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Review Article

Vascular tumors of infancy and childhood: beyond capillary hemangioma

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Abstract

Vascular tumors of infancy and childhood represent a number of clinicopathologically distinct entities for which precise histopathological diagnosis is often essential in determining effective therapeutic approach. Unfortunately, pathologists and clinicians alike have traditionally tended to lump these tumors, in addition to small vessel vascular malformations, under overly generic terms like *capillary hemangioma* that do little, if anything, to guide proper clinical management. In the last decade this nosologic oversimplification has begun to wane as important new diagnostic tools and better understanding of etiology have evolved, facilitated by international recognition of the need for a multidisciplinary approach in dealing with these perplexing and often clinically devastating lesions. This article provides a brief historical perspective on this progress, and then focuses on the current clinical, histological, and immunophenotypical features that distinguish the major types of vascular tumors of infancy and childhood, also reviewing new evidence regarding their mechanisms of pathogenesis.

Keywords: Hemangioma; Tufted angioma; Kaposiform hemangioendothelioma

1. Introduction

1.1. History and nomenclature

A growing body of clinical, histological, radiological, and biological evidence supports the conclusion that vascular tumors and malformations of childhood represent a number of distinct entities with diverse etiologies and clinical behaviors. Immunohistochemical and gene expression analyses have recently yielded a number of important clues regarding these etiologies and have also provided important new diagnostic tools. Molecular analyses are currently underway in many laboratories in hopes of better defining the underlying mechanisms of disease and therefore targets of intervention. An absolute requisite of meaningful diagnosis and study of these lesions is precise histopathological description, combined with knowledgeable clinical and radiological evaluation. Unfortunately, traditional overgeneric use of the term *hemangioma* by clinicians and pathologists alike has led to inappropriate grouping of a number of entities that we now know are biologically as well as clinically dissimilar, hampering research efforts in the field and causing problems when making comparisons between cases reported in the literature.

In recognition of this problem, the International Society for the Study of Vascular Anomalies (ISSVA) agreed in 1996 upon a biology-based nosologic classification system derived in part from that proposed by Mulliken and Glowacki in which vascular anomalies were divided into tumors and malformations based on endothelial cell mitotic activity [1]. According to this classification system, the suffix *-angioma* (as in hemangioma) should be reserved for benign vascular tumors arising through

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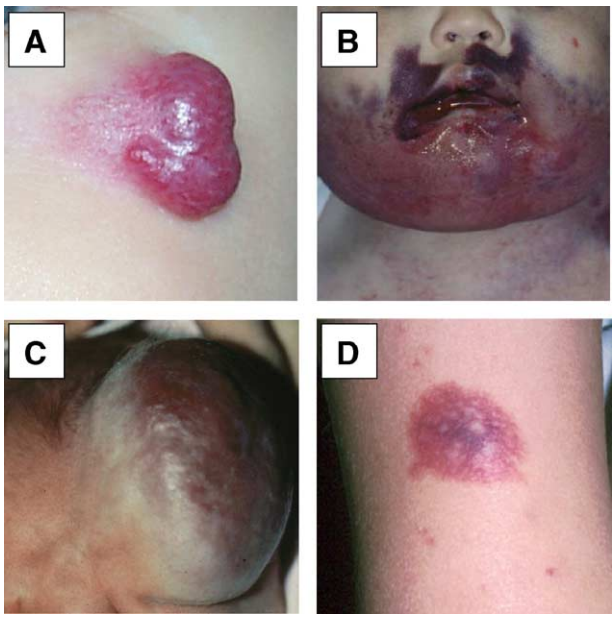

Fig. 1. The clinical heterogeneity of "capillary hemangioma." (A–D) Four patients with vascular tumors, vastly different in clinical characteristics, which share composition by benign, capillary-sized vessels (corresponding histologies are shown in Fig. 2A–D). None are adequately described by the overly generic diagnostic term capillary hemangioma.

cellular hyperplasia—whether congenital or acquired and whether monoclonal or polyclonal. The term *malformation*, on the other hand, should designate true errors in vascular morphogenesis, usually (but not always) clinically evident at birth, which exhibit growth commensurate (±) with that of the patient and little endothelial mitotic activity, for example, venous malformation.

