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Case Report

Paediatric Lipoblastoma of the Extremities

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Abstract

Paediatric lipoblastomas are rare benign lesion arising in areas of embryonic fat tissue of the body. Their presentation in the extremities has been documented in single sae reports and small case series thus the exact prevalence for the orthopaedic surgeon is unknown. When an 18-month-old boy with a painless mass of the left calf presented in the emergency department, imaging studies revealed a homogenous mass with benign characteristics. Complete resection was diagnostic for lipoblastoma which lead to a review in the current literature regarding these lesions in the paediatric population. This minireview focuses on the differential diagnostic steps and prevalence paediatric lipoblastomas of the extremities.

Keywords: *Paediatric Lipoblastomas (PLs); Adipose Tissue*

Introduction

Paediatric Lipoblastomas (PLs) are rare benign lesions arising from embryonic fat tissue usually located in areas of abundant adipose tissue [1]. Representing 4 - 5% of pediatric adipose tumors, they present as painless growing or persistent well identified masses [2,3]. When reviewing the literature PLs demonstrate a slight male predominance in infants and children [4-6]. Complete surgical resection is the treatment of choice but may be challenging due to location or size. As a result, recurrence rates vary from 9 to 25% [4,7]. Unfortunately, statistics are only available for PLs throughout the body not specifically the ones located in the extremities. Thus, their exact prevalence for the orthopaedic surgeon is unknown.

There are two variants of lipoblastoma: a superficial, localized and encapsulated lesion -lipoblastoma and an infiltrative, non-capsulated, diffuse form- lipoblastomatosis [5]. Both, demonstrate a spectrum of cellular differentiation and maturation with primitive mesenchymal cells, lipoblasts, mature adipocytes and spindle cells [1,8].

Through a case treated in our department we came across a well-defined left calf lesion which demonstrated benign characteristics but could not be differentially diagnosed from liposarcoma. Complete resection was mandatory in order to define the histological signs of lipoblastoma while the rare location lead to a review of the current literature on PLs located in the extremities and identify the main differential diagnostic steps from lipoblastomatosis and liposarcomas.

Case Report

An 18-month-old male presented to the emergency department of our institution with his parents due to a painless mass in his left calf. They stated that the mass appeared the last 2 days and did not affect the baby's gait or movement. On clinical examination the mass was well defined, painless with no signs of inflammation. The child was in excellent general condition, afebrile with normal blood tests.

An anteroposterior and lateral radiograph of his right tibia was performed. Both views revealed a soft tissue prominence at the site of the lesion which did not seem to affect the bone. Ultrasound was additionally available revealing a homogenous and hyperechoic mass of the left calf. Unfortunately, liposarcoma could not be excluded thus, MRI imaging was ordered.

On magnetic resonance a lobular 6 x 3.5 x 2.6 cm mass in the left calf between the flexor hallucis longus and soleus muscles was identified. The tumor expressed high signal intensity in both T1 and T2 weighted images while fat suppression sequencing on T1 revealed an adipose tumor with benign characteristics (Figure 1). Lipoblastoma was the most probable diagnosis, but histopathologic examination of the lesion was mandatory for definitive diagnosis. Complete excision of the lesion was performed, and the post-surgical course of the patient was uneventful.

