Applied Cancer Research 2009;29(4)188-191

Case Report

Angiosarcoma in a 3-year-old Child with Congenital Lymphedema

Pricila Bernardi,MD;[1] Paulo Ricardo Gazzola Zen, MD, PhD;[1] Rafael Fabiano Machado Rosa, MD;[1] Roque Domingos Furian,MD; [2] Cristina Medina,MD;[1] Carla Graziadio,MD;[1] Giorgio Adriano Paskulin, MD,PhD;[1]

1 Universidade Federal de Ciências da Saúde de Porto Alegre (UFCSPA), Porto Alegre, Brazil

2 Complexo Hospitalar Santa Casa de Porto Alegre (CHSCPA), Porto Alegre, Brazil

Abstract

Angiosarcoma occurring in chronic lymphedema has been described in more than 200 cases, especially in the upper extremity following radical mastectomy (Stewart-Treves syndrome). However, angiosarcoma developing in congenital lymphedema is quite rare and the literature presents only 14 cases. Our patient is a girl with congenital lymphedema of the left lower limb that developed an angiosarcoma at 3 years of age, noted initially as a painful nodular lesion on the left thigh. This seems to be the earliest presentation of angiosarcoma associated with lymphedema. It claims attention to a careful evaluation of any lesions in a child with lymphedema to provide a better prognosis, which is allowed by precocious diagnosis and rapid interventions.

Keywords: Congenital abnormalitus,Lymphedema, Sarcoma, Hemangiosarcoma, Upper extremity

Introduction

Primary lymphedema can be broadly classified into congenital and non-congenital types. When the edema develops in infancy or early childhood, the condition is classified as congenital and it may either hereditary (Nonne-Milroy-Meige syndrome) or nonhereditary. The form of idiopathic lymphedema that is non-congenital is termed praecox, because it occurs commonly in early adolescence; otherwise it appears after 35 years of age and the entity is named "forme tarde".[1]

Angiosarcoma is a rare and aggressive vascular neoplasm arising in chronic congenital or acquired lymphedema. It is responsible for around 2% of all soft tissue sarcomas and can occur in any location in the body, usually in the skin or superficial soft tissues.[2-5] Despite their rarity, angiosarcomas display remarkable clinical heterogeneity.[4]

Cutaneous lesions often present as ill-defined, bruise-like lesions that can progress to nodular and ulcerated lesions.[3] Although angiosarcomas are most frequently associated with post-mastectomy lymphedema (Stewart-Treves syndrome), they can exceptionally arise in congenital hereditary lymphedema (Nonne-Milroy-Meige syndrome) and non-hereditary lymphedema (congenital, praecox or *forme tarde* lymphedemas).[6-7]

In this case report, we report a girl with congenital lymphedema that secondarily developed angiosarcoma.

Case Report

Our patient is a white girl with congenital lymphedema of the left lower limb. She is an only child of healthy, young and non-consanguineous parents. At birth was observed a congenital lymphedema of the left

Correspondence
Paulo R. G. Zen
Rua Sarmento Leite, 245 - 403
90050170, Porto Alegre-Brazil
Phone: +55 51 33038771
E-mail: paulozen@ufcspa.edu.br

lower limb, with no other congenital anomalies. She presented a painful nodular lesion on the left thigh when she was 3 years of age. One year later she was admitted in a pediatric hospital with a 1.8 x 3.5 cm ulcerated lesion on the left thigh associated to multiple blue (bluish) and papillomatous nodules on the same limb (Figure 1). These nodules were not present at birth, but

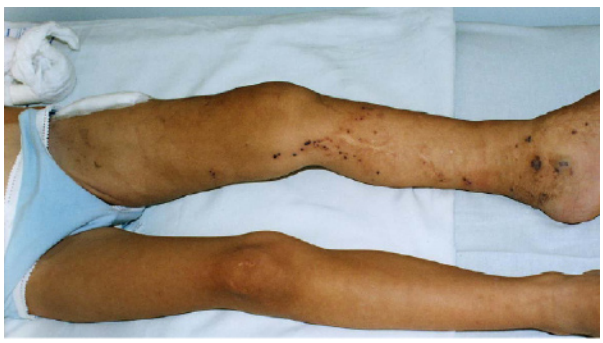

Figure 1 - Ulcerated lesion associated to multiple blue (bluish) and papillomatous nodules on the left thigh.

reminiscent of congenital malformations of lymphatic system-like **congenital lymphangiomatosis.** No other abnormalities were observed at the physical examination. There were no other cases of lymphedema in her family.

