Pediatric Hematology and Oncology, 22:447–451, 2005

ISSN: 0888-0018 print / 1521-0669 online
DOI: 10.1080/08880010591002215

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AGGRESSIVE INTRA-ABDOMINAL FIBROMATOSIS IN CHILDREN AND RESPONSE TO CHEMOTHERAPY

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□ *Intra-abdominal fibromatosis (IAF) is a rare benign neoplasm arising from the abdominal fibrous tissue, mostly in the mesentery. IAF is characterized by a tendency to infiltrate the surrounding vessels and vital structures and recurrence after usually incomplete surgical removal. Accordingly, IAF is associated with considerable morbidity and mortality. The authors report on a boy who presented with a large IAF at the age of 5 years. Within 6 months after initial presentation, he underwent 4 subsequent abdominal explorations for diagnosis, tumor reduction, and intestinal obstructions. IAF was confirmed by the presence of vimentin and absence of other biological cell markers. Due to accelerated tumor growth and deteriorated general condition, as a last resort, a chemotherapy trial with vincristin and methotrexate was carried out. This regimen proved to be effective in reducing the tumor burden and improving the patient's general condition. Outcome of IAF depends on early diagnosis and complete tumor resection, and, if indicated, timely employment of neo/adjuvant chemotherapy. Radiotherapy must be considered in life-threatening conditions as the last resort in a growing child [2–4].*

Keywords aggressive fibromatosis, chemotherapy, childhood, intra-abdominal

Intra-abdominal fibromatosis (IAF) is a rare tumor in children, accounting for less than 0.1% of all tumors (2–4 per 1,000,000 capita per year), and affects mostly girls aged 4–5 years [1–3]. It originates from the fibrous tissue in the mesentery or retroperitoneum and less commonly the intestinal wall

Received 27 January 2005; accepted 28 April 2005.
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[2, 4]. Dysregulation of β-catenin production, e.g., its elevation, may account for the accelerated proliferation of tumor cells [5]. IAF is classified according to its histopathological features and biological behavior as a benign tumor with no potential for metastasis. However, it has a notable tendency to infiltrate the adjacent structures, thus compromising vital organ functions and vascular structures, and causing morbidity and mortality. Surgical tumor resection has been so far considered the first-line treatment modality for IAF and other localized desmoid tumors. However, a complete tumor excision is usually not feasible. Recurrence of the residual tumor (gross or microscopic) is another characteristic of IAF, and a serious complication, which might necessitate repeated surgical interventions and compromise the prognosis quad vitam. Adjuvant chemotherapy is an option that must be taken into consideration once the tumor is unresectable or takes an aggressive turn [6–9]. Results of radiotherapy for IAF in adolescents and adults have been variable, but it might prove beneficial in some patients [6, 10–12]. Considering the immediate and long-term side effects of of irradiation, this option must be considered as last resort in growing young children [3, 6, 10]. Due to the rarity of IAF in children there is only limited experience with either therapeutic approach. The following report demonstrates the clinical course of such a tumor and the usefulness of chemotherapy as an option in a child with aggressive IAF.

CASE REPORT

A.H.S, a 5-year-old male, complained in March 2002 of malaise and persistent abdominal pain, and presented soon after with a conspicuous mass in the left abdominal flank. After thorough clinical investigations and imaging procedures, including abdominal CT scan and MRI, he underwent an exploratory laparotomy. The well-vascularized tumor proved to be inoperable due to its intra- and retroperitoneal extension and attachment to descending colon, sigmoid, part of small bowel and left renal bed, and infiltration of the aorta, mesentery, and iliac vessels. Therefore, only careful tumor size reduction was carried out. The histopathological study of the surgical specimen indicated fibromatosis (Figure 1). This was confirmed by immunohistochemical findings: positive vimentin, negative smooth muscle actin, S 100, c-kit, and CD34. A.H.S. underwent 3 more laparotomies for recurrent tumor growth and intestinal obstructions. The last laparotomy was carried out in Germany in October 2002 and a short segment of proximal jejunum was removed because of kinking and tumor infiltration. An attempt to reduce the tumor mass surgically failed because of massive hemorrhage from tumoral vessels.

After recovery, A.H.S. was sent home and referred to our department for follow-up. At first presentation in early 2003, he was markedly dystrophic, had

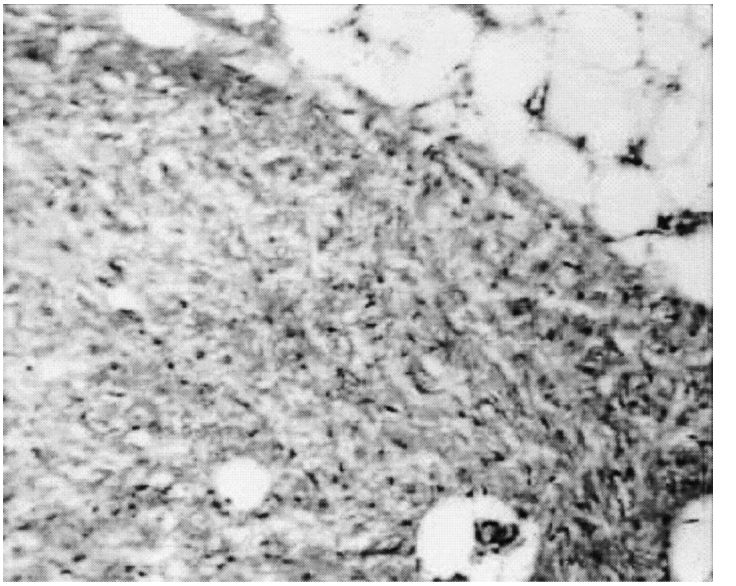

FIGURE 1 Microscopic feature of the mesenteric tumor biopsy.