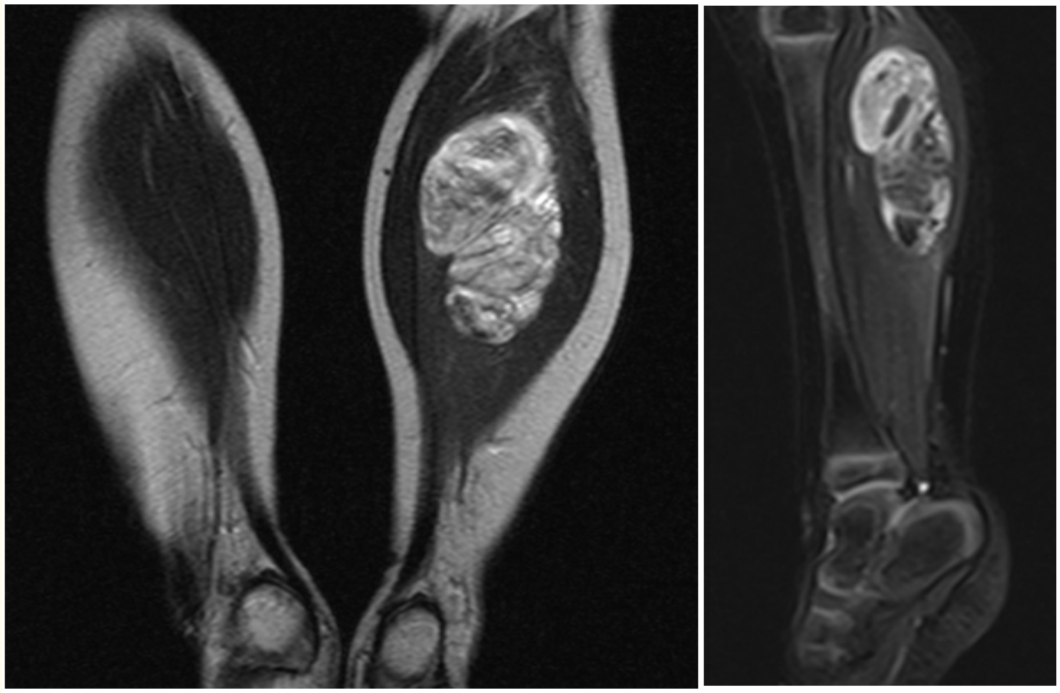
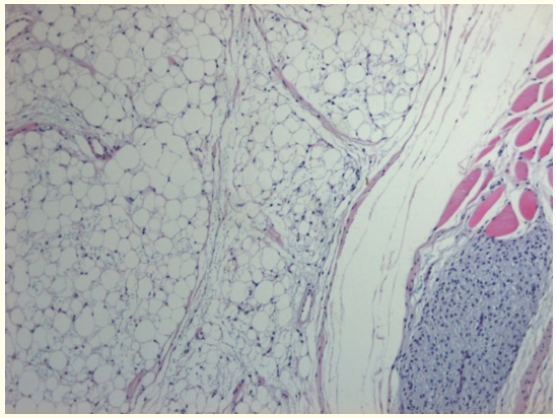
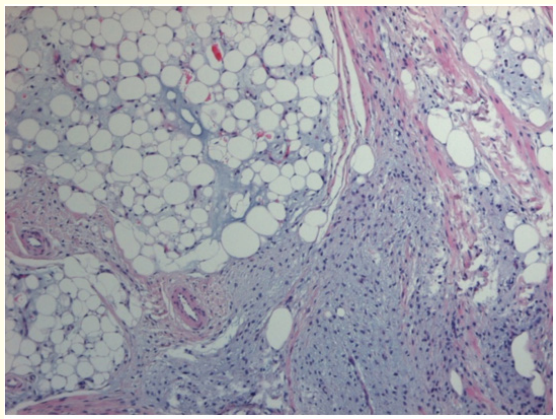


Figure 1: *MRI T2 imaging of the lesion of the left calf laying between flexor hallucis longus and soleus muscles with lobular characteristics.*

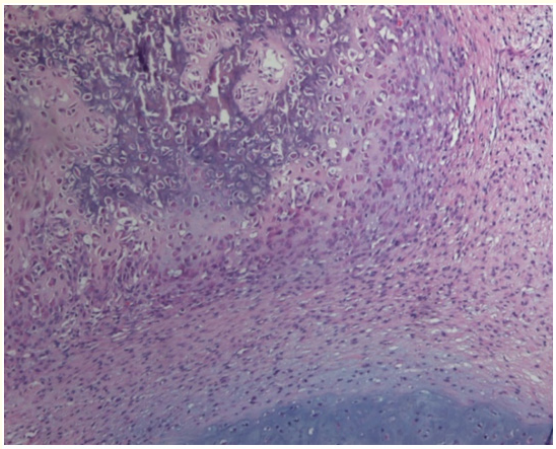
Macroscopically, a well-defined, lobular, elastic mass with fibrous diaphragms and an area of more solid content and signs of ossification was noted. Microscopically, 60% of the lesion consisted of adipose tissue lobules in various stages of differentiation, primarily embryonic fat, and fewer lobules of fully differentiated -adult type- fat tissue (Figure 2). The rest of the lesion (30 - 40%), consisted of fibroblasts with no signs of atypia or mitotic activity and a small area of fully mature hyaline cartilage surrounded by well-defined osteoid tissue and osteoblasts. While the largest portion of the specimen demonstrated a well-circumscribed pattern, an area of skeletal muscle infiltration was additionally noted. Immunohistochemical staining positive for CD34, desmin, S-100 protein and SOX-9, CD56/NCAM, WT-1 protein and bcl-2 protein. Limited expression of Ki-67/MIB-1 marker in less than 10% of the fibroblasts nucleus was consistent with the low mitotic activity.



