CONGENITAL MULTISEGMENTAL LYMPHATIC DYSPLASIA WITH SYSTEMIC INVOLVEMENT – EVALUATING PRIMARY LYMPHOEDEMA

Afthab Jameela Wahab1, V. Anandan2, K. P. Saradha3, Nithya Baskar4

1Associate Professor, Department of Dermatology, Stanley Medical College.
2Professor, Department of Dermatology, Stanley Medical College.
3Associate Professor, Department of Dermatology, Stanley Medical College.
4Junior Resident, Stanley Medical College.

ABSTRACT

A ten-year old girl presented with unilateral swelling of right half of her body since birth. She developed itchy, oozing, painful skin lesions over right lower leg for the past three months. Clinical examination and investigations revealed unilateral lymphoedema with elephantiasis nostras verrucosa cutis and visceral involvement in the form of pericardial effusion, ascites and intestinal lymphangiectasia. She was diagnosed as a case of multisegmental lymphatic dysplasia with systemic involvement. We report this rare case of primary lymphoedema, highlighting the approach to a case of primary lymphoedema.

KEYWORDS

Primary Lymphoedema, Multisegmental Lymphatic Dysplasia, Lymphangiectasia.

INTRODUCTION

Primary lymphoedema results from an inherent developmental abnormality of the lymphatic system. Multisegmental Lymphatic Dysplasia with Systemic Involvement (MLDSI), a subtype of primary lymphoedema, is characterized by a segmental pattern of lymphoedema affecting different body parts associated with systemic involvement.

CASE REPORT

A 10-year-old girl, who had hypertrophy of the entire right half of the body since birth presented with painful, itchy, oozing skin lesion over her right leg of three months duration (Figure 1). She was the second child of non-consanguineous parents with a birth weight of 6.5 kg, delivered by caesarean section. The hemihypertrophy had increased proportionately to her growth, uninfluenced by postural changes. She had developed recurrent cellulitis over her right leg swelling for which she was on intermittent treatment.

The patient gives history of recurrent upper respiratory tract infections. There was no history suggestive of cardiovascular, gastrointestinal and central nervous system involvement clinically.

The patient’s vital signs, general and systemic examination was normal. There was increased girth of right half of face and body and right limbs indicating right unilateral lymphoedema with soft tissue hypertrophy. There was no warmth or tenderness and no length discrepancy between right and left upper and lower limbs.

The swelling over the right lower limb was non-pitting, non-pulsatile, non-reducible and non-compressible. The hemihypertrophy was not influenced by postural changes. The patient had developed recurrent cellulitis over right leg swelling for which she was on intermittent treatment.

Patient gives history of recurrent upper respiratory tract infections. There was no history suggestive of cardiovascular, gastrointestinal and central nervous system involvement clinically.

The patient’s vital signs, general and systemic examination was normal. There was increased girth of right half of face and body and right limbs indicating right unilateral lymphoedema with soft tissue hypertrophy. There was no warmth or tenderness and no length discrepancy between right and left upper and lower limbs.

The swelling over the right lower limb was non-pitting, non-pulsatile, non-reducible and non-compressible. The hemihypertrophy was not influenced by postural changes. The patient had developed recurrent cellulitis over right leg swelling for which she was on intermittent treatment.

CASE REPORT

A 10-year-old girl, who had hypertrophy of the entire right half of the body since birth presented with painful, itchy, oozing skin lesion over her right leg of three months duration (Figure 1).

She was the second child of non-consanguineous parents with a birth weight of 6.5 kg, delivered by caesarean section. The hemihypertrophy had increased proportionately to her growth, uninfluenced by postural changes. She had developed recurrent cellulitis over her right leg swelling for which she was on intermittent treatment.

Patient gives history of recurrent upper respiratory tract infections. There was no history suggestive of cardiovascular, gastrointestinal and central nervous system involvement clinically.

The patient’s vital signs, general and systemic examination was normal. There was increased girth of right half of face and body and right limbs indicating right unilateral lymphoedema with soft tissue hypertrophy. There was no warmth or tenderness and no length discrepancy between right and left upper and lower limbs.
DISCUSSION

Lymphoedema is defined as swelling of tissues resulting from accumulation of lymph caused by inadequate drainage. It may be primary or secondary. Primary lymphedema implies an intrinsic developmental or functional fault in lymph drainage. Secondary lymphedema occurs when previously normal lymphatics suffer from an external insult such as disease, infection, tumors, trauma or surgery with loss of functional capability. Primary lymphoedema may be classified into four types:

1. Isolated primary lymphedema.
2. Primary lymphedema associated with systemic or visceral involvement.
3. Primary lymphedema associated with disturbed growth/cutaneous/vascular anomalies.
4. Primary lymphedema as part of syndromes.

Isolated primary lymphoedema is lymphoedema confined to skin and soft tissue only. It may be of congenital onset (<1 year) or of late onset (>1 year), further subtyping depending on the limb or segments involved.

