

Transumbilical laparoscopic treatment of Congenital Infantile Fibrosarcoma of the Ileum

Trattamento trans-ombelicale video assistito di un fibrosarcoma ileale

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Abstract

Congenital-Infantile Fibrosarcoma (CIF) is a malignant mesenchymal tumor representing 10-20% of soft-tissue tumors. Complete surgical resection is generally the treatment of choice.

The most recurrent cytogenetic abnormality was identified as the traslocation $t(12;15)(p13;q25)$, which bears the fusion of *Tel* gene *EVT6* with *TrkC* gene.

This study describes a case of infantile fibrosarcoma of the ileum in a female newborn examined for intestinal occlusion and its laparoscopic treatment.

Introduction

Congenital-Infantile Fibrosarcoma (CIF) defines fibrosarcomas diagnosed at birth or in the early years of life. It is a malignant mesenchymal tumor representing 10-20% of soft-tissue tumors. Soft-tissue tumors, 25% of which are of malignant nature, account for 25% of congenital tumors. 40% of CIFs involve subjects < 3 months of age and can also be diagnosed prenatally. The infantile presentation is less aggressive than CIF in adults; survival rate is 80-

100% and the incidence of metastases ranges between 1% and 13%. Characteristically, most frequent sites of presentations are extremities, head, neck and trunk but unusual anatomical regions such as ovary, mesentery, retroperitoneum as well as gastrointestinal tract have also been described. Morphologically, CIF shows high cellularity, prominent mitoses, necrosis and atypia. Some of its characteristics are similar to Gastrointestinal Stromal Tumors (GIST) and Infantile Myofibromatosis.^{1,2,3,4,5}

Complete surgical resection is generally the treatment of choice for this neoplasm.

This study describes a case of infantile fibrosarcoma of the ileum in a female newborn examined for intestinal occlusion and its laparoscopic treatment.

Case Report

A full term female baby born vaginally developed progressive food intolerance starting from 9 days after birth. Due to suspected SIP abdominal ultrasounds were performed. This excluded hypertrophy of the pyloric region but showed an invagination, not well localized, in the hypogastric region. Conventional bowel enemas could not resolve the clinical situation so US scan was performed after enteroclysis. This allowed observation of the intestinal invagination with thickening of the relevant portion of the intestinal wall. Due to a worsening of the patient's conditions, it was decided to perform trans-umbilical laparoscopic exploration during which it was not possible to observe any invagination; instead, a 2.5 cm solid mass was found in the middle ileum. The mass was totally resected through enlargement of the umbilical incision and termino-terminal direct anastomosis. (Figure 1)

At the time of procedure there was no evidence of pathologic lymph nodes or other intra-abdominal findings. The postoperative period was uneventful.

Pathologic examination of the specimen revealed a pale tan-whitish tumor infiltrating the entire intestinal wall. (Figure 2) (Figure 3)

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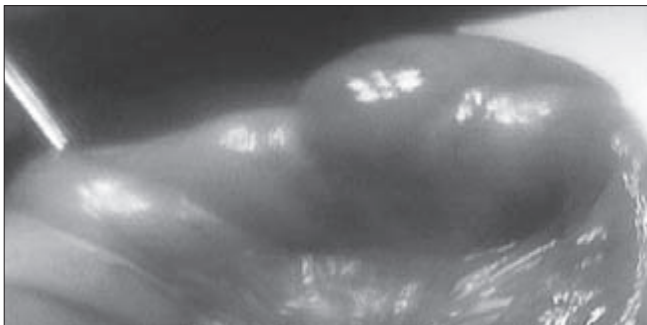


Figure 1.

