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Large Ulcerating Congenital Infantile Fibrosarcoma of the Lower Leg: Case Report and Literature Review

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Abstract

Congenital infantile fibrosarcoma (CIFS) is a rare pediatric soft-tissue sarcoma and is typically detected in children <1 year of age. They usually present at birth but some present late up to the third moth of life. Histologically composed of relatively uniform spindle-shaped cells often organized in a herring-bone pattern, with a range of mitotic activity and differentiation.

Keywords: Congenital; Tumours; Gene fusion

Background

Well-differentiated tumors are typically composed of slender, elongated cells while poorly differentiated tumors have more round cells and tend to have less collagen deposition [1-3]. CIFS is highly associated with (12;15) (p13;q25) translocation, which creates an ETV6/NTRK3 gene fusion, although ETV6/NTRK3 fusion negative cases also have been described [4,5].

Case Presentation

A 45 days old full-term boy presented with a large mass over the right leg. He was born by normal vaginal delivery 40 weeks after uncomplicated pregnancy. At the time of delivery, he was noted to have approximately 5 × 5 cm mass on his right leg. Initially it was misdiagnosed and treated conservatively as congenital hemangioma. However, the mass had rapidly increased in size, upon presentation examination show a firm, non-pulsatile mass approximately 15 × 10 × 10 cm in size, with an overlying skin telangiectasia and tortuous subcutaneous veins (Figure 1A). There was no lymph node swelling in the inguinal region. Musculoskeletal ultrasound revealed huge mass involving almost all flexor compartment of the leg with scattered necrotic zone. Mass was negative on Doppler study. MRI revealed a large, well-defined intramuscular mass replacing the muscles of the entire calf and extend beyond the knee joint, mass was heterogeneous with area of high T1? Hemorrhage, high T2 necrosis and enhancing solid mass completely encasing the neurovascular bundles (Figure 1B). The MRI findings were interpreted as being consistent with rhabdomyosarcoma. A biopsy was performed to ascertain the diagnosis. The histopathological examination showed dense cellular neoplastic spindle cells arranged in short interlacing fascicles with mild pleomorphism, and frequent mitoses. Immunohistochemistry stains were negative for SMA, myogenin and CD34, and positive for vimentin, scattered view cells show immune reactivity for S100. Based on these findings, a diagnosis of CIF was made. A staging with CT scan of the chest was performed and revealed (2 mm) nodules within the left upper and right lower lobes the rest is unremarkable. Her initial full blood count also showed hemoglobin of 6.3 g/patient receive packed RBCs before surgery. Above knee amputation was done, resection margin was involving with tumor the child was kept on close follow-up only, patient currently on remission with no evidence of local recurrence.

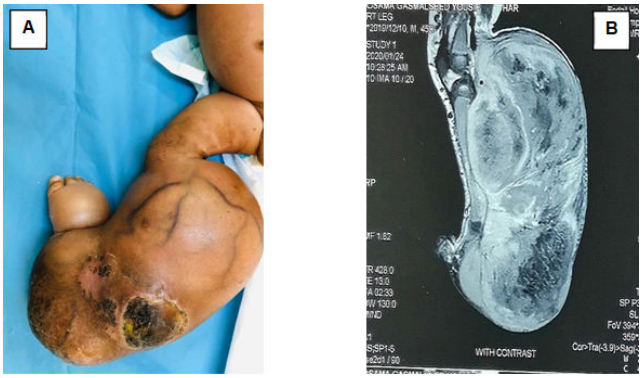

Figure 1: (a) Appearance of the distal limb before surgery, show approximately 15 × 10 × 10 cm mass with an overlying skin telangiectasia and tortuous subcutaneous veins. (b) Preoperative MRI studies revealed a large, well-defined intramuscular heterogeneous mass replacing the muscles of the entire calf and extend beyond the knee joint.

Discussion

Congenital infantile fibrosarcoma (CIFS) is a rare pediatric soft-tissue sarcoma and is typically detected in children <1 year of age [1,2]. Although 40% present of the cases present at birth some present late up to the third moth of life, as well as the antenatal period [3-7]. With some rare cases reported late in childhood [8], CIFS most frequently occur in the extremities with lower limbs more often affected than upper limbs [1,9]. But it also has been reported in the trunk and other extra skeletal locations [10-12]. Clinically, CIFS is classically presents

at birth or shortly after as a growing mass that progressively enlarges into a firm, shiny tumor, often ulcerate and fixed to underlying tissues, as in our case [13]. CIFS is usually slow-growing, and tends to be more benign than fibrosarcoma in older children, which behaves more like the type found in adults although they are histologically similar [14]. Large ulcerating tumor early in life (Table 1) can present with significant hemorrhage or disseminated intravascular coagulopathy requiring emergency resuscitation [15]. The incidence of metastatic spread of disease is 5%-8%, rises to 26% when considering patients with axial tumors [16]. The organs commonly affected in metastasis are the lungs and lymph nodes. Metastatic disease may be verified on fluorodeoxyglucose positron emission tomography [17]. Being vascular lesions, in addition to occasional cutaneous clinical presentation, CIFS may mimic vascular lesions on clinical grounds and in ultrasound evaluation, most frequently misdiagnosed as an infantile hemangioma or congenital hemangioma, contributing to a delay in diagnosis and treatment as was seen in the present case [18]. Other common differential diagnosis includes spindle cell rhabdomyosarcoma, infantile myofibroma and dermatofibrosarcoma protuberans may also resemble CIFS clinically and histologically.

