156:Neurologic conditions in congenital lymphangiomas

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INTRODUCTION

Lymphangioma, is an infrequent congenital malformation of the lymphatic and vascular system and is recognized as a benign tumor. It accounts for 6% of all pediatric soft tissue tumors.

The International Society for the Study of Vascular Anomalies (ISSVA) has established the classification of lymphangioma on the basis of clinical manifestations and complications (Fig 1) (1).

Although benign, depending on their location, they can have functional, aesthetic and even vital repercussions when they occur in critical areas. The clinical management and evolution of lymphangiomas depend on the clinical manifestations and locations, as well as their complexity (2).

ISSVA classification for vascular anomalies ©
(Approved at the 20th ISSVA Workshop, Melbourne, April 2014, last revision May 2018)

This classification is intended to evolve as our understanding of the biology and genetics of vascular malformations and tumors continues to grow

Vascular Anomalies					
Vascular Tumors	**Vascular Malformations**				
	Simple	***Combined***	***Of Major Named Vessels***	***Associated with Other Anomalies***	
Benign	Capillary malformations	defined as two or more vascular malformations found in one lesion	abnormalities in the origin/course/number of major blood vessels that have anatomical names	syndromes in which vascular malformations are complicated by symptoms other than vascular anomalies	
Locally aggressive or Borderline	Lymphatic malformations				
	Venous malformations				
	Arteriovenous malformations *				
Malignant	Arteriovenous fistula *				

Fig 1: The international society of the study of vascular anomalies classification of lymphatic malformations (1).

OBJECTIVES

Here, we report medical and genetic assessment of a Tunisian child from Sfax town, who harbor an inoperable neonatal lymphangioma of the axilla complicated by neurologic conditions.

METHODS

A 22-month-old male child from a non consanguineous couple (the unique son of the couple) was seen at our genetic counselling for the genetic management of an inoperable lymphangioma of the right axilla.

Physical, morphological were conducted.

Cytogenetic exploration of the child and his parents was carried out using RHG banding.

Molecular screening was not possible.

Fig 2: Clinical presentation of the lymphangioma of the axilla

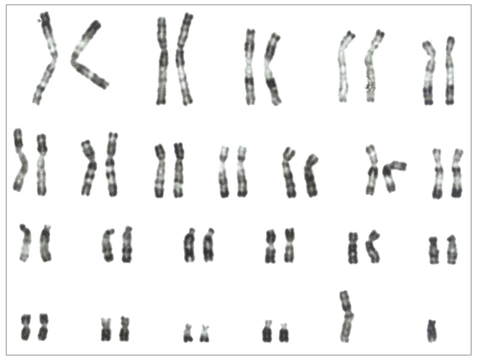

Fig 3: 46,XY RHG banding karyotype of the index case

RESULTS

The lymphangioma was diagnosed prenatally as a small cyst.

At birth, it was initially small and then progressively increasing in size leading to **neurologic deficits of the right hemi body (paresis).**

There was also:

- **A delay in achieving motor milestones**
- **Speech and hearing disorders**
- **Repeated epileptic crisis leading to a west disease appeared at the age of five months**
- **An intellectual disability (mental retardation)**

Cerebral imaging revealed multiples **brain lymphangiomatic cysts that intercommunicate**. The notion of **hydrocephalus** was also reported.

Ophthalmologic assessment did not show abnormalities.

On physical examination, the child's body showed many other multiples angiomas. The mass of the right axilla was covered by healthy skin, well-circumscribed with a smooth non-pulsatile surface, of renitent consistency, mobile on the superficial plane, and fixed on the deep plane, measuring 12 cm × 10 cm in diameter (Fig 2).

Imaging of the axilla showed multiple encapsulated vascular malformations.

The medical history of the parental families showed many disorders like epileptic seizures, aneuploidies, anophtalmia and cancer.

Cytogenetic analysis was without abnormalities (Fig 3).

CONCLUSION

This case of disseminated lymphangioma was complicated by neurologic deficits and epileptic crisis.

Most lymphangiomas occur in the cervical and axilla regions (almost 80%) and they can coexist with genetic syndromes as Rasopathies and chromosomal aneuploidies (Tab 1) (3,4). Better understanding of the pathogenesis of this case of disseminated lymphangioma and a whole genomic investigation are required to more effective clinical management.

Recent studies indicated that many signaling pathways may be involved during embryogenesis of such malformations, like RAS, Wnt/β-Catenin and PI3K/AKT/MTOR Signaling Pathways.

Specific inhibitors targeting these pathways have been investigated for clinical applications and clinical trials. Some drugs already currently in clinical use for other diseases were found to be effective for lymphangiomas.

Gene	Name
AKT1	v-akt murine thymoma viral oncogene homolog 1
CCBE1	collagen and calcium binding EGF domains 1
COL18A1	collagen, type XVIII, alpha 1
FAT4	FAT atypical cadherin 4
IDH1	isocitrate dehydrogenase 1 (NADP+), soluble
IDH2	isocitrate dehydrogenase 2 (NADP+), mitochondrial
PTEN	phosphatase and tensin homolog
PTH1R	parathyroid hormone 1 receptor
SOX18	SRY (sex determining region Y)-box 18
TSC1	tuberous sclerosis 1
TSC2	tuberous sclerosis 2

Syndrome	Genetic defect
Down	Trisomy 21
Edward	Trisomy 18
Patau	Trisomy 13
Turner	Monosomy X
Noonan	PTPN11 mutations
Rasopathies	RAS/MAPK mutations
Cloves	PIK3CA mutations
Klippel-Trenaunay	PIK3CA mutations

Tab 1: Genes and syndromes associated to congenital lymphangiomas

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