

Unusual localization and aggressive progression of large infantile fibrosarcoma

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ABSTRACT

Infantile fibrosarcoma is a very rare soft tissue tumor in infants and children most commonly located in extremities. It constitutes less than 1 percent of all childhood cancers. Prognosis and clinical course of it is relatively good compared to adult forms. Local recurrence is common but metastasis is infrequent.

In this case report we present infantile fibrosarcoma with relapse and lung metastasis despite neoadjuvant chemotherapy, pelvic reconstruction surgery with wide surgical excision and adjuvant chemotherapy protocol. The patient was a 2-year-old girl at the time of diagnosis, and there was a huge mass in pelvic region. After neoadjuvant chemotherapy, type 1 pelvic resection and pelvic reconstruction with bone cement performed. The patient presented with relapse and lung metastasis 6 months after the surgery.

This is the first report of pelvic infantile fibrosarcoma with pelvic resection surgery. This case suggests that these tumors may exhibit unpredictable clinical behavior.

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Introduction

Infantile fibrosarcoma (IFS) is a very rare early childhood soft tissue malignancy. The incidence of IFS is 5 cases per one million infants.¹ Tumor is typically found in extremities, followed by head, neck and trunk.^{2,3} Standard treatment is primarily wide surgical excision.³ However if it is impossible, preoperative chemotherapy should be given.⁴ Amputation may be considered as an alternative surgery in patients whose neurovascular structures are invaded by the tumor and cannot be operated with limb-sparing surgery.⁴ Although being histologically similar to fibrosarcomas occurring in adults, the IFS has better prognosis. Metastases are rare compared to the adult type.^{3,4}

The case is presented because of its rare localization and aggressive course with lung metastasis.

Case report

A 2 year-old-girl was referred to our clinic following a pelvic mass prediagnosis after physical and radiologic examination at another clinic. When she came to our clinic, her body weight was 11.3 kg. (3rd-10th percentile) and height was 84 cm. (25th percentile). Physical examination revealed an unclear marginal mass with a solid surface but without local heat nor erythema. Her family had noticed swelling 2 months prior to visiting and had felt pain during palpation on the mass. The mass was extending from her lower back to the right gluteal and proximal lateral thigh. Laboratory analyses included a white blood cell count of 13.40 k/UL. Erythrocyte sedimentation rate and C-reactive protein levels were normal. The thorax computed tomography (CT) scan did not reveal any metastatic nodule. Magnetic resonance imaging (MRI) revealed a solid heterogeneous mass in the right hemipelvis measuring approximately 12×8×8 cm which is centrally cystic and necrotic. The lesion is hypointense in T1-weighted non-fat-suppressed axial images (TR:400.0/TE:10.0) (Fig. 1A), hyperintense in T2-weighted images (TR:4220.0/TE:54.0) and had peripheral contrast in T1-weighted contrast enhanced fat-suppressed coronal images (TR:497.0/TE:11.0) (Fig. 1B). A tru-cut biopsy was performed for diagnosis. After histopathological evaluation the specimen was reported to be inadequate, and open biopsy was thus performed

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Fig. 1. Magnetic resonance imaging (MRI) revealed a solid heterogeneous mass in the right hemipelvis measuring approximately 12×8×8 cm which is centrally cystic and necrotic. The lesion is hypointense in T1-weighted non-fat-suppressed axial images (TR:400.0/TE:10.0) (A) and had peripheral contrast in T1-weighted contrast enhanced fat-suppressed coronal images (TR:497.0/TE:11.0) (B).

under general anesthesia. Histopathologic evaluation deemed, the tumor to be comprised of atypical mesenchymal cells characterized by zonal necrosis, narrow cytoplasm, and nuclei with large vesicles. High proliferative activity was identified by positive staining with Ki67 (90% index). The mitosis index was 36 in each zoom area of 10 and the diagnosis was reported as infantile fibrosarcoma. The patient was evaluated according to the American Joint Committee on Cancer (AJCC) system for staging of soft tissue sarcomas and delineated as stage IIB. Chemotherapy was performed because the tumor's volume was too large for excision. The child received 3 alternate cycles of preoperative VAC (vincristin 1.5 mg/m, actinomycin D 1.25 mg/m, cyclophosphamide 750 mg/m) and 4 cycles of VACA (vincristin 1.5 mg/m, adriamycin 60 mg/m, cyclophosphamide 750 mg/m, actinomycin D 1.25 mg/m) chemotherapy once every three weeks. There was minimal regression in the tumor after neoadjuvant chemotherapy (Fig. 2). After 3 weeks of such protocol, the patient was recommended for surgery.

