SYNDROMIC CLASSIFICATION OF HEREDITARY LYMPHEDEMA

K.A. Northup, M.H. Witte, C.L. Witte

Department of Surgery, University of Arizona College of Medicine, Tucson, Arizona, USA

“Vertebrate development is constrained into only a very few final or common developmental pathways; therefore, no developmental anomaly seen in humans is unique to (‘pathognomonic of’) one syndrome.”

JM Opitz (1)

ABSTRACT

Since the late 1800's, the familial occurrence of peripheral lymphedema has been well-documented in Milroy and Meige syndromes. However, the presence of lymphedema in many other hereditary dysmorphic syndromes has not been fully appreciated. In order to establish more standardized and detailed clinical phenotypic criteria as the basis for rational classification and for greater precision in screening and genetic linkage studies, we conducted a comprehensive literature search and review of OMIM-identified and non-identified hereditary syndromes in which lymphedema was reported as a feature. Modes of inheritance, associated clinical features and images, and specific organ involvement were inventoried and suggested pathophysiologic mechanisms noted. The findings support the recommendation that when peripheral lymphedema of undetermined etiology is found, further careful, comprehensive clinical, including detailed dysmorphic, evaluation along with lymphatic imaging with subsequent syndromic classification is warranted. This information can provide clues to underlying pathogenesis and form the basis for genetic counseling and prognostication as well as offer guidance to the clinical investigator translating research at the molecular level into new approaches for evaluation and therapy.