<table>
<thead>
<tr>
<th>One Limb</th>
<th>Lower limb Non-familial Unilateral</th>
<th>Lower limb Non-familial Bilateral</th>
<th>Lower limb Familial</th>
<th>Lower limb and Genitalia</th>
<th>Multiple Segments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital unisegmental lymphedema</td>
<td>Congenital unisegmental lymphedema</td>
<td>Milroy disease, VEGFR3</td>
<td>Milroy like disease, KIF11, VEGFC</td>
<td>Lower limb + genital lymphedema</td>
<td>Congenital multisegmental lymphedema without systemic involvement</td>
</tr>
</tbody>
</table>

Table 1: Congenital onset Lymphoedema subtypes
Matro's disease, an autosomal dominant disease caused by failure of lymphangiogenesis secondary to inactivation of VEGFR-3 with familial, bilateral below-knee lymphoedema.3

<table>
<thead>
<tr>
<th>Lymphedema with Distichiasis</th>
<th>Lower limbs Familial</th>
<th>Lower limbs Non-familial Bilateral</th>
<th>Lower limbs Non-familial Unilateral</th>
<th>Lower limb and genitalia</th>
<th>4-limb</th>
<th>Segmental</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoedema-Distichiasis Syndrome FOXC2</td>
<td>Meige GJC2</td>
<td>Meige like</td>
<td>Late onset unilateral leg lymphoedema</td>
<td>Lower limb + genital lymphoedema GATA2</td>
<td>4-Limb lymphoedema a GJC2</td>
<td>Late onset uni or multisegmental lymphoedema</td>
</tr>
</tbody>
</table>

Table 2: Late onset Lymphoedema

Lymphoedema–distichiasis syndrome is an autosomal dominant disease caused by mutations in FOXC2 (MFH-1). Congenital accessory eyelashes are present along the posterior eyelid borders. Lymphoedema may occur from puberty to fifth decade.4 Meige's disease is familial, mild bilateral below-knee lymphoedema developing at or soon after puberty in adolescent female.5

Primary lymphedema associated with systemic or visceral involvement

Individuals have widespread developmental abnormality of the lymphatic system. There may be prenatal hydrothorax, hydrops fetalis, dysmorphic facial features with epicantic folds, broad nasal bridge, neck webbing and low set ears. Postnatal pericardial and pleural effusions, chyloous ascites and pulmonary and intestinal lymphangiectasia may develop. The lymphedema may be multisegmental or generalized. Accordingly, they can be further divided into two categories.

Multisegmental Lymphatic Dysplasia with Systemic Involvement (MLDSI)

Associated with the above systemic involvement, there is congenital segmental lymphoedema affecting different body parts, probably due to somatic mosaicism. There may be ipsilateral hemifacial and conjunctival oedema. Intelligence is normal. There are no associated structural abnormalities. Sibling and offspring recurrence risk is low.3

Generalized Lymphatic Dysplasia (GLD)- Hennekam or lymphangiectasia- lymphoedema-mental retardation syndrome.

An autosomal recessive disease due to mutations in collagen and calcium binding EGF-domain 1 (CCBE1).6 It is characterized by uniform, widespread lymphoedema affecting all segments of the body from birth to 12 years, intestinal lymphangiectasia, hypoproteinemia, learning difficulties and characteristic facial features.

Primary Lymphedema associated with disturbed growth and/or cutaneous/vascular anomalies

Lymphoedema and lymphatic malformations can be seen in conjunction with growth disturbances or vascular/cutaneous anomalies resulting from somatic mosaicism.

<table>
<thead>
<tr>
<th>Syndromes</th>
<th>Clinical Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLOVES syndrome PIK3CA</td>
<td>Congenital lipomatous overgrowth, vascular malformations, epidermal naevi, skeletal abnormalities</td>
</tr>
<tr>
<td>Klippel-Trenaunay syndrome E133K</td>
<td>Lymphoedema, capillary malformation, venous disease, limb overgrowth</td>
</tr>
<tr>
<td>Parkes Weber syndrome RASA1</td>
<td>High flow capillary-Arteriovenous Malformation (AVM) or capillary-lymphatic-AVM, vascular stain, limb overgrowth</td>
</tr>
<tr>
<td>Proteus syndrome AKT1, P10</td>
<td>Asymmetrical overgrowth of any body part, macroacaly, palmpoplantar cerebriform overgrowth, verrucous epidermal naevi, lymphangiomatous swelling</td>
</tr>
<tr>
<td>WILD syndrome Sporadic</td>
<td>Warts, immunodeficiency, lymphoedema, anogenital dysplasia</td>
</tr>
<tr>
<td>Maffucci’s syndrome.7 Sporadic</td>
<td>Haemangioma, venous malformations, cavernous lymphangiomasses, dyschondroplasia, enchondromas</td>
</tr>
</tbody>
</table>

Table 3: Syndromes associated with disturbed growth/vascular or cutaneous anomalies

Primary lymphedema as a part of syndromes

Turner’s syndrome 45X0 Chromosomal testing is essential in neonates/children with primary lymphoedema.

Noonan’s syndrome PTPN11,

Hypothrichosis-lymphoedema -telangiectasia syndrome SOX18.

Microcephaly-lymphoedema–chorioretinal dysplasia KIF11.

Cholestasis-lymphoedema syndrome (Aagenaes’s syndrome).

Yellow nail syndrome.

CONCLUSION

An algorithmic approach to evaluate a case of primary lymphoedema would be to first assess the extent of lymphoedema, systemic/visceral lymphatic involvement and then to exclude associated syndromes, growth disturbances, vascular/cutaneous anomalies. In our case associated syndromes were ruled out by clinical examination and chromosomal analysis. Further investigations excluded vascular malformations, cutaneous anomalies and growth disturbances. Systemic lymphatic involvement (intestinal lymphangiectasia, pericardial effusion, ascites) ruled out isolated primary lymphoedema. Unilateral congenital lymphoedema with normal intelligence excluded GLD, confirming the diagnosis of “Multisegmental lymphatic dysplasia with systemic involvement.” This rare-case report attempts at highlighting an algorithmic approach in evaluating primary lymphoedema.

REFERENCES


Journal of Evolution of Medical and Dental Sciences/ eISSN- 2278-4802, pISSN- 2278-4748/ Vol. 4/ Issue 100/ Dec. 14, 2015 Page 16582