A type 1 pelvic resection was performed. The tumor was excised with wide margins, including the right ilium (Fig. 3). Following type 1 internal hemipelvectomy with wide margins,

cementation was applied to fill the iliac defect and stabilization of the cementation was achieved by lumbopelvic, iliopubic and ilioischial fixation with plates and screws. Reconstruction was strengthened with a polypropylene mesh to increase hip stabilization and to prevent a possible hip dislocation (Fig. 4). A diagnosis of grade 3 infantile fibrosarcoma was made. The margins were considered negative upon pathology review. The tumor is 10 mm at the closest proximity from the soft tissue surgical margin. Histopathological examination showed macroscopically poorly circumscribed, lobulated, with tan-gray, fleshy cut surface and necrosis (Fig. 5a). Additionally, the tumor is infiltrated with adjacent soft tissue of irregular margins and zonal necrosis (H&Ex40) (Fig. 5b), composed of uniform and moderately atypical spindle cells with oval to fusiform nuclei (H&Ex200) (Fig. 5c), increased mitotic figures (H&400) (Fig. 5d), as well as focal positivity with SMA (x200) and desmin (x200) (Fig. 5e). Immunohistochemical studies revealed, a focal positive staining with Sma, Desmin, CD 34 and CD 68. Minimal positive staining was detected with HHF35 and Factor 13a. Stainings with CK, S100, Myogenin and beta-catenin were negative.

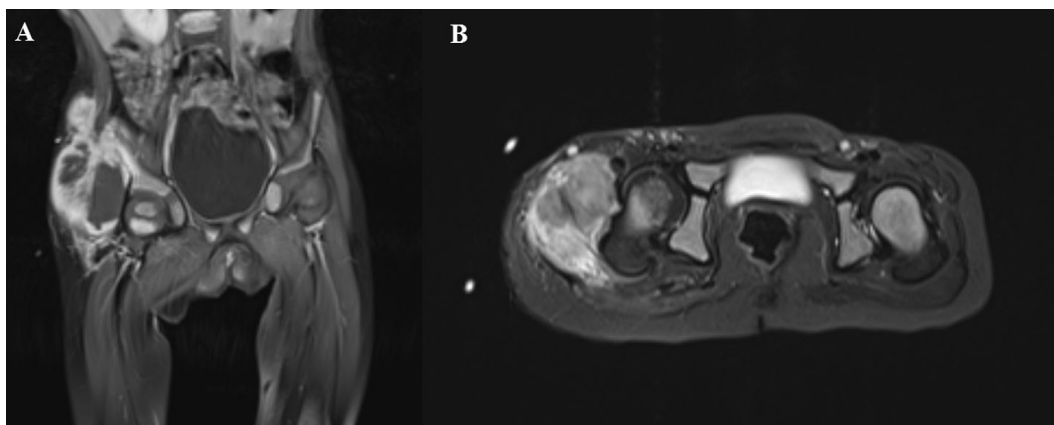


Fig. 2. Postcontrast coronal T1 (TR:497.0/TE:11.0) (A) and T2-weighted fat suppressed axial (TR:4220.0/TE:54.0) (B) MR images revealed that there was minimal regression in the tumor after neoadjuvant chemotherapy.