Intra-operative view

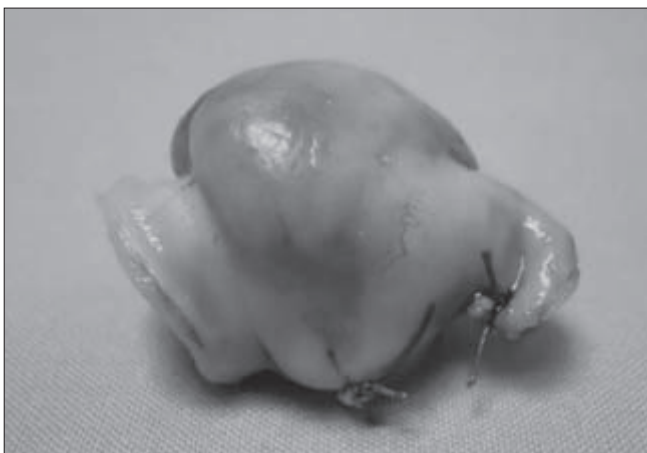


Figure 2.

Macroscopic view of tumor

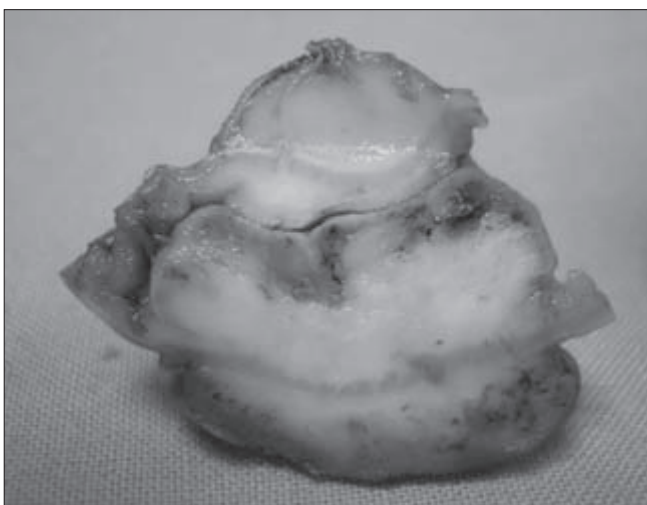


Figure 3.

Section of macroscopic tumor

The tumor was highly cellular and it was composed of spindle cells arranged in diffuse sheets; mitotic activity was high (10x10 HPF) and necrosis was not observed. Immunohistochemistry was done with a large panel of markers: cytokeratin 8-18, vimentin, sm-actin, desmin, β -catenin, CD31, CD34, myoglobin, myogenin, caldesmon, CD99, DOG-1, CD117, S100 protein, HMB45, Podoplanin, EBV-LMP1, HHV8, CMV, CD68, CD56. The tumor showed

positivity only for vimentin, CD34 and β -catenin. Cytogenetic analysis revealed the translocation $t(12;15)(p13;q25)$ bearing the fusion of Tel gene ETV6 with TrkC gene compatible with fibrosarcoma. Margins of resection were disease free. Follow up at 9 months showed good general health conditions and US did not show alterations. (Figure 4)

Discussion

CIF is a rare soft-tissue tumor and it was first recognized by Stout in 1962.^{1,6} It is a rapidly growing and poorly circumscribed tumor and it can infiltrate both superficial and deep soft tissues. Currently literature reports about 200 cases of CIF, most of which diagnosed before 2 years of age with 5-10% found during the neonatal period. This tumor usually presents axial (20% of cases) or limbs (71% of cases) localization. Only few cases report a different localization, such as tongue and oral cavity, ovary, retroperitoneum, chest wall, heart and bowel. Macroscopically CIF varies from a small nodule to large tumor, with a pale tan or fleshy appearance and the consistency varies from firm to soft. Literature reports 6 cases of intestinal CIF, 5 located in the ileum and only 1 located in the colon. In 1975 Shearburn et al reported a case of a 2-month-old girl affected by CIF causing duodenal obstruction, while in 2003 Shima et al reported a case of intestinal perforation with consequent meconium peritonitis in a premature baby born at 34 weeks of gestation due to CIF of the jejunum diagnosed before birth.¹ Also Salem et al in 2008 observed a case of meconium peritonitis in a full-term baby following CIF in the colon.⁴ A M Buccoliero in 2008 described a case of CIF in the form of a 4 cm solid mass in the right colic flexure¹ while in 2010 Van Niekerk described a case of obstructive CIF in the ileum.³ The most recent case was observed in 2011 by Rizkalla H in the form of acute abdomen caused by ileal perforation.⁵

All these cases were treated ONLY surgically: exploratory laparotomy with intestinal resection and anastomosis.

