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Dermatofibrosarcoma Protuberans Masquerading as Vascular Anomaly: A Diagnostic Challenge in Pediatric Patients

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Abstract: ***Soft tissue sarcoma in pediatric patients, particularly dermatofibrosarcoma protuberans (DFSP), poses a diagnostic challenge due to their clinical resemblance to other vascular lesions. This retrospective study analyses pediatric sarcoma cases, including 4 misdiagnosed DFSP cases initially treated as hemangiomas. Patient 1, a 10-year-old boy, exhibited aggressive DFSP progression despite surgical intervention, leading to a fatal outcome. Patient 2, a 10-year-old girl, experienced DFSP recurrence after initial surgery, declining further intervention and remaining alive with the disease. Patient 3, a 5-month-old boy underwent multiple surgeries due to recurrent DFSP, ultimately leading to a modified Chopart amputation. These cases highlight the critical importance of accurate diagnosis through biopsy before surgical intervention in pediatric vascular lesions. Enhanced clinical awareness and vigilance are imperative to differentiate DFSP from other conditions, ensuring appropriate treatment strategies and improved patient outcomes.***

Keywords: Soft tissue sarcoma, Dermatofibrosarcoma protuberans, Vascular anomaly

1. Introduction

Soft tissue sarcoma constitutes a diverse category of extra-skeletal mesenchymal malignancies. The occurrence of soft tissue sarcoma in the pediatric population is notably rare, accounting for approximately 10%(1,2). Among the varied tumors observed in this age group, infantile hemangioma is one of the common tumors. Unlike many other tumors, hemangiomas lack specific clinical characteristics and growth patterns(3). Consequently, certain lesions may mimic hemangiomas, namely kaposiformhemaioendothelioma, dermatofibrosarcoma protuberans (DFSP), infantile fibrosarcoma, and infantile myofibroma(4). This results in a diagnostic challenge. These mimickers offer differing prognosis, underscoring the critical importance of early and accurate diagnosis for appropriate management strategies.

2. Methods and Patients

This is a retrospective study. We analyzed patient records spanning the period from 2011 to 2022 within our institute. Our focus was on pediatric patients diagnosed with various forms of sarcomas. Among the cohort, a total of 57 cases were identified with skeletal sarcomas, comprising 35 cases of osteosarcoma and 22 cases of Ewing sarcoma. Additionally, six patients were diagnosed with soft tissue sarcoma, including one case of rhabdomyosarcoma, one teratoma, and four instances of DFSP.

Upon further analysis, we identified 4 cases of DFSP initially misdiagnosed and treated as hemangioma due to the absence of typical clinical features. Subsequent evaluation led to the re-identification of these lesions as dermatofibrosarcoma protuberans (DFSP). This observation underscores the intricate diagnostic challenges associated with DFSP and underscores the critical importance of enhanced clinical awareness and vigilance in distinguishing these lesions. Thus, this study aims to delve into the intricate clinical challenges encountered in the diagnosis of DFSP, helping the clinician to differentiate DFSP from other similar conditions.

3. Result

Table 1: Patient summaries initially diagnosed as hemangioma, reassessed and identified as DFSP

Patient / Sex	Age at 1st presentation	Age: Referred in HKL / DFSP diagnosis	Parents' input on lesion	Site	Clinical differential diagnosis	Treatment	Oncological outcome
1 / Male	10 years old	13 years old	Noted since childhood as blueish indurated lesion	Left thigh	Infected hemangioma	Wide local excision with free anterolateral thigh flap	Intra-abdominal and pelvic tumour recurrence at 17 years old, passed away due to post operative complication
2 / Female	3 years old	10 years old	"Dimple" like lesion since birth	Dorsum of left foot	Hemangioma	Parents currently still refused oncological intervention	Alive with disease – On surveillance
3 / Male	5 months old	2 years old	Blueish discoloration	Dorsum of left foot	Hemangioma	Modified chorpart amputation	Disease free survival – On surveillance
4 / Male	13 years old	17 years old	Indurated lesion noted at 13 years old	Left thigh	Hemangioma	Wide local excision	Disease free survival – On surveillance

Patient 1

In this case, a 10-year-old boy presented with a longstanding blueish induration on the left thigh since childhood. Initially, he was diagnosed with an infected hemangioma and surgically excised. However, recurrence prompted a referral to our center at the age of 13, manifesting as a fungating mass. A subsequent biopsy was performed, and histopathological examination revealed DFSP. The patient underwent extensive treatment involving wide local excision and soft tissue reconstruction utilizing a free anterolateral thigh flap. Despite the initial intervention, the disease exhibited aggressive behavior, leading to intra-abdominal and pelvic tumour recurrence at the age of 17. Unfortunately, the patient succumbed to the disease's progression.