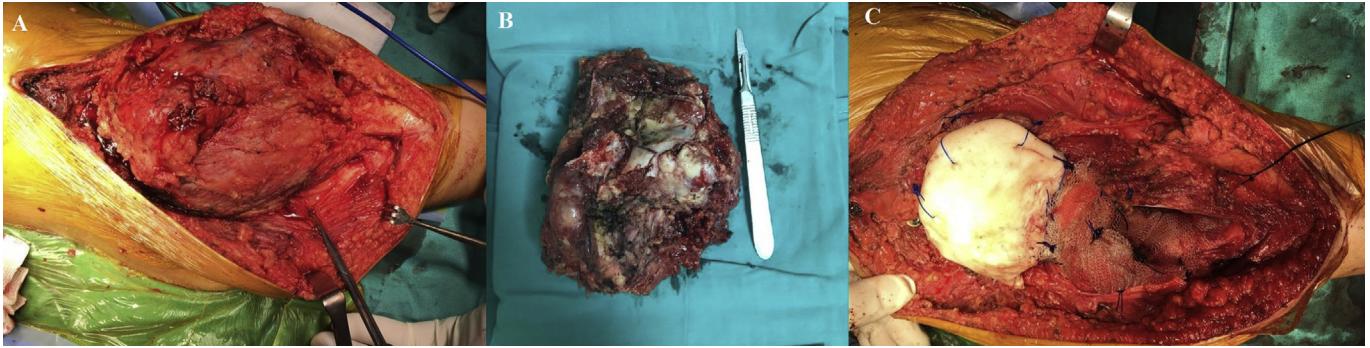


Fig. 3. A: Intraoperative photograph of mass B–C: Gross appearance of the tumor after excision and photograph of reconstruction. Polypropylene mesh was used to increase hip stabilization and prevent a possible hip dislocation.

The child was consulted with the pediatric oncology clinic for adjuvant chemotherapy and received 3 cycles of adjuvant VAC (vincristin 1.5 mg/m, actinomycin D 1.5 mg/m, cyclophosphamide 1000 mg/m) chemotherapy. Taking the minimum time needed for an optimal health status of the patient and adequate wound healing into consideration, the first adjuvant chemotherapy session was planned to be given 2 months after the surgery. Succeeding sessions were planned for every month following the first. The patient was monitored at 1.5 month intervals for postoperative follow-up. Controls revealed that the patient had not been on the chemotherapy protocol as planned due to systemic complications. Six months after the surgery, CT angiography was performed instead of routine MRI evaluation for recurrence because the patient could not tolerate any sedation for MRI due to her poor health status. Radiological findings on CT angiography revealed an irregular confined mass compatible with relapse. The iliac artery and surrounding veins were both invaded by the mass. The thorax CT revealed widespread multiple metastatic mass lesions in both lungs. The largest one was 20×14 mm in the superior segment of the lower lobe of the right lung (Fig. 6). Palliative radiotherapy was planned for relapse with a dose of 1.8 Gy/fraction with 25.2 Gy.

However, the radiotherapy could not be implemented. 9 months after the operation, while the patient was on the third session of adjuvant chemotherapy, she died of cardiopulmonary arrest, with an overall survival time of 3 months from metastasis. A written informed consent was obtained from the parents for publication of this case report.

Discussion

IFS is a rare, soft-tissue mesenchymal tumor that is generally diagnosed within the first year of life.⁵ Although its etiology remains unknown, gene fusion and translocations have been reported.⁶ The common sites of involvement are on the extremities, especially on the foot, ankle, lower leg, hand, forearm and wrist.⁷ Boys are more often affected than girls. IFS is a highly vascular tumor so it may be confused with hemangiomas and hemangiopericytomas.⁸ Clinically, the most common symptom is a local, progressive, necrotic or ulceric mass in distal parts of extremities.⁹

Histologically, IFS presents with some variants. It is a highly proliferative cellular tumor and its considerable vascularity should be distinguished from infantile hemangiopericytoma and