A: *Adipose tissue lobules separated by fibrous septa.*



B: *Area of muscle skeletal muscle infiltration.*



C: *Mature hyaline cartilage surrounded by well-defined osteoid tissue and osteoblasts.*

Figure 2: *Histopathologic examination of the lesion -Hematoxylin and Eosin staining.*

Based on the above characteristics and review of the current literature the diagnosis of lipoblastoma with rare characteristics of fibrous and cartilaginous component was made. Follow-up time of 22 months was uneventful with no local remission on imaging and clinical examination. These rare findings of PLs led to a throughout search of epidemiologic data concerning PLs and the differential diagnostic challenges the orthopaedic surgeon must face [9-11].

Written consent form was obtained by the patient's family for the above data to be used.

Discussion

We performed a comprehensive search for articles concerning PLs located in the extremities.

A total of 85 patients aged from 4 weeks to 14 years of age (mean 12,02 months) were diagnosed with PLs of the extremities. Thirteen case reports and 15 case series involving PIs of the extremities were published between 1982 - 2018.The largest series of lipoblastomas was conducted by Alison L Speer., *et al.* in 2008 with 32 patients while among the 15-case series 71 patients out of a total of 191 had PLs of the extremities (37.17%) (Table 1).

First author, country	Study design	Number of patients with lipoblastomas of the extremities	Mean age	Gender
G.Stringel., *et al.* 1982, Canada	Case series	1 out of 4		
MM Al Qattan., *et al.* 1995 Canada	Case series	1 out of 4	2-month-old	Female
T J Gilbert., *et al.* 1996 USA	Case report	1	168-month-old	Male
Miller GG., *et al.* 1997 Canada	Case series	4 out of 9	50.28-month-old	3 M: 1F
Collins MH., *et al.* 1997 USA	Case series	11 out of 25	21-month -old	3.8 M:1 F
T Reiseter., *et al.* 1999 Norway	Case series	1 out of 4	13-month-old	Female
Hicks J., *et al.* 2001 USA	Case series	9 out of 24	20-month-old	0.79 M:1 F
CM Papendieck., *et al.* 2003 Argentina	Case report	1	1-month-old	Female
Shih-Ming Jung., *et al.* 2005 China	Case series	5 out of 16	22.2-month-old	1.7 M:1 F
Marcene R. McVay., *et al.* 2006 USA	Case series	5 out of 16	28.2-month-old	4 M: 1 F
Kaufman D., *et al.* 2007 USA	Case report	1	24-month-old	Female
Anjum Syed., *et al.* 2007 India	Case report	1	30-month-old	Male
Speer., *et al.* 2008 USA	Case series	12 out of 32	30-month-old	1.9 M: 1 F
Kok KY., *et al.* 2010 Brunei	Case series	5 out of 10	28.2-month-old	4 M: 1 F
Akhtar T., *et al.* 2012 India	Case report	1	12-month-old	Male
MS.Anikumar., *et al.* 2013 India	Case report	2	15-month-old	2 Female
G.N.Srinivas., *et al.* 2013 India	Case report	1	48-month-old	Male
Kamal AF., *et al.* 2014 Indonesia	Case series	2 out of 3	24-month-old	2 Female
Vorona G *et al.*2014 USA	Case report	1	22-month-old	Male
Panda SS., *et al.* 2014 India	Case report	1	108-month-old	Male
Parul Ghosh., *et al.* 2015 India	Case series	1 out of 6	24-month-old	Male
Susam-Sen H., *et al.* 2016 Turkey	Case series	2 out of 12	13.5- months-old	2 Female
Lisa Y Shen., *et al.* 2017 USA	Case series	2 out of 13	10.5-months-old	2 Female
Hashimoto S.., *et al.* 2017 Japan	Case report	1	23-month-old	Female
Giraldo Mordecay L.., *et al.* 2018 Colombia	Case report	1	5-month-old	Female
Rashmi Patnayak., *et al.* 2018 India	Case report	1	42- month–old	
Jamshid Abdul – Ghafar., *et al.* 2018 Pakistan	Case series	10 out of 13	99-month-old	4 Female/6 Male
Mayrim V.Rios Perez., *et al.* 2018 Puerto Rico	Case report	1	168-month-old	Female

Table 1: *Review of the Current Literature on Paediatric Lipoblastomas of the extremities.*

The exact location of PLs of the extremities was available in 53 patients including our case report. The thigh was the most common site of PLs of the extremities with 18 patients diagnosed (33.96%). The foot was next with 10 patients (18.87%), 9 PLs were diagnosed in the gluteal region (16.98%), 8 in the lower leg below the knee (15.09%), 4 in the forearm (7.54%), 3 in the proximal humerus area (5.66%) and 1 in the hand (1.89%).

