Pilocytic astrocytoma and pleomorphic xanthoastrocytoma: glioneuronal tumors or variants of ganglioglioma?

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Neoplasms of the central nervous system (CNS), when examined macroscopically, may be circumscribed or diffusely infiltrating. Circumscribed glial and mixed glial-neuronal neoplasms include, among others, pilocytic astrocytoma (PA), pleomorphic xanthoastrocytoma (PXA) and ganglioglioma (GG). Besides being circumscribed, these neoplasms share several similarities: they affect mostly children, adolescents and young adults; they are often cystic; they may present a mural nodule; they have low proliferative potential[1, 2]. Among the microscopic findings, we highlight the presence of eosinophilic granular bodies (PA, PXA and GG), Rosenthal fibers and microvascular proliferation (PA and GG), a network of reticular fibers and perivascular lymphocytic infiltrate (PXA and GG) and invasion of the leptomeninges (PA, PXA and GG). The variable mix of neurons and glial cells is the major finding for the diagnosis of GG. However, neurons can also be found in some PAs and PXAs[1], including tumors resulting from the combination of GG and PXA[5], which maximizes the similarity among these neoplasias.

The eosinophilic granular bodies are so denominated from their visualization as granular or globular aggregates of varying size, intensely eosinophilic, hyaline and periodic acid-Schiff (PAS) positive, related to astrocytic extensions. The presence of eosinophilic granular bodies in PA, PXA and GG, as well as in other neoplasias of low proliferative potential such as papillary glioneuronal tumor[8], and rarely in schwannoma[6], suggests that the finding of these structures support the diagnosis of a circumscribed, slow-growing and well-differentiated neoplasia, despite the fact that they are rarely identified in anaplastic astrocytomas and glioblastomas. When examined by immunohistochemistry, eosinophilic granular bodies are positive for α-1-antichymotrypsin, α-1-antitrypsin, lysozyme, ubiquitin, membrane proteins associated with lysosome 1 and 2, cathepsin D and α-B-crystalline, indicating lysosomal origin[4, 7]. They may also exhibit immunoreactivity for glial fibrillary acidic protein (GFAP), although there are variations in the immunoreactivity pattern. Electron microscopy reveals membrane-bound round bodies, containing electron-dense homogeneous material with occasional myelin figures or loose granular profiles. The formation mechanism of eosinophilic granular bodies has not yet been fully elucidated. According to some authors, the presence of nuclei in some of these structures evinces that eosinophilic granular bodies may originate from degenerated cells, while others believe that they are derived from lysosomes and disposed outside the cells.

In an article published in this issue of the Brazilian Journal of Pathology and Laboratory Medicine (JBPML), Moreira *et al.*[3] analyzed the presence of neurons and eosinophilic granular bodies in 14 cases of PA, eight PXA and eight GG. They used morphological analysis with hematoxylin and eosin and immunohistochemistry for synaptophysin, neurofilament and GFAP. Neurons were observed in six out of 14 cases of PA and all eight cases of PXA and GG. Eosinophilic granular bodies were identified in four out of six cases of PA with neuronal component and five out of eight cases with no neuronal component, in four out of eight cases of PXA and seven out of eight cases of GG. There was immunostaining for synaptophysin and/or neurofilament in eosinophilic granular bodies associated with the three types of tumor with neuronal component. Nevertheless, it was negative

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in eosinophilic granular bodies associated with cases of PA without neuronal component. GFAP immunostaining was positive in one out of five cases in which it was assessed. In some eosinophilic granular bodies, an image suggestive of nucleus was identified. In view of these findings, the authors conclude that PA with neuronal component and PXA may be classified as glioneuronal tumors or variants of GG and eosinophilic granular bodies with positive immunostaining for synaptophysin and neurofilament may represent degenerated neurons.

It is the first time that neuronal markers are identified in eosinophilic granular bodies. Moreover, the positive immunostaining for GFAP, observed in one case by the authors and described in the literature, as well as immunohistochemical and ultrastructural findings indicating the presence of lysosomes, suggest that these structures may have neuronal and astrocytic origins, representing degenerated cells. As there was no difference in postoperative progression of PA with and without neuronal component in relation to PXA and GG, the presence of the neuronal component does not seem to influence the biological behavior of these circumscribed astrocytic tumors.

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