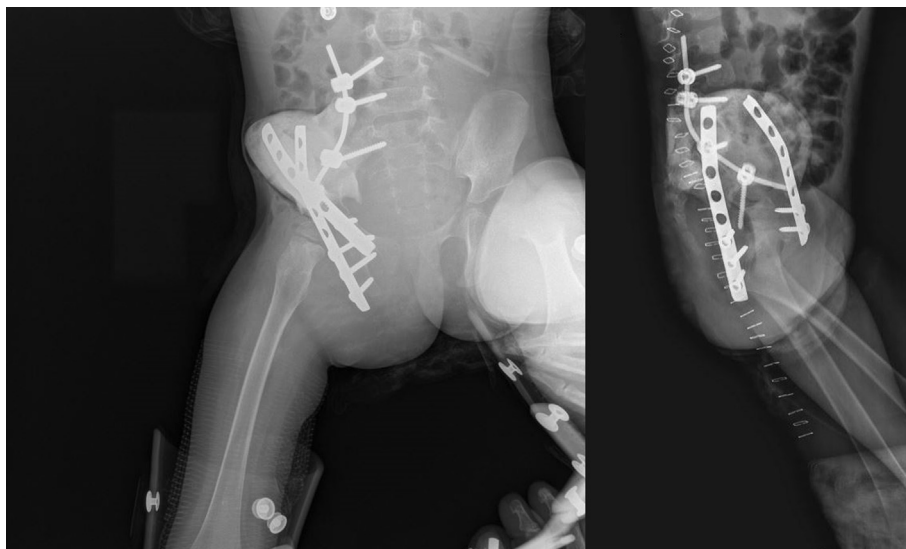


Fig. 4. Postoperative pelvis antero-posterior and lateral radiographs. Following type 1 internal hemiplevectomy with wide margins, cementation was applied to fill the iliac defect and stabilization of the cementation was achieved by lumbopelvic, iliopubic and ilioischial fixation with plates and screws.

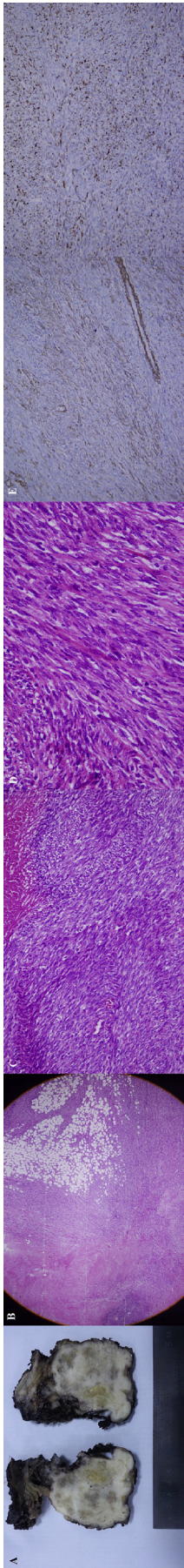


Fig. 5. A: Macroscopic poorly circumscribed, lobulated, with tan-gray, fleshy cut surface and necrosis. B: The tumor is infiltrated adjacent soft tissue with irregular margins and zonal necrosis (H&Ex40) C: The tumor is composed of uniform, moderately atypical spindle cells with oval to fusiform nuclei (H&Ex200) D: Increased mitotic figures (H&Ex200) E: Focal positivity with SMA (x200) and focal positivity with desmin (x200).

myofibromatosis. It may be difficult to distinguish IFS from infantile myofibromatosis because of overlapping morphological features but a translocation, t(12; 15) between ETV6 gene on chromosome 12p13 and NTRK3 gene on chromosome 15q25, as well as the presence of a fusion protein distinguish fibrosarcomas from other forms.^{3,7,10}

IFS does not have a unique MRI appearance. Generally, IFS shows well-demarcated low-signal-intensity masses on T1 weighted images and inhomogenous high-signal-intensity masses on T2 weighted images. Magnetic resonance imaging is a good choice for diagnoses and follow-up and superior to other imaging modalities in the assessment of soft tissue masses.^{3,5,9} In our patient, CT angiography was performed instead of routine MRI evaluation in the follow-up. For sure, this preference shouldn't be interpreted as a routine practise but rather as a medical indispensability because the patient could not tolerate any sedation for MRI due to her poor health status.

IFSs biological behavior is better than of adult counterpart. It has a good prognosis.⁹ The 5-year survival rate is 80–100 percent. Local recurrence is common problem, it is reported nearly 30 percent but metastasis is uncommon.^{9,10} Distant metastasis was reported only in four percent of cases.⁹

Current treatment in IFS involves wide surgical excision or amputation.^{3,4,7,9,10} Preoperative chemotherapy can be useful in patients who have unresectable tumors at diagnosis. If the disease is metastatic at presentation or wide excision is not possible because of tumor volume, then chemotherapy should be considered.¹¹ The role of adjuvant chemotherapy in this disease is controversial because the tumor is so rare that there is no established protocol for comparing the effectiveness of this treatment.¹⁰ In cases of irresectable tumors, recurrences or incomplete surgical resections, chemotherapy is a common adjuvant therapeutic tool.¹² In this case, surgery was followed by chemotherapy because of the huge pelvic mass and due to the insufficient response to neoadjuvant chemotherapy.