When reviewing the literature 80 - 90% of these lesions are diagnosed in patients younger than 3 years of age and with a slight male predominance [4-7]. In the largest series found in current literature of Alison L Speer., *et al.* the male to female ratio was 1.9:1 but was calculated based on the prevalence of PLs throughout the body and the authors did not verify the gender of patients with PLs of the extremities. It is important to underline that Mahour., *et al.* in their series demonstrated an equal male to female ratio of PLs [12]. On the other hand, Dilley., *et al.* reported a female predominance in a series of 25 patients [13]. The above conflict in data is because PLs are rare, reported mostly in case studies and thus their exact prevalence is unknown. In our review of the current literature data on gender were available in 47 patients. A total of 24 male had PLs of the extremities and 23 female suggesting a male to female ratio of 1.04:1. Thus, PLs of the extremities may have an equal prevalence in both genders.

Additionally, no specific epidemiologic references are found in current literature for PLs located in the extremities compared to non-extremity distribution with a range of 11% to 72% [3,5,11-14]. Speer., *et al.* in their review of 186 patients with PLs calculated a prevalence of 47% in the extremities with no left or ride side predominance [15]. Compared to the non- extremity distribution of PLs Kok., *et al.* showed an equal prevalence while more recent studies suggest than PLs of the extremities are more uncommon [1,3,16]. In our review a prevalence of 37.17% for PIs of the extremities compared to other locations was found.

Differential diagnosis includes local inflammation, benign and malignant lesions such as liposarcoma, fibrolipoma, fibrosarcoma, fibroliposarcoma, hibernoma and hemangiomas [2,17,18]. Clinicians must keep in mind that PLs are virtually indistinguishable from liposarcomas radiographically and clinically, thus complete resection and biopsy is mandatory. On MRI the tumor expressed high signal intensity in both T1 and T2 weighted images while fat suppression sequencing on T1 revealed an adipose tumor with benign characteristics. Unfortunately, non-of these features is pathognomonic for lipoblastoma and the only separation that may be made is with lipoma due to the lower intensity on T1 [3,12,19].

Histologically, there are two variants of lipoblastoma: a superficial, localized and encapsulated lesion (lipoblastoma) and an infiltrative, non-capsulated, diffuse form (lipoblastomatosis) [5]. Grossly they appear as large pale, yellow masses with myxoid and cystic foci [20]. Both forms demonstrate a spectrum of cellular differentiation and maturation encompassing primitive mesenchymal cells, lipoblasts, mature adipocytes and spindle cells [8]. The tumor is separated by prominent fibrous septa that may be cellular while the presence of lipoblasts differentiates them from lipomas [21]. The lesion has a plexiform vascular pattern and abundant myxoid stroma and may have prominent extracellular mucinous pool. Lipoblastomatosis has a less lobulated appearance and the tumor infiltrates the skeletal muscles which was found in a small portion of our lesion. Compared to the rest of the specimen, which had clear characteristics of lipoblastoma, this finding did not affect our final diagnosis. Future research is necessary to reveal whether lipoblastomas may demonstrate small areas of muscle infiltration. It is important to underline that cellular atypia and mitoses, as seen in liposarcoma, are not features of lipoblastoma while on the other hand fibrous and cartilaginous components may be rare but are possible features PLs [12,22].

To further delve into the pathogenesis, cytogenic breakpoint abnormalities have been identified in lipoblastomas. It has been proposed that PLAG1 developmental gene at 8q12 is the presumed target oncogene responsible for lipoblastoma development causing escape of adipose maturation, resulting in lipoblastoma [23,24].

Conclusion

To conclude, the clinical diagnosis of PLs in extremely challenging for the orthopaedic surgeon. It is difficult to address a growing mass of the extremities with benign radiological characteristics with certainty especially when epidemiologic data are lacking. Thus, the collaboration amongst specialists is of paramount importance in order to set definitive diagnosis. Complete resection may offer complete remission, but surgeons should keep a close follow-up on their patients since local recurrence is a possibility.

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