Although seemingly obvious, this nosologic distinction between "angiomas" and malformations represents a significant departure from the traditional diagnostic approach in which the term hemangioma was overapplied without regard to etiology or clinical behavior, at best modified by morphological descriptors such as *cavernous* and *capillary*. For instance, it remains entrenched even today in the pathology literature to refer to *venous* and *capillary venous malformations*, which consist of mitotically quiescent collections of developmentally abnormal capillaries and/or veins, as *cavernous hemangiomas*. This inadvertently encourages the prevalent but erroneous belief that these lesions, which in reality are embryonic errors in vascular morphogenesis, can arise through vascular dilatation within intrinsically hyperplastic *capillary hemangiomas*. Likewise, developmental abnormalities of lymphatic vessel beds (*lymphatic malformations* by the new scheme)

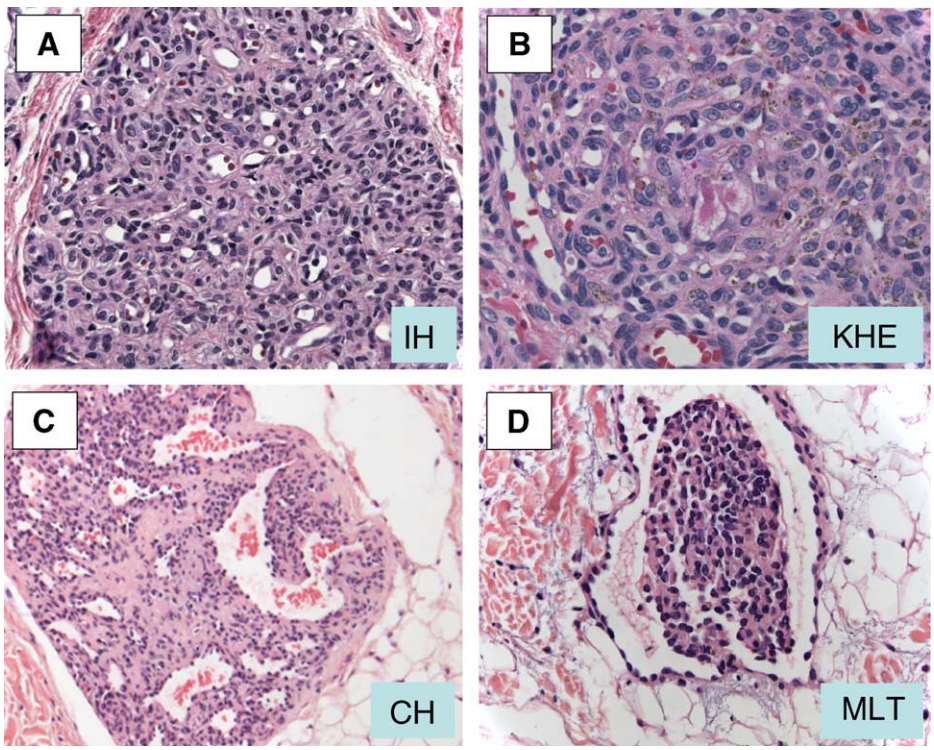

Fig. 2. The histological heterogeneity of capillary hemangioma. (AD) The histological appearances of the four clinical entities depicted in Fig. 1, in the same quadrant pattern. Despite common composition by vessels of capillary size, they are distinguishable in architecture and immunophenotype as well as in clinical presentation. Specific clinicopathological diagnoses for the four are (A) infantile hemangioma (IH) in the proliferative phase, (B) kaposiform hemangioendothelioma (KHE), (C) congenital nonprogressive hemangioma (CH), and (D) multifocal lymphangioendotheliomatosis with thrombocytopenia (MLT). Hematoxylin and eosin, original magnifications: ×400 (A, D), ×600 (B), and ×200 (C).