When we reviewed the literature, we found extremity localized studies of IFS cases. Tarik et al⁴ reported an IFS located in the left arm and axilla associated with a hand malformation in a new-born female. They performed shoulder disarticulation after chemotherapy. Hamidah et al⁷ reported a full-term infant girl with fibrosarcoma involving her left forearm. They performed neoadjuvant chemotherapy and complete excision of the tumor. They also reported follow-up procedures with their patients with no relapses. Kraneburg et al⁸ reported a large and destructive IFS of the lower leg. They performed a knee disarticulation and reported a follow-up without any local recurrence and metastasis. Hashemi et al⁹ reported a nine-year-old girl with a mass in her left hand. After excisional surgery, the treatment was completed with chemotherapy. Ertürk et al¹⁰ reported a right leg fibrosarcoma, for which they performed wide surgical excision. They referred the patient to a chemotherapy center but her family refused the treatment. Recurrence was observed 12 months later in the leg; then performed an amputation because of the local recurrence.

Pelvic bone tumors has already been reported to be associated with lower survival rates and potentially more aggressive biological behaviour due to difficulty to achieve negative margins, the prolonged diagnostic time periods, larger tumor size and high intra-operative neurovascular complication rates compared to tumors in appendicular skeleton.¹³

We believe that present case report is unique because its pelvic location, huge size and aggressive course with distant metastasis. Despite neoadjuvant chemotherapy, wide excision with negative margins and adjuvant chemotherapy, we detected relapse and distant metastasis after 6 months in our case.

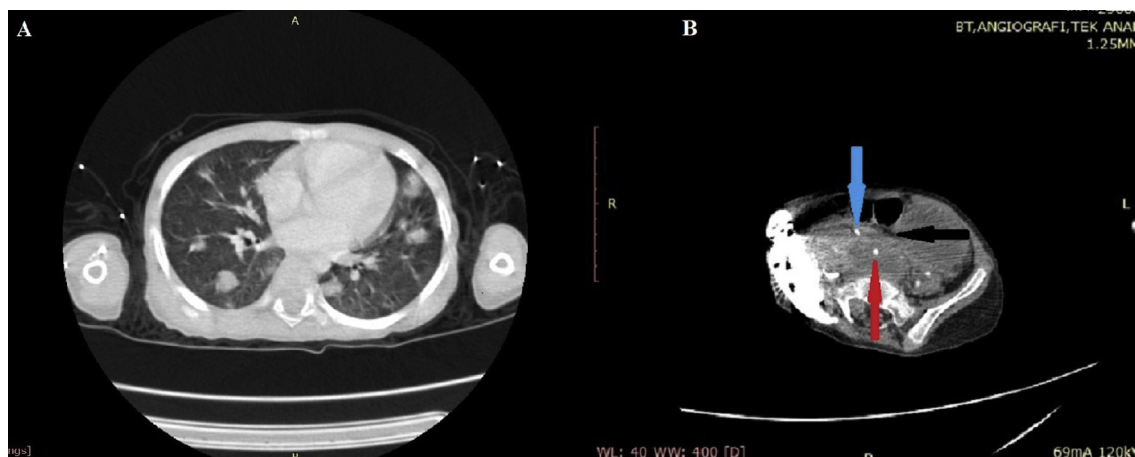


Fig. 6. A: Thorax CT revealed widespread multiple metastatic lesions in both lungs at postoperative 6 months. B: Image of axial CT angiography showed border of irregular mass compatible with relapse (black arrow). The external (blue arrow) and internal iliac (red arrow) arteries were invaded by the mass.

Conclusion

Our case suggests that these tumors may exhibit unpredictable clinical behavior. Although it is known as tumors with good prognosis, the present case shows that it can be quite aggressive.

Funding

None.

Conflict of interest

The authors declare that there is no conflict of interest regarding the publication of this article.

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