Inflammatory Myofibroblastic Tumor of the Small Intestine

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Inflammatory pseudotumor, inflammatory myofibroblastic tumor, and plasma cell granuloma are terms that have been used interchangeably for a variety of lesions ranging from some that are inflammatory in nature, to those that are clearly neoplastic. Although neoplastic lesions generally pursue a benign clinical course, intraabdominal and retroperitoneal lesions of this type have typically shown higher local recurrence rates and even distant metastases. Lesions have been reported in a variety of intraabdominal organs, but small bowel tumors are particularly rare. The authors report a small bowel inflammatory myofibroblastic tumor (IMFT). The literature is reviewed; the clinical and pathologic features of this tumor and controversies in nomenclature are discussed.

CASE REPORT

A 3-year-old girl presented with a 3-week history of worsening abdominal pain. Her pain was initially intermittent and diffuse across her lower abdomen and was treated as constipation. Five days before her hospital admission, the pain became constant and more severe. Located in both lower quadrants, it was somewhat worse on the right. She had no associated nausea, vomiting, bloody stool, or diarrhea.

On physical examination, a 12-cm, nonmobile, palpable mass was found in the right lower quadrant. The mass was nontender, as was the rest of her abdomen. Abdominal ultrasonography revealed an 11 × 6 × 9-cm solid mass in the right iliac fossa. Other abdominal structures, including her liver, spleen, kidneys, ovaries, and uterus, were normal.

A CT scan confirmed the presence of a mass and the normal appearance of other intraabdominal and retroperitoneal organs. Seemingly well encapsulated, the origin of the mass was still unclear. Further workup included a bone scan, chest x-ray, and a CT scan of the chest, all of which were normal. Laboratory values, including ferritin and lactate dehydrogenase, were normal. A 24-hour urine collection for vanillylmandelic acid and homovanillic acid was negative.

On laparotomy, a large tumor with prominent vascularity was found to arise from the antimesenteric border of a small bowel loop in the distal jejunum. The tumor also involved the mesentery, and multiple mesenteric lymph nodes were enlarged. There was no evidence of metastasis. The mass was resected, along with involved sections of small bowel and mesentery, and a primary small bowel anastomosis was performed. The girl did well postoperatively.

Pathologic examination revealed IMFT throughout the wall of the jejunum, with focal infiltration of the overlying mucosa, but encapsulation by the serosa (Fig. 1). All resected lymph nodes were negative. Histologically, the tumor was composed of a proliferation of spindle-shaped cells arranged into storiform and fascicular growth patterns (Fig. 2). Cellularity varied in different portions of the tumor. In some areas, the cells were widely spaced and deposited in a myxoid stroma reminiscent of nodular fasciitis. In other areas, the cells were compact and had overlapping cell borders. The nuclei had open chromatin and variably prominent nucleoli; mitotic counts ranged from 3 to 5 mitotic figures/10 high-power fields. Small zones of hemorrhage and necrosis were present. Scattered collections of lymphocytes and plasma cells were found throughout the tumor, sometimes forming nodular aggregates.

The patient has been followed with physical examination and abdominal CT scan every 6 months and with head and chest CT scans on a yearly basis. She has been free of local and metastatic disease after 2 years of followup.
DISCUSSION

Inflammatory myofibroblastic tumor is a distinctive pseudosarcomatous lesion that occurs in the viscera and soft tissue of children and young adults. The lesion has a distinctive histologic appearance and usually pursues a benign clinical course. Although original descriptions of this lesion focused on their occurrence in the lung, subsequent reports have described this lesion in virtually every anatomic location. This entity has been referred to by many different names, including plasma cell granuloma, plasma cell pseudotumor, inflammatory myofibroblastic proliferation, omental-mesenteric myxoid hamartoma, and most commonly, inflammatory pseudotumor. But inflammatory myofibroblastic tumor is preferred because the term inflammatory pseudotumor has been applied to many different entities, including reparative pseudosarcomatous lesions of the lower genitourinary tract, infectious lesions, including those secondary to mycobacterium avium intracellulare infection, and Epstein-Barr virus-associated follicular dendritic cell tumors that are usually found in the liver or spleen. Meis and Enzinger proposed the term inflammatory fibrosarcoma to describe a group of intraabdominal lesions characterized by the presence of cytologically atypical spindle-shaped cells and a more aggressive clinical course.

The most common sites of extrapulmonary inflammatory myofibroblastic tumor are the mesentery and omentum. In the study by Coffin and associates, of cases (43%) arose in these sites. Although the age range is broad, extrapulmonary tumors show a predilection for children, with a mean age of approximately 10 years. Females are affected slightly more commonly than males. Presenting symptoms depend on the site of primary tumor involvement. Patients with intraabdominal tumors most commonly present with abdominal pain, abdominal mass with increased girth, or occasionally, with intestinal obstruction. Some patients have prominent systemic manifestations, including fever, night sweats, weight loss, and malaise. Laboratory abnormalities are present in a minority of patients and include an elevated erythrocyte sedimentation rate, anemia, thrombocytosis, and hypergammaglobulinemia, which often resolve with excision of the lesion.