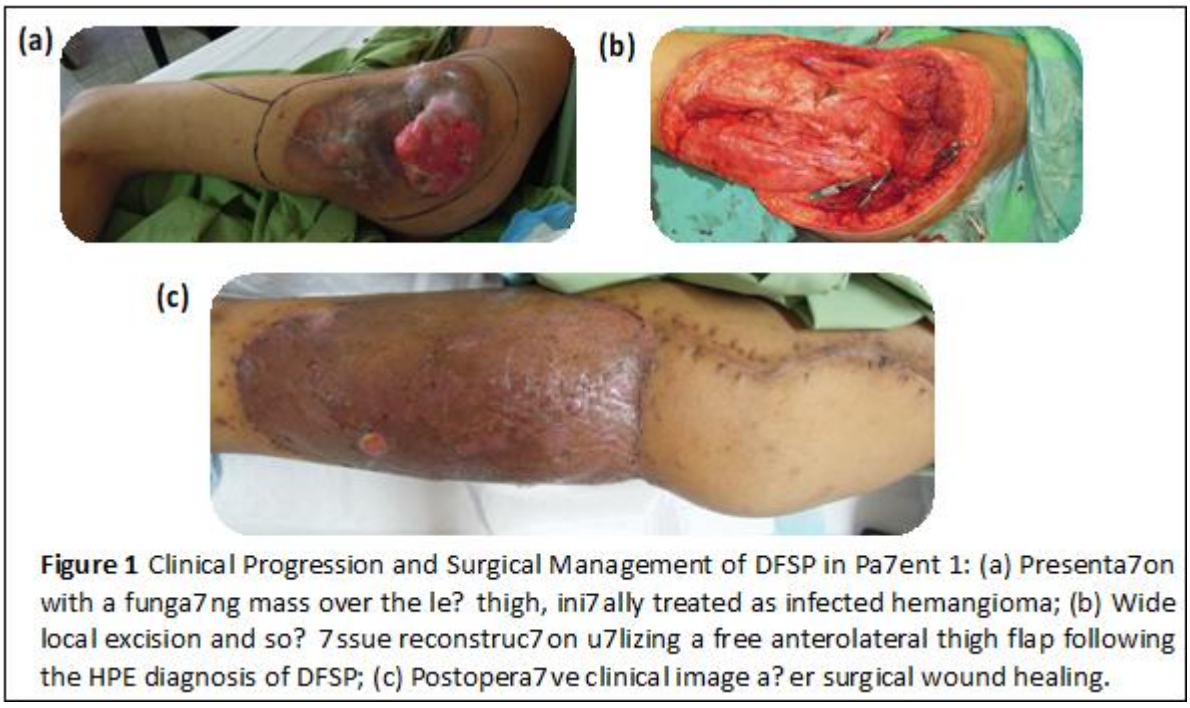

Figure 1 Clinical Progression and Surgical Management of DFSP in Pa7ent 1: (a) Presenta7on with a funga7ng mass over the le? thigh, ini7ally treated as infected hemangioma; (b) Wide local excision and so? 7ssue reconstruc7on u7lizing a free anterolateral thigh flap following the HPE diagnosis of DFSP; (c) Postopera7ve clinical image a? er surgical wound healing.

Patient 2

A 10-year-old girl whose parents have observed a "dimple" at the dorsum of the left foot since birth and gradual growth had been noted since the age of 3. Initially, the patient was diagnosed with hemangioma and underwent surgery at the age of six. The HPE was reported as epithelioid hemangioendothelioma. However, a year post-surgery, the swelling recurred, leading to a second surgical procedure. The histopathological examination at this stage indicated DFSP with involvement of the surgical margin. Consequently, the patient was referred to our center for further management. Subsequently, imaging assessments, including an MRI of the left foot identified a residual tumour lesion within the surgical site. Surveillance CT scans revealed no evidence of distant metastases. Regrettably, the parents declined further surgical intervention. At present, the patient remains alive with the disease and is under surveillance.