While there are no particular imaging findings to differentiate CIFS from other soft tissue tumors, MRI can often help to discriminate CIFS from benign vascular lesions, and is important for defining the extent of the lesion [19]. Furthermore, histologic evaluation remains critical for the early detection of CIFS, and FISH for The ETV6/NTRK3 gene fusion plays a vital role in uncovering the correct diagnosis and ultimately the proper therapy when microscopic appearance is equivocal. Histopathologic characteristics include a solid, dense proliferation of spindle cells in interlacing bundles; positive for vimentin, and occasionally for desmin, SMA, and cytokeratin [20]. Our case it was positive for vimentin, and negative for SMA, and myogenin, in addition to positive immune reactivity to S-100 protein. We could not test for the ETV6-NTRK3 gene fusion due to technical resource constraints. ETV6-NTRK3 transcript was present in 87.2% of patients where the investigation was performed by the European Pediatric Soft Tissue Sarcoma Study Group [21]. Previously, therapy for CIFS consisted primarily of surgical resection, often necessitating amputation in patients with extremity involvement [22]. Both neoadjuvant and adjuvant chemotherapies have been used to reduce the risk of metastasis [23-25]. Recently, dual neoadjuvant therapy with vincristine actinomycin-D has been shown to be effective in a conservative, multidisciplinary approach to preserve functionality in the involved tissues by avoiding mutilating surgery [21]. Wide local excision, without any mutilating surgery, is the mainstay of management [26]. In cases of huge tumor size, where functional or anatomical derangement might jeopardize the quality of life in these children, neoadjuvant chemotherapy with vincristine and actinomycin-D (VA) might prove beneficial [6,27]. In cases, where a tumor-free margin is achieved, close follow-up without any adjuvant chemotherapy is sufficient.

Although the role of adjuvant chemotherapy has not been established, chemotherapy has been used postoperatively in cases with positive surgical margins or with residual tumor [24,28]. The European Pediatric Soft Tissue Sarcoma Study Group (Intergroup Rhabdomyosarcoma Study; IRS) has developed conservative treatment recommendations according to initial resectability of the tumor [21]. Initial surgery is suggested only if possible without mutilation. Patients with initial complete (IRS group I/R0) or microscopic incomplete (group II/R1) resection have no further therapy. Patients with initial inoperable tumor (group III/ R2) receive first-line VA chemotherapy. Delayed conservative surgery is planned after tumor reduction. Aggressive local therapy (mutilating surgery or external radiotherapy) is discouraged. The VA regimen is recommended as the first-line therapy in order to reduce long-term effects [21]. The risk of Local recurrence is considerably high, being 17%-43% of patients after conservative surgery alone [29]. Fortunately, they are usually treatable and rarely metastasize; with a reported curative rate of greater than 80% [30]. In the present case, complete gross excision with microscopic incomplete (group II/R1) tumor resection was the result of surgery the child was kept on close follow-up only, no evidence of local recurrence until date.

References	Gender	Age	Location	Size, cm	Surgical procedure	Chemotherapy	Outcome
Salman et al. [30,31]	Male	2 months	Left arm	8.3 × 5 × 2.7 cm	Gross resection	Neo-adjuvant, VAC; 2 cycles	In remission at 3 years of treatment
Kraneburg et al. [13]	Male	36 w	Left lower leg	11.8 × 9.3 × 8.5 cm	Knee disarticulation amputation	No	In remission at 2 years old
Dumont et al. [7]	Male	Prenatal	Right leg	10.7 × 7.3 × 8.6 cm	Leg amputation	No	Died at day 8 of life
Kerl et al. [32]	Female	Newborn	Left elbow	10 cm (in diameter)	Resection	Yes, VAC; 9 cycles	In remission at 4 years old
Duan et al. [33]	Male	4 days	Left forearm, recurrent	8 × 7 × 6 cm	Resection; Amputation at Supracondylar level at	No	In remission

					Recurrence		
Hashemi A et al. [8]	Female	9 year	left hand recurrent	4 × 5 cm	Resection	Yes oncovin, actinomycin	In remission
						and endoxan.	
Hamidah Alias [15]	Female	7-week	right arm	6 × 5 × 7	Resection	Yes, Yes, neo- adjuvant VAC; 5 cycles	In remission at 3 years
				cm		postopraive	

Table 1: Case report of large CIFS of extremity.

Conclusion

In conclusion, CIFSs should be kept in the differential diagnoses of soft tissue tumors in infants, even in congenital cases. The clinical picture is similar to some more common lymph vascular malformations which might lead to misdiagnosis. Surgical resection still the main treatment option aiming for complete excision. However, chemotherapy does have a good response and can be considered to avoid Aggressive local therapy (mutilating surgery or external radiotherapy). Overall survival in these tumors is excellent.

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