CIF should be distinguished from other causes of intestinal obstruction and other abdominal masses. In particular, it is important to make a diagnosis of exclusion with intestinal duplication cysts, intestinal invagination, neoplasms such as GIST, rhabdomyosarcoma, leiomyosarcoma, MPNST and intestinal myofibromatosis.^{1,3}

In literature only one case presented CIF as a paraneoplastic condition with secretion of parathormone-like substances and consequent hyperkalemia.⁴

In the case reported in this study CIF was a lesion of about 2.5 cm located in the mid-ileum showing intestinal invagination at Ultrasounds.

Histologically, CIF varies from well-differentiated collagen-forming fibrosarcomatous pattern to a highly cellular, non collagenous spindle to oval cell tumor arranged in fascicles or diffuse sheets. There are often several mitosis. At a morphological point of view, the differential diagnosis with spindle cell and poorly differentiated embryonal rhabdomyosarcoma have to be considered, especially in

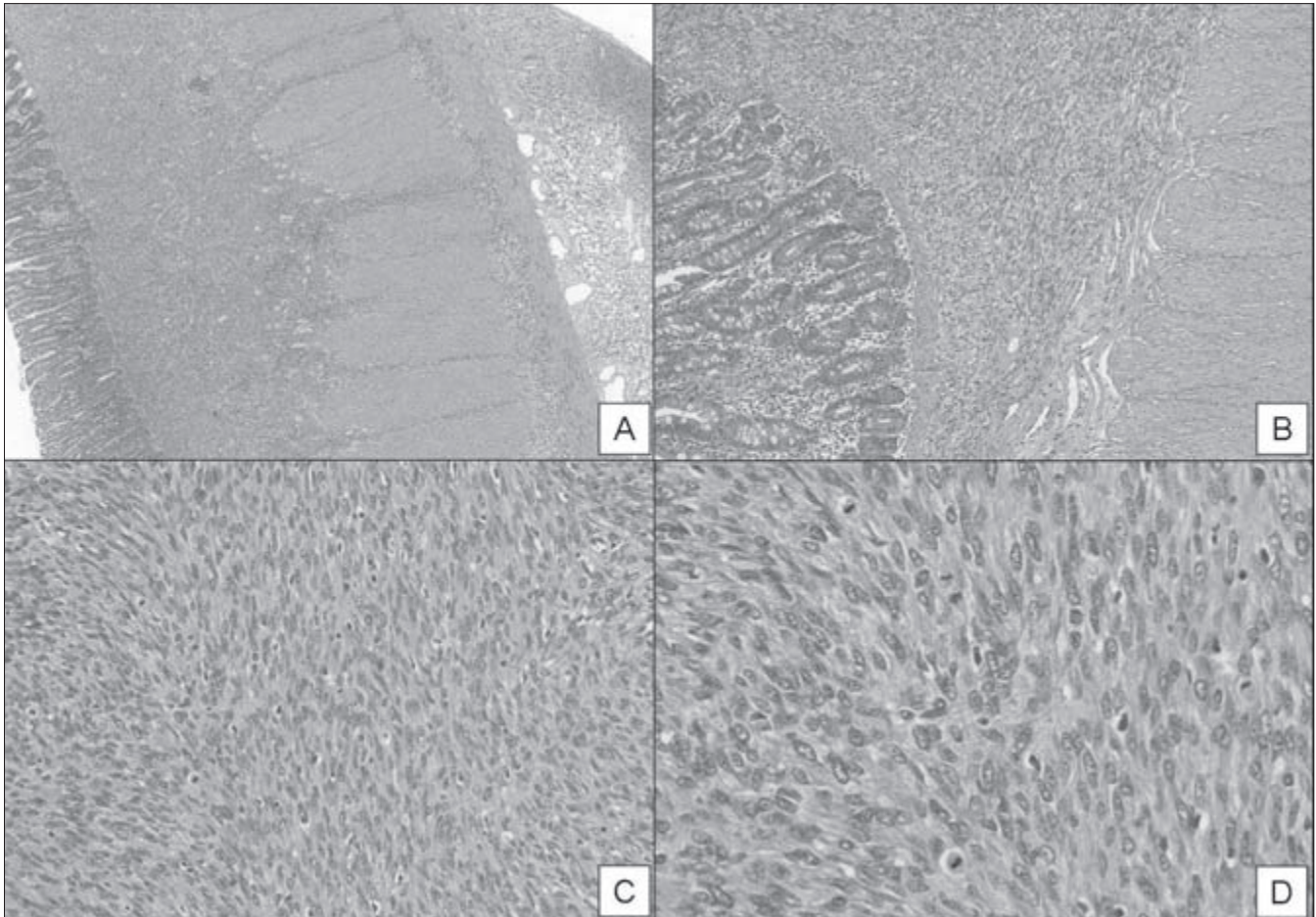


Figure 4.

Microscopic images stain with Hematoxylin&Eosin, showing the tumor at different magnification. 4A. Tumor infiltrate the entire intestinal wall (4x); 4B. Detail showing the involvement of the submucosa (10x); 4C and 4D. High magnification images (20x and 40x respectively) showing the tumor with high cellularity, composed of neoplastic spindle cells arranged in diffuse sheets; mitotic activity was high (figure 4D).

case involving the genital region, pelvis and abdomen. Immunohistochemistry is always required in differential diagnosis of such cases. Other overlapping histological features have been reported between CIF, infantile myofibromatosis and congenital haemangiopericytoma.⁷

Immunohistochemically, CIF is positive for vimentin and variably positive for actins. Some cases show nuclear positivity for β -catenin.⁸ Negative results have been reported for desmin, cytokeratins, EMA and S100 protein.

The most recurrent cytogenetic abnormality was identified as the translocation $t(12;15)(p13;q25)$, which bears the fusion of *Tel* gene *EVT6* with *TrkC* gene.⁹⁻¹⁰

Trisomy of chromosome 11 and variable trisomies of the other chromosomes^{17,20,8,10} also occurred as non-random cytogenetic changes.