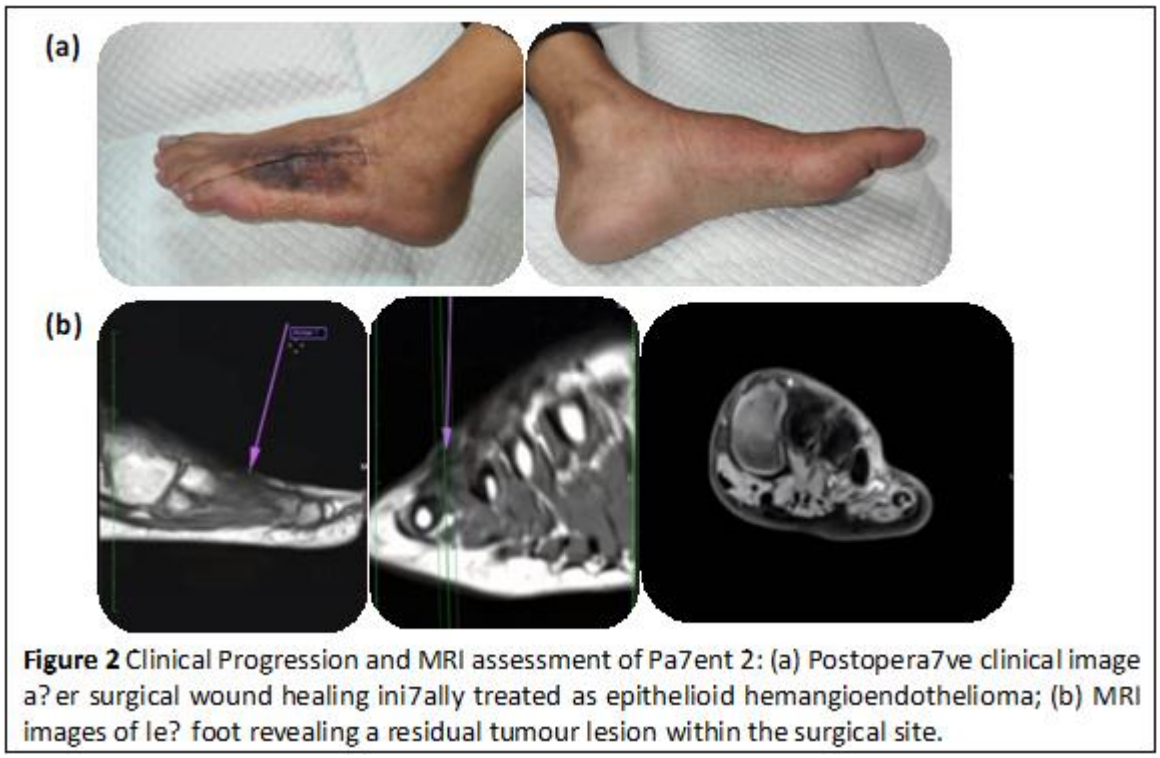

Figure 2 Clinical Progression and MRI assessment of Pa7ent 2: (a) Postopera7ve clinical image a?er surgical wound healing ini7ally treated as epithelioid hemangioendothelioma; (b) MRI images of le? foot revealing a residual tumour lesion within the surgical site.

Patient 3

A 5-month-old boy presented with a bluish discoloration on the dorsum of his left foot since birth, accompanied by a progressively enlarging swelling. An initial ultrasound examination revealed characteristics consistent with a venous malformation. The patient was closely monitored until the age of 2 years when the swelling continued to enlarge. Subsequent MRI revealed an avidly enhanced mass on the dorsum of the left foot, suggesting a hemangioma. Patient was diagnosed as an infected vascular lesion. Surgical excision of the swelling was performed, but an unexpected finding emerged upon histopathological examination, indicating DFSP. The patient was subsequently referred to our institute for further management. Following the initial excision, recurrence transpired within a few months, necessitating a wide resection. Despite this intervention, the swelling recurred 6 months later, leading to a ray amputation. Unfortunately, the recurrence persisted prompting a modified Chopart amputation. Presently, the patient maintains ambulatory function, demonstrating the ability to run and jump. Encouragingly, he remains disease-free under surveillance.

