, pH: 9</td>
<td>1/100</td>
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<tr>
<td>Vimentin</td>
<td>Autoclave</td>
<td>Citrate, pH: 6</td>
<td>1/100</td>
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<tr>
<td>Cytokeratin</td>
<td>Autoclave</td>
<td>Tris, pH: 9</td>
<td>1/100</td>
</tr>
<tr>
<td>S-100 protein</td>
<td>Proteinase K</td>
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tasis within months or a few years. 4, 14, 22 Controversy exists as to whether multiple lesions represent multifocality or the tumor has the ability to metastasize. 5

Rarely, recurrent IMT may undergo transformation to large-cell histiocytoid neoplasm resembling histiocytic sarcoma. 2

IMT is still referred to as a lesion of unknown etiology. Previously, it was suggested that IMT is of nonneoplastic etiology of fibroblastic and myofibroblastic nature, 5, 6, 8, 11, 13, 15–17, 21 considering immunologic or infectious factors playing a role in its pathogenesis in view of the presence of systemic symptoms, 10, 14 and detection of organisms such as Coxiella burnetii, Klebsiella pneumoniae, 4 Epstien-Barr virus, 14, 16 and a case report following Campylobacter jejuni enteritis. 10

The neoplastic nature of IMT was first suggested in 1991 14 and 1995. 2 Recently, Tsuzuki et al 18 demonstrated ALK gene translocation or ALK protein expression in IMT. They reported that almost 75% of IMTs in their patients expressed ALK-1 immunohistochemically, which was confirmed by fluorescence in situ hybridization as well. 18, 19 Thus, it appears that ALK-1 expression is highly specific for IMT and confirms its neoplastic nature, originating probably from follicular dendritic cells. 3, 20 Ploidy analysis and P53 staining have limited value in the study of IMTs, but it is notable that P53 is consistently demonstrated in IMT, yet another manifestation of their neoplastic character. 3, 20

Differential diagnosis of IMT is extensive and includes benign and malignant lesions with spindle cells. Sclerosing retroperi toneitis, sclerosing mesenteritis, sclerosing cholangitis, sclerosing mediastinitis, tumefactive fibroinflammatory lesions of head and neck, and Reidel’s thyroiditis are a group of diffuse processes, rather than discrete tumeformations, which are clinically distinct from the majority of IMTs because of their progressive clinical course, although they share the same cellular constituents with IMTs. The differential diagnosis also includes postoperative spindle cell nodule, fibrous induration (ligneous perityphilitis) due to ruptured appendix, nodular fascitis and other pseudosarcomas, fibromatosis, myofibroblastoma, fibrous histiocytoma, low-grade inflammatory fibrosarcoma, myxoid leiomyosarcoma, rhabdomyosarcoma, sarcomatoid sarcoma, inflammatory malignant fibrous histiocytoma, gastrointestinal stromal tumors, and other predominantly spindle cell sarcomas. Many of these can be successfully differentiated from IMT by meticulous attention to histopathologic findings, use of adjunctive diagnostic techniques such as immunohistochemistry and electron microscopy, and attention to clinical details of age, affected site, and accompanying signs and symptoms. 2, 10, 11, 14, 15, 20, 21

Newly-developed immunohistochemical stains are of particular importance in diagnosing difficult cases. 3

Complete resection is the treatment of choice even in those with multiple recurrences. 2, 10, 18, 20, 22 There is no proven role of chemotherapeutic intervention. 2, 6, 17, 22 For selected cases, however, radiation therapy is an option. 20 Long-term follow-up is highly recommended to detect local recurrence or possible metastasis. 2, 5, 6, 9, 14

Our cases appear to be the third case of rectal IMT and the fourth case of appendiceal tumor being reported with microscopic and immunohistochemical features similar to previously-reported cases. The latter had also omental and mesenteric involvement (multifocal). Since IMT can be misdiagnosed as benign or malignant spindle cell neoplasm, 2, 14, 15 this entity should be considered in differential diagnosis.

Chapters are still being written on IMTs and new markers are developing and it may be premature to close the books on the IMT story. 3

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References

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