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Congenital Lymphedema : Another Unique and Gender Specific Stigmata of Tuberous Sclerosis?

We report a child of tuberous sclerosis with a rare association of congenital lymphedema and cardiac rhabdomyoma since birth.

A 3-month-old female child, born of non-consanguineous marriage , was detected soon after birth to have nonpitting edema of left lower limb extending from thigh to foot. Neurosonogram and USG abdomen were normal. Echocardiography revealed a 9 x 9 mm rounded pedunculated mass in LV outflow tract, attached to aorto-mitral continuity junction. Physical examination revealed multiple hypopigmented macules in right upper limb and trunk suggestive of ash leaf macules. X-ray chest and ECG was normal for age. Blood investigations were normal. The child's father had a history of seizure disorder and was on antiepileptic drugs. His physical examination revealed hypopigmented to depigmented macules in both upper limbs and trunk, skin colored plaques with irregular border in lumbosacral region and multiple hyperpigmented to erythematous papules and small plaques over face suggestive of ash leaf macules, shagreen patches, and angiofibromas respectively.

Lymphedema is a chronic tissue swelling that is most commonly manifested in a limb. This condition results from impaired lymph drainage in the presence of normal capillary filtration. The three main consequences of lymphatic failure are lymphedema, infection and, very rarely, cancer [1]. Most forms of primary lymphedema are thought to be caused by a congenital abnormality of the lymphatic system and present at or soon after birth. Cardiac rhabdomyomas are intracavitary or intramural tumors that are present in nearly 50 to 70% of infants with tuberous sclerosis (TSC). Most children are asymptomatic. Symptoms are attributed to the presence of intracardiac obstruction, myocardial involvement, and rhythm disturbances [2].

Congenital lymphedema is a rare association with tuberous sclerosis with only few cases reported earlier [3,4]. The previous reported patients were females but unlike our child, they presented with history of multiple seizures while our child had no seizures but instead had a cardiac rhabdomyoma detected incidentally. It is interesting to note that pulmonary lymphangio-myomatosis seen in tuberous sclerosis similarly occurs only in women which is hypothesized to be due to the fact that estrogen regulates TSC gene signalling and, perhaps, also the migration of TSC2-deficient cells [3].

The pathophysiology of congenital lymphedema in tuberous sclerosis is yet unclear. Previous authors have suggested that it could be due to the dysplastic development of lymphatic system in the affected limb as part of TSC gene mutation as this gene regulates cell growth, proliferation and migration. Congenital lymphedema may also be due to the abnormal smooth cell hypertrophy in subcutaneous tissue which externally compresses the superficial lymphatics. An increased awareness of this association may help pediatricians suspect tuberous sclerosis in a female child when congenital lymphedema is the sole external manifestation.

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