Histologically, a variety of patterns can be seen in this neoplasm, and different patterns can be found within the same tumor. Some cases are composed predominantly of cytologically bland spindle- or stellate-shaped cells loosely arranged in a myxoid stroma with scattered inflammatory cells, somewhat resembling nodular fasciitis. Others are composed of a compact proliferation of spindle-shaped cells arranged in a storiform or fascicular growth pattern. Mitotic figures can be seen. Rare tumors can show cells with more pronounced cytologic atypia, with cells containing large nuclei and distinct nucleoli.

Regardless of the terminology used, lesions with the histologic features described previously, occurring in the
abdomen and retroperitoneum, have a propensity for more aggressive clinical behavior than their extra-abdominal counterparts. A recent report by Sanders and colleagues documented four cases of IMFT of the alimentary tract, one at the gastroesophageal junction, one in the rectum, one involving the appendix, and one involving the appendix and sigmoid colon. One patient (25%) had two recurrences; the first occurred within 2 months and was treated by surgical resection. The second recurrence was discovered 6 months later and regressed without surgical intervention, while the patient was on oral antiinflammatory therapy. In the study of extrapolummary tumors by Coffin and associates, of 53 cases with followup, 13 patients (25%) had one or more recurrences from 1 to 24 months after initial excision. Nine of the 13 patients who developed recurrence had retroperitoneal or intraabdominal tumors, including 2 tumors that underwent histologic transformation into a higher grade sarcoma. Although none of the patients developed metastatic disease, including the two patients whose tumors showed histologic progression, two patients with mesenteric tumors died as a direct result of their tumors. Tumors that were more likely to result in aggressive behavior included those in an intra-abdominal or retroperitoneal location, those that were in close proximity to vital structures, and multinodular tumors, all of which compromised complete surgical excision.

IMFT of the abdomen and retroperitoneum has been associated with higher degrees of cellular atypia and a more aggressive clinical course than tumors in other sites. Meis and Enzinger reported 38 such cases, preferring the term inflammatory fibrosarcoma. In this series, 10 of 27 patients (37%) in whom followup information was available, developed at least one local recurrence, a median of 5 months after initial excision. Three patients (11%) had histologically proved metastases, including one with multiple lung metastases at presentation, another with brain metastases at presentation, and one who developed pulmonary metastases 4½ years after initial excision. In eight cases, there was invasion or metastases to adjacent parenchymal organs, including the liver, spleen, kidney, pancreas, and adrenal gland. Overall, five patients died as a complication of their tumor, four of whom were older than 10 years of age, suggesting that children can have a more favorable prognosis than adults. Morphologic features of the tumors were not predictive of the ultimate biologic behavior. Evaluation of additional cases of inflammatory myofibroblastic tumor with cytologic atypia (inflammatory fibrosarcoma) will be necessary to more fully appreciate the clinical behavior of these rare tumors.

Although we prefer to group all of these tumors under the term inflammatory myofibroblastic tumor, use of the terms inflammatory pseudotumor, IMFT, and inflammatory fibrosarcoma will likely persist. If so, the term inflammatory pseudotumor would more accurately be reserved for those lesions associated with an infectious or other clear inflammatory process. Defined as such, cases of inflammatory pseudotumor clearly are neoplastic. But there is sufficient evidence to support the fact that the inflammatory myofibroblastic lesions described above are true neoplasms, albeit typically benign. Clonal cytogenetic abnormalities have been demonstrated in some cases, particularly abnormalities on chromosome 2. Biselli and coworkers recently found that almost 50% of pediatric extrapolummary IMFT are aneuploid. Finally, there are reports of IMFT merging into frankly malignant-appearing neoplasms, further supporting the neoplastic nature of these lesions.

The question as to whether IMFT and inflammatory fibrosarcoma are the same tumor, distinct entities, or represent a continuous spectrum separated by degree of cytologic atypia, remains unresolved. Certainly, these two entities share clinical and pathologic features in common, and, as stated by Coffin and associates, the distinction of inflammatory fibrosarcoma “from inflammatory myofibroblastic tumor may be more semantic than real.” Some cases of IMFT do show more pronounced cytologic atypia, but given the generally benign clinical behavior of this group of lesions, we prefer to group all of these tumors under the term inflammatory myofibroblastic tumor.

The mainstay of therapy for IMFT is surgical resection, with reexcision of recurrent tumors. Steroid therapy has been reported to achieve regression in a single case of renal IMFT, and there have been anecdotal reports of the successful use of nonsteroidal antiinflammatory drugs. The benefit of chemotherapy and radiation therapy remains to be proved. Given the high local recurrence rate for intraabdominal lesions, and their potential, albeit low, for metastasis, close followup with physical examination, radiographic imaging, and serial erythrocyte sedimentation rates is recommended.
REFERENCES