a protruding abdomen with a firm tumor mass occupying the whole abdominal cavity and engorged superficial abdominal wall veins. In the following months the tumor grew and the patient's general condition deteriorated further. By late 2003, he complained of lassitude, anorexia, orthopnea, and insomnia. He had developed scrotal and pretibial edema. His abdominal circumference measured 87.5 cm and the abdominal MRI demonstrated a huge tumor mass displacing small bowel, compressing liver and spleen and extending into the pelvis (Figure 2). At this point, we decided to carry out a chemotherapeutic trial. This consisted of weekly intravenous vincristin (1.5 mg/m^2) and weekly oral methotrexate (10 mg/m^2). Chemotherapy was

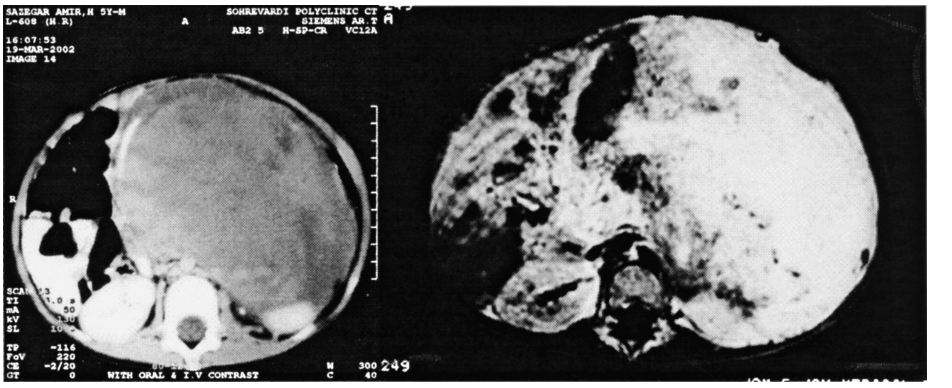

FIGURE 2 Abdominal CT scan and MRI before chemotherapy.

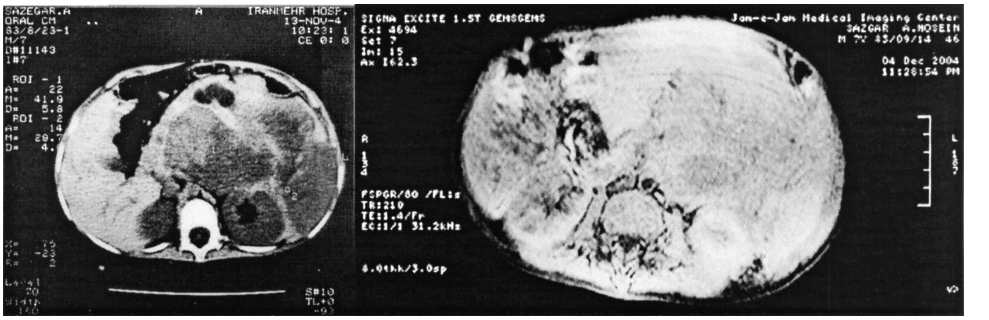

FIGURE 3 Abdominal CT scan and MRI, 9 months after chemotherapy.

commenced in early January 2004 and within a few weeks tumor shrinkage was observed. At the same time, the patient's general condition improved remarkably and respiratory complaints and edema disappeared. A.H.S. now attends elementary school and is physically active. His abdominal circumference measures 60 cm 12 months after beginning of chemotherapy, and the follow-up abdominal MRI demonstrates significant tumor shrinkage with necrotic areas (Figure 3).

DISCUSSION

Intra-abdominal fibromatosis is a rare, benign neoplasm in children. However, in our patient the tumor took an aggressive path, complicated by recurrent intestinal obstructions. Repeated surgical interventions were of only temporary relief. There are few reports about the usefulness of chemotherapy in IAF [3, 8, 9]. The decision to initiate chemotherapy in our patient was made as the tumor expansion accelerated and the patient's condition worsened rapidly. The combination of vincristin and methotrexate proved to be efficient and well tolerated. This regiment can be applied on an outpatient basis and is economically affordable. Follow-up by MRI provides an opportunity to monitor the tumor regression and necrosis accurately [3]. According to current reports, there is no consensus about the duration of chemotherapy and the necessity for maintenance therapy [3, 9] Other cytostatic drugs, such as cyclophosphamide, actinomycin-D, doxorubicin, and vinblastin, have also proved to be effective in controlling tumor growth. Another therapeutic option in aggressive IAF is the application of carboplatin and hyperthermia [1]. Radiotherapy will be of benefit to adolescents and adults with incompletely resected IAF [11, 12]. There is no recommendation to apply radiotherapy in children unless there is a life-threatening condition [3, 10]. In our patient chemotherapy will be continued as long as tumor shrinkage continues and, if necessary, another attempt to excise the remaining tumor tissue will be performed.

Clinically and therapeutically it is important to distinguish between IAF and other childhood desmoid tumors with visceral presentation, e.g., infantile myofibromatosis, juvenile fibrosarcoma, leiomyosarcoma, neurofibromatosis, fibromyxoid sarcoma, and gastrointestina stromal tumor. Accurate differentiation between these rare entities can be done by refined histochemical and immune marker studies [2–4] and appropriate treatment can be initiated [13–17].

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