Moreover, CIF is histologically identical with but clinically different from adult-type fibrosarcoma (AF) which does not show gene rearrangement. Behavior of AF is more aggressive with easy metastatic spread and poor prognosis. Kihara et al. showed that apoptotic index is higher for IF/CIF if compared to AF while the opposite occurs for cell proliferation index.¹¹

For these reasons diagnosis of CIF outside the usual localizations should include morphological, immunohistochemical, molecular and ultrastructural analyses.

Complete surgical resection is generally the treatment of choice for this neoplasm.

If the margins of resection are disease free, there is no need of either additional chemo or radiotherapy. If resection is not possible because it would affect vital structures or could be mutilant or because it would result in an incomplete procedure, then chemotherapy can be used as adjuvant therapy.

Mignon L et al reported extremely favorable results obtained with the support of adjuvant chemotherapy; also, it is important to remember that the surgical approach may lead to relevant long-term morbidity especially if the tumor is located in specific regions. Adjuvant chemotherapy in the pre-operative stages showed really favorable results if used with different combinations of drugs: regimens have included vincristine, adriamycin and cyclophosphamide (adria-VAC); vincristine, actinomycin-D, and cyclophosphamide (actino-VAC); also etoposide and ifosfamide have been proposed. However, chemotherapy usually requires at least a diagnostic biopsy and this is not always possible to obtain.¹²

The rate of metastases is low (1-13%), although literature reports rare cases of metastases in the liver and lung. Prognosis is usually favorable with long-term survival rate of 90% except for retroperitoneal fibrosarcoma. Close clinical and radiological follow-up is recommended.¹

The case in this study probably shows an unusual situation because the possible presence of neoplasia was never suspected. However, the laparoscopic approach resulted very useful to identify and better understand this condition. Once the suspected neoplasia was identified surgical resection was performed following all the safety measures involved in standard oncological surgery. Histological examination was not performed during surgery because resection removed the mass completely and there were not findings of suspect lymph nodes or other abdominal masses.

