New Frontiers in Our Understanding of Lymphatic Malformations of the Head and Neck

Natural History and Basic Research

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KEYWORDS

• Lymphatic malformations • Head and neck • Natural history • Basic research

KEY POINTS

- Head and neck lymphatic malformation (HNLM) is not a result of disrupted vasculogenesis but arises from sporadic genetic abnormalities in specific cells.
- Clinical research into HNLM has focused on nomenclature, diagnosis, the assessment of natural history, and the evaluation of invasive treatment efficacy.
- Because of the rarity and clinical variability of HNLM, the evidence created by this research is low quality (levels 2–4), but the gap between experience-based decision-making and evidence-based practice is closing.

The future of head and neck lymphatic malformation (HNLM) evaluation and treatment is changing because of 2 decades of clinical research and the recent basic science investigation. HNLM is not a result of disrupted vasculogenesis but arises from genetic abnormalities in specific cells within the malformation.[1,2] Clinical research into HNLM has focused on nomenclature, diagnosis, assessment of natural history, and evaluation of invasive treatment efficacy.[3–8] Because of the rarity and clinical variability of HNLM, the evidence created by this research is low quality (levels 2–4); but the gap between experience-based decision-making and evidence-based practice is closing.[8] Basic science investigation using cellular biology and molecular genetics has revealed the genetic cause of some HNLMs, which has created the possibility of medical treatment specific to HNLM.[1,9] This

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article summarizes the clinical and basic science research that will likely influence the future of HNLM assessment and treatment.

The nomenclature for all vascular anomalies (VAs) has slowly evolved based on clinical phenotypic observation and the availability of improved high-resolution imaging. The descriptive terms of *cystic hygroma* for large fluid-filled neck masses and *lymphangioma* for infiltrative lymphatic channels seen in oral and oropharyngeal lymphatic malformation (LM) have been changed to the more inclusive *common LMs* by the International Society for the Study of Vascular Anomalies (ISSVA) (See **Table 1** in Paula E. North's article, "Classification and pathology of congenital and perinatal vascular anomalies of the head and neck," in this issue for further details).[10,11] The ISSVA nomenclature for all VAs enabled providers to better distinguish different congenital vascular lesions, particularly congenital and acquired lymphatic disease. Careful categorization of VA and lymphatic diseases allowed for improvements in clinical research and provided a framework to direct basic science investigation. Categorization of HNLM based on anatomic location and laterality led to a staging/grading system for intraoral and head and neck lesions (**Fig. 1**).[12,13] Treatment outcomes have been measured comparing differences between HNLM stages.[5,7,14] Further refinement of our understanding of HNLM has been accomplished with radiographic imaging that categorizes these lesions as macrocystic and microcystic. This information often directs the type of invasive treatment.[15–17]

Prenatal diagnosis of HNLM is frequently made with in utero ultrasound imaging. Lucency in the soft tissue of the posterior/dorsal neck with nuchal thickening is still called cystic hygroma in obstetrics literature. Radiolucent lesions in the nuchal region indicate an increased risk for abnormal fetal karyotype, whereas radiolucent anterior or ventral neck lymphatic lesions do not confer this same risk (**Fig. 2**).[18] There are now highly sensitive and specific screening tests (noninvasive prenatal testing) that allow direct sampling of fetal DNA from maternal blood, without the need for invasive amniocentesis or chorionic villus sampling.[19] In utero characterization of HNLM can be further functionally assessed with in utero MRI and 3-dimensional duplex imaging of the upper aerodigestive tract in mothers with polyhydramnios to guide high-risk delivery planning and airway management.[4]

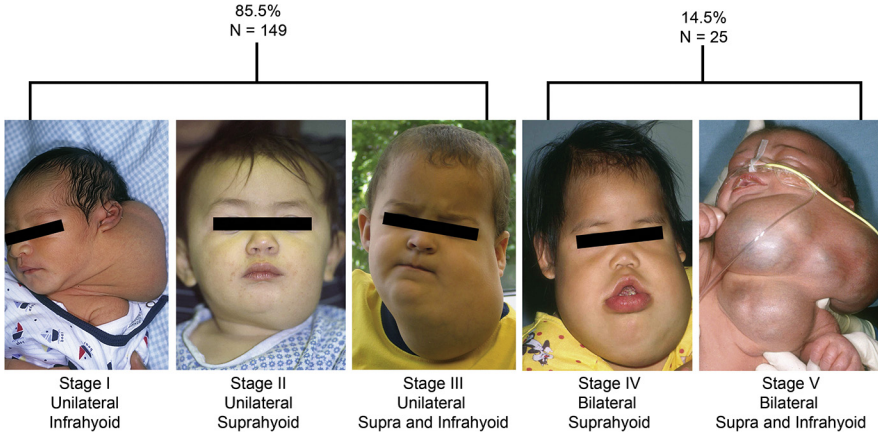

Fig. 1. The deSerres head and neck LM staging system used to improve treatment outcome measurement and allow for quantitative data analysis. In a series of 174 HNLMs, 85.5% were stages 1 to 3 and 14.5% were stages 4 or 5; in lower stage lesions, surgery and sclerotherapy had the same efficacy.