Because of asymmetrical limbs, we considered the differential diagnosis of chromosomal mosaicism and Klippel-Trenaunay syndrome; however the Doppler ultrasonography and the x-ray of the limb were normal. The skin karyotype of the affected limb was 46,XX. Hemihyperplasia was also considered but this condition usually is not a lymphatic abnormality.

The anatomopathological study of a skin biopsy in left thigh ulcerated lesion diagnosed an angiosarcoma grade 2 (Figure 2). This lesion was removed, and the histological analysis showed that the tumor was at the deep limits of resection. There was no sign of the presence of metastases. The family decided not to go further with the treatment and we do not have more information after that.

Discussion

The Stewart-Treves syndrome has been described in more than 200 cases. However, angiosarcoma associated to a congenital lymphedema (hereditary and non-hereditary) is quite rare and was described in only 14 cases in the literature.[6-12]

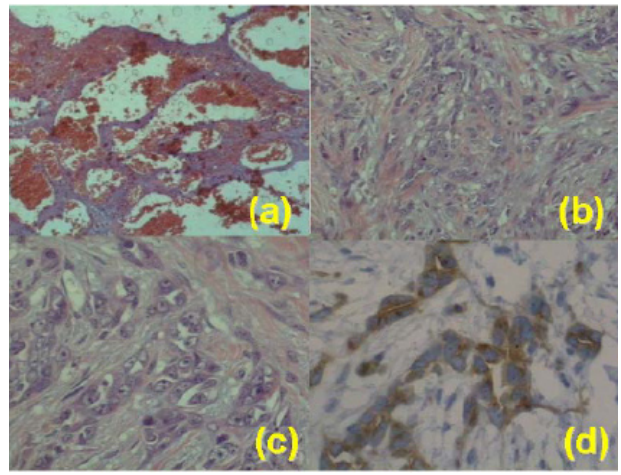

Figure 2 - (a-d). The anatomopathologic study showing: (a) angiomatous proliferation (haematoxylin and eosin, 45x objective); (b & c) angiosarcoma lesion (haematoxylin and eosin, 200x objective); and (d) immunohistochemical analysis (staining with CD34, 200x objective).

Offori et al. (1993)[6] described a 10-year-old boy with angiosarcoma and provided a good review about these 14 cases. His patient had a lymphedema at the left lower limb and the clinical appearance of the tumor was the presence of blue and red nodules. Two patients cited by the authors were classified by Offori et al.[6] as a praecox lymphedema, because the lymphedema was first noted at the age of six and seven months, respectively. Nevertheless, according to the definition of Dubin et al.[1] we considered these two cases above as congenital lymphedema. Besides three patients had a hereditary lymphedema and eight had a lymphedema in the upper limb (one was not informed).

The age of patients at time of diagnosis of angiosarcoma ranged from 4 to 85 years, whereas our patient presented the disease earlier in relation to others. The delay in diagnosis ranged from two months to three years (in five cases was not stated), and 10 of 15 patients were female. The aspect of the malignant lesions was described as ulceration (7 cases), apparent traumatic ecchymoses (2 cases) and violaceous nodules or papules which tend to form satellite lesions (9 cases). Ulcerated lesions and blue nodules presented by our patient at the diagnosis were the most frequently observed. The clinical features observed are described in Table 1. The authors emphasized that these kinds of lesions should be considered as a diagnostic warning in lymphedematous extremities.

Angiosarcoma is an uncommon malignant neoplasm that is known to have a very poor prognosis. Much of the literature regarding this tumor has been in relation to the angiosarcoma associated with post-

Table 1- Clinical features observed in patients with angiosarcoma associated with congenital lymphedema described in the literature (modified from Offori et al., 1993).

Author	Sex	Age at diagnosis	Tumor site	Clinical appearance	Delay in diagnosis	Treatment	Survival
Present case	F	4y	LLL	Ulcerated lesion/ blue nodules	1y	Local excision	Alive at 14m
Liszauer et al.[9]	M	28y	RLL	Ulcerated lesion	4m	Local excision	Died at 11m
Scott et al.[10]	F	50y	LUL	Papillomatous nodules	>7m	Local excision / amputation	Died at 37m*
Taswell et al.1962§	M	17y	LUL	Ulcerated lesion	Not stated	Disarticulation	Died at 24m
Bunch., 1968§	F	13y	UL	Not stated	Not stated	Interscapular amputation	Died at 1y
Finlay-Jones, 1970§	M	34y	LLL	Ulcerated blue tumor	Not stated	Excision and combined therapy	Died at 31m
Merrick et al., 1971§	M	52y	LUL	Swelling/blue nodules	6m	Wide local excision / amputation / radiotherapy	Died at 36m
Mackenzie, 1971§	M	64y	RLL	Nodules/ulceration	2m	Hindquarter amputation / radiotherapy	Alive at 24m
Dubin et al.[1]	F	29y	LUL	Ulcerated lesion	3y	Disarticulation	Died at 45m*
Laskas et al.[11]	F	85y	RUL	Purple papules and blisters/ulceration	10m	Palliative mid-humeral amputation	Died at 14m
Banathy et al.[12]	F	50y	LUL	Purple nodules	Not stated	Mid-humeral amputation	Died at 26m
Sordillo et al 1981§	F	23y		Not stated	Not stated	Hemipelvectomy	Alive at 19y
Bostrom et 1989§	F	19y	RUL	Infected lesion	4m	Amputation / disarticulation	Died at 12m
	F	10y	LLL	Blue/red nodules	8m	Amputation / disarticulation	Alive at 10m
Offori et al.[6]	F	43y	LLL	Blue/purple nodules	2m	Amputation	Alive at 9m