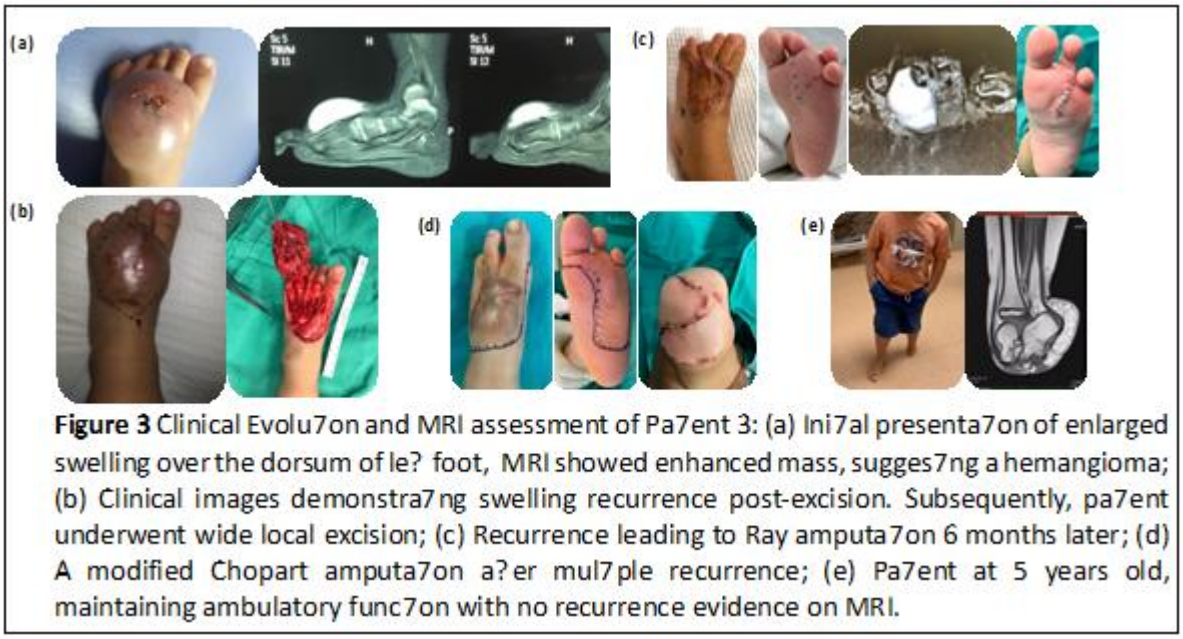

Figure 3 Clinical Evolu7on and MRI assessment of Pa7ent 3: (a) Ini7al presenta7on of enlarged swelling over the dorsum of le? foot, MRI showed enhanced mass, sugges7ng a hemangioma; (b) Clinical images demonstra7ng swelling recurrence post-excision. Subsequently, pa7ent underwent wide local excision; (c) Recurrence leading to Ray amputa7on 6 months later; (d) A modified Chopart amputa7on a?er mul7ple recurrence; (e) Pa7ent at 5 years old, maintaining ambulatory func7on with no recurrence evidence on MRI.

4. Discussion

Dermatofibrosarcoma protuberans (DFSP) stands as a rare soft tissue sarcoma characterized by its fibrohistiocytic origin (4). Despite its rarity, it poses significant clinical challenges due to its locally aggressive nature and propensity for recurrence (3,5). While the incidence in both adults and children is low, McKee et al shed light on its

prevalence. In their analysis of 36 DFSP cases, 5.9% were identified in patients below the age of 13, underscoring the presence of this condition in the pediatric demographic (6).

A supernumerary ring chromosome is found in DFSP. A unique fusion between platelet derived growth factor B (PDGFB) and the COL1A1 gene on chromosomes 22 and 17 is identified by cytogenetic analysis(7). This fusion is specific to DFSP (t(17;22)(q22;q13)) and expressed in 90% of patients with DFSP. The PDGFB and COL1A1 fusion are thought to upregulate PDGFB expression which will activate the RAS mitogen-activated protein kinases and PI3K-AKY-mTOR in intracellular cell cycle signaling pathways and stimulate cell growth (8). This fusion has a low amplifying rate hence the slow-growing nature of DFSP(8). About 8% of patients do not carry t(17;22)(q22;q13) fusions(8). Other rare translocations such as t(2;17)(q33;q35), 11t(x,7)(q21.2;q11.2), 12t(5;8)(q14;p21) and t(9;22)(q32;q12.2) have been reported(8).