In the pediatric age the differential diagnosis between oncologic and malformative pathologies is often difficult to make. For this reason explorative laparoscopy is always suggested in all cases where radiological findings can not give a definitive diagnosis.

References

- ¹ Buccoliero AM, Castiglione F, Degl'Innocenti DR, Maio V, Taddei M, Sardi J, Nocchioli B, Franchi A, Taddei GL. Congenital/Infntile Fibrosarcoma of the colon, morphological, Immunohistochemical, Molecular and Ultrastructural features of a relatively rare tumor in an extraordinary localization. *J Pediatr Hematol Oncol* 2008; vol 30, num 10.
- ² Dumont C, Monforte M, Flandrin A, Couture A, Tichit R., Boulot P. Prenatal management of congenital infantile fibrosarcoma: unexpected outcome. *Ultrasound Obstet Gynecol* 2011; 37: 733-735.
- ³ Van Niekerk ML, Nel WA, Slavik T. Infantile fibrosarcoma of the ileum presenting with congenital bowel obstruction. *J Pediatr Surg* 2010; 45: 461-2.
- ⁴ Salem I, Soldes OS, Ruiz R, Geiger JD. Primary colonic congenital infantile fibrosarcoma presenting as meconium peritonitis. *Pediatr Surg Int* 2008; 24: 621-623.
- ⁵ Rizkalla H, Wildgrove H, Quinn F, Capra m, O'Sullivan MJ. Congenital fibrosarcoma of the ileum: case report with molecular confirmation and literature review. *Fetal Pediatr Pathol* 2011; 30:156-60.
- ⁶ Stout AP. Fibrosarcoma in infants and children. *Cancer* 1962; 15: 1028-1040.
- ⁷ Alaggio R, Barisani D, Ninfo V, Rosolen A, Coffin CM. Morphologic overlap between infantile myofibromatosis and Infantile Fibrosarcoma: a pitfall in diagnosis. *Pediatr Dev Pathol.* 2008 Sep-Oct;11(5):355-62.
- ⁸ Carlson JW, Fletcher CD. Immunohistochemistry for beta-catenin in the differential diagnosis of spindle cell lesions: analysis of a serie and review of the literature. *Histopathology.* 2007 Oct;51(4):509-14.
- ⁹ Knezevich SR, Mc Fadden DE, Tao W, Lim JF, Sorensen PH. A novel ETV6-NTRK3 gene fusion in congenital fibrosarcoma. *Nat Genet.* 1998 Feb;18(2):184-7.
- ¹⁰ Dubus p, Coindre JM, Groppi A, Jouan H, Ferrer J, Cohen C Rivel J, Copin MC, Leroy JP, de Muret A, Merlio JP. The detection of Tel-TrkC chimeric transcripts is more specific than TrkC immunoreactivity for the diagnosis of congenital fibrosarcoma. *J Pathol.* 2001 Jan; 193(1): 88-94.
- ¹¹ Kihara S, Nehlsen-Cannarella S, Kirsch WM, Chase D, Garvin AJ. A comparative study of apoptosis and cell proliferation in infantile and adult fibrosarcoma. *Am J Clin Pathol* 1996;106:493-7.
- ¹² Loh ML, Ahn P, Perez-Atayde AR, Gebhardt MC, Shamberger RC, Grier HE. Treatment of infantile fibrosarcoma with chemotherapy and surgery: results from the Dana-Farber Cancer institute and Children's Hospital Boston. *J Pediatr Hematol/Oncol* 2002; vol 24, n 9.