LLL: left lower limb; RLL: right lower limb; LUL: left upper limb; RUL: right upper limb; m: months; y: years; § Cited by Offori et al.(1993); ⋆ Cases considered like praecox lymphedema by Offori et al. (1993).

mastectomy lymphedema of the upper extremities (Stewart-Treves syndrome).[7-8] Although angiosarcoma has been originally described only in patients with post-mastectomy chronic lymphedema due to breast cancer, many other cases of angiosarcoma have been observed in chronic lymphedema unassociated to previous malignancy, which has made it clear that chronic lymph stasis (and not the primary cancer) predisposes to the onset of the angiosarcoma. There is considerable evidence that lymphedema contributes to local immune compromise with decreased immune surveillance. Thus, the immune compromise and possibly other effects of the deregulated local environment with lymphedema appears to be a common cofactor in development and/ or progression at least some cases of angiosarcoma and other cutaneous neoplasms, as Kaposi's sarcoma and non-Hodgkin's lymphoma.[4,7]

Treatment of angiosarcoma is still unsatisfactory. Early recognition associated with radical ablative surgery and the addition of radiation can result in best chance for survival.[4] Our report claims attention to a careful evaluation of any lesions in children with lymphedema as an early diagnosis and rapid intervention to provide a better prognosis.

References

1. Dubin HV, Creehan EP, Headington JT. Lymphangiosarcoma and congenital lymphedema of the extremity. Arch Dermatol 1974;

110:608-14.
2. Ohguri T, Imada H, Nomoto S, Yahara K, Hisaoka M, Hashimoto H, et al. Angiosarcoma of the scalp treated with curative radiotherapy plus recombinant interleukin-2 immunotherapy. Int J Radiat Oncol Biol Phys 2005; 61:1446-53.
3. Koch M, Nielsen GP, Yoon SS. Malignant tumors of blood vessels: angiosarcomas, hemangioendotheliomas, and hemangioperictyomas. J Surg Oncol 2008; 97:321-9.
4. Abraham JA, Hornicek FJ, Kaufman AM, Harmon DC, Springfield DS, Raskin KA, et al. Treatment and outcome of 82 patients with angiosarcoma. Ann Surg Oncol 2007; 14:1953-67.
5. Itakura E, Yamamoto H, Oda Y, Tsuneyoshi M. Detection and characterization of vascular endothelial growth factors and their receptors in a series of angiosarcomas. J Surg Oncol 2008; 97:74-81.
6. Offori TW, Platt CC, Stephens M, Hopkinson GB. Angiosarcoma in congenital hereditary lymphoedema (Milroy's disease)--diagnostic beacons and a review of the literature. Clin Exp Dermatol 1993; 18:174-7.
7. Ruocco V, Schwartz RA, Ruocco E. Lymphedema: an immunologically vulnerable site for development of neoplasms. J Am Acad Dermatol 2002; 47:124-7.
8. Merrick TA, Erlandson RA, Hajdu SI. Lymphangiosarcoma of a congenitally lymphedematous arm. Arch Pathol 1971; 91:365-71.
9. Liszauer S, Ross RC. Lymphangiosarcoma in lymphoedema. Can Med Assoc J 1957; 76:475-7.
10. Scott RB, Nydick I, Conway H. Lymphangiosarcoma arising in lymphedema. Am J Med 1960; 28:1008-12.
11. Laskas JJ, Shelley WB, Wood MG. Lymphangiosarcoma arising in congenital lymphedema. Arch Dermatol 1975; 111:86-9.
12. Banathy LJ. Lymphangiosarcoma arising in a congenitally lymphoedematous arm: case report. Pathology 1977; 9:65-7.