DSFP predominantly manifests on the trunk, followed by occurrencesin the proximal extremities and then the head and neck region (4, 6). Remarkably, its onset can be traced back to infancy, emphasizing its early emergence(5). At our institutional cohort, patients consistently reported the presence of swelling sine birth or early childhood, aligning with existing literature. Notably, the lesions were localized on the thigh and foot, with two cases identified each site. This variation in lesion location adds to the complexity of DFSP manifestations and highlights the need for more precise diagnostic approaches in diverse anatomical regions.

The diagnostic process of DFSP is inherently complex owning to its inconspicuous clinical presentation. Typically appearing as a painless, solitary, and indurated nodule, often exhibiting pink or blue, characteristic that are shared with benign lesions (9, 10). Its slow growth rate and painlessness further obscure its malignant potential. This clinical resemblance often confounds differentiation between DFSP, hemangioma, or vascular malformation based solely on physical examination, leading to potential misdiagnosis and delayed treatment initiation(4,11). In our experience, the atypical clinical presentation led to all referred patients being initially treated as hemangioma, which further highlighting the challenges encountered.

Clinically, DFSP often presents as an indolent lesion, yet its deceptively benign appearance masks its potential for aggressive local invasion. This aggressive behavior significantly elevates the risk of local recurrence(4,8,12)Our series mirrors this trend, with three patients referred to our institutionfollowing local recurrence after the initial surgical excision, originally misdiagnosed as hemangioma.

To overcome these challenges, clinicians rely on various imaging modalities. Plain radiographs typically show an unmineralized nodular mass. T1 weighted MRI depicts a well-defined lesion, often displaying areas of high signal intensity indicative of hemorrhage. The T2-weighted MRI sequences exhibit signals higher than fat. Post-gadolinium contrast-enhanced images highlight lesion enhancement, aiding in differentiation.

Despite these imaging insights, biopsy remains the gold standard for definitive diagnosis. Histopathological examination of DFSP specimens demonstrates an infiltrating subcutaneous lesion characterized by collagenous or myxoid stroma. Distinctive intersecting fascicles of spindle cells form a storiform “cartwheel” pattern, a hallmark feature aiding in accurate identification (12). Immunohistochemical staining (IHC) plays a pivotal role, with DFSP typically exhibiting positive CD34 expression (13). Conversely, it shows negativity for CD31, S100, and factor XIIIa further confirming the diagnosis (13). The combination of clinical, imaging, histopathological, and immunohistochemical assessment is crucial for the accurate and timely diagnosis of DFSP.

The management of DFSP remains to achieve wide local resection, serving as the fundamental approach to treatment (10). Despite its seemingly benign nature, DFSP exhibits a distinct proclivity for recurrence, often manifesting after a substantial period of latency. Additionally, it displays both local invasiveness and low potential for metastatic spread, necessitating comprehensive therapeutic strategies to mitigate its progression. While radiotherapy as adjuvant therapy in DFSP management, especially in cases featuring a positive surgical margin or inoperable cases (14,15).

In recent years, targeted immunotherapy has introduced novel therapeutic avenues, particularly the use of tyrosine kinase inhibitors as a viable medical treatment option. One such inhibitor is Imatinib, which effectively inhibits the activation of PDGFB receptors (4, 15). This treatment finds its relevance in cases where surgery poses challenges or proves unfeasible, as well as in the context of metastatic tumors. Additionally, it serves as neoadjuvant therapy for managing large tumors, enhancing the prospects of a successful surgical outcome (15).

5. Conclusion

DFSP is a rare occurrence in the pediatric population, presenting a unique diagnostic challenge owing to its clinical resemblance to vascular anomalies. Given this diagnostic complexity, any vascular lesion displaying atypical clinical features or behavior mandates a biopsy before contemplating any surgical intervention. This cautious approach ensures accurate diagnosis and guides the subsequent implementation of appropriate and effective treatment strategies ultimately improving patient outcomes.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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