Angiogenesis in congenital vascular malformations: a dynamic view on a static lesion

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Nerves in congenital vascular malformations - a painful association?

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With great interest we read the manuscript by Gokani and colleagues in a recent issue of JPRAS on the histopathological evaluation of nerve profiles in surgically resected congenital vascular malformations of 29 patients. With the use of immunohistochemical markers specific for nerve tissue, the authors studied the archived samples of venous (VM), capillary (CM) and arteriovenous (AVM) types of vascular malformations, in which they found significantly increased numbers of interstitial nerves compared to control tissues and lymphatic type (LM) of malformations.

The nerve profile in vascular malformations is an interesting subject of investigation, since vascular malformations arise from embryonic errors in vasculogenesis, while at the same time a congruency in development of peripheral nerves and blood vessels has emerged. This could implicate a relationship also between vessels and nerves in vascular malformations, as is indeed supported nicely by these histomorphological observations. It is clearly of clinical importance to speculate whether or not such an increase in nerves inside vascular malformations might contribute to the discomfort of patients. As is cited correctly in the manuscript, pain is a symptom in >90% of patients with VMs, but the authors believe that the observed aberrant nerve profiles in VMs cannot be held responsible for such discomfort, since in their studies also AVMs and CMs showed a similar intralesional increase in nerves. To our opinion such a statement is arguable, since pain can be a serious symptom also in cases of AVMs, especially in the craniofacial region. This contrasts indeed to CMs which are painless lesions, but at this point the results of this study contradict with the findings of Smoller and colleagues who investigated 11 cases of CMs with the use of S100 immunostains, and found a significant decrease of nerve innervation in this specific type of malformation. Therefore, we believe that the situation appears to be more complicated, which can be illustrated by our own histopathological observations on nerve profiles in vascular malformations in a much larger series of patients. In the October 2009 issue of Human Pathology we published a study on the neural component of various types of vascular malformations of skin and soft tissue in 130 patients. Using basically the same methods, numbers of anti-S100 immunostained nerves were counted per cm² of the resected vascular malformations, we observed a significant increase of intralesional mature nerve elements in 96 of 130 specimens (74%). Our series revealed at first that certainly not all cases have a distinct neural component, but also that there is a remarkable difference between AVM (increased nerve density in 87% of cases, n = 83) and VM (55% of cases, n = 33). Particularly AVM lesions in the head and neck area showed such an increase: 45 out of 47 (96%) in this topographic area were affected. Moreover, in our large
series we were able to rule out prior surgery as a potential trigger for nerve proliferation in vascular malformations. It probably relates to the small sample size that Gokani and colleagues did not find a significance difference in nerve profiles between AVMs and VMs. The authors published only the median number of nerves per type of malformation, making it impossible to find out whether or not all malformations were involved. We agree with the authors that well known complications such as thrombosis, hemorrhage, formation of phleboliths and chronic inflammation will lead to clinical discomfort including pain, but this does not rule out the possibility that local nerve increase could at least aggravate such symptoms. For example, inflammatory cytokines, sensory perception, mass-forming effects of hemorrhage and pressure could trigger the neural component in the affected subgroup of patients with many intralesional nerves.

References