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LETTER TO THE EDITOR

Melanocytic colonization of choroid plexus papilloma: A previously undocumented source of pigment storage in the plexogenic epithelium

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Sir, – Primary central nervous system (CNS) tumors that are intrinsically defined as being melanized encompass less than a handful of entities (i.e., meningeal melanocytoma and malignant melanoma, melanotic neuroectodermal tumor of infancy, melanotic psammomatous Schwannoma) [1]. Conversely, aberrant pigment production by tumor cells as a seemingly erratic secondary phenomenon has been documented in several unrelated CNS neoplasms. The better-known examples include pigmented variants of pilocytic astrocytoma [2], pleomorphic xanthoastrocytoma [3], ependymoma [4], ganglioglioma [5], dysembryoplastic neuroepithelial tumor [6], glioblastoma [7], medulloblastoma [8], and choroid plexus papilloma [9, 10, 11, 12].

From case to case, the intracellular pigment may be either of melanosomal origin [3, 5, 7, 8] or neuromelanin/lipofuscin [2, 11], and has variously been interpreted as reflecting neoplastic transformation of pluripotent embryonal-like cells, lineage infidelity, or as a “wear-and-tear” phenomenon in prematurely senescent tumor cells.

In contrast to pigment storage due to the synthesis of melanin/neuromelanin by the neoplastic cells themselves, melanocytic colonization refers to an unusual form of symbiosis established between an otherwise conventional neoplasm and a scatter of melanocytes secondarily percolating from the lesion’s melanocyte-containing micro-anatomical neighborhood. Most examples of this altogether rare pattern of cohabitation involve cutaneous-related sites [13, 14, 15].

As for primary CNS tumors, to the best of our knowledge, only three previous occurrences of melanocytic colonization – each involving a meningioma as a substrate – have been reported [16, 17, 18].

Recently, we had the opportunity to study a hitherto unreported variant of the above scenario, one wherein melanocytes grafted themselves upon a choroid plexus papilloma. This was a consultation case from Cameroon, and the rather sparse clinical data indicated that the sample had been resected from a 13-year-old boy of African ethnicity. Located within the right parietal lobe, the tumor was described as a homogeneously enhancing intraparenchymal mass communicating with the posterior horn of the lateral ventricle.

Light microscopy revealed a moderately cellular epithelial proliferation with tightly packed papillary to confluent, near-solid, architecture (Figure 1A). Irregularly lined up along nondescript vascular axes, individual tumor cells had copious cytoplasm with roundish contours, and harbored a subtly atypical nucleus. There was no detectable mitotic activity. The lesion’s most arresting feature was the presence of abundant brown intracytoplasmic pigment granules throughout the neoplastic cell population (Figure 1B). The pigment turned intensely black with Masson-Fontana’s silver impregnation (Figure 1A – inset), and was partially sensitive to bleaching by hydrogen peroxide, whereas Prussian Blue staining gave a negative result.

The yield of immunohistochemistry was felt to have been hampered by suboptimal preanalytical handling; nevertheless, appropriate expression of cytokeratin (clones AE1/AE3; Dako, Glostrup, Denmark) was able to confirm the epithelial nature of tumor cells (Figure 1C). While the latter also exhibited faint to moderate reactivity with the melanosomal marker MELAN-A (clone A103; Dako), testing for this epitope surprisingly revealed a quite intensely stained secondary population of nonepithelial cells with dendritic to stellate morphology, not readily appreciated on routine slides (Figure 1D). Ubiquitously dispersed, these melanocytes tended to intri-
cately intermingle with the tumor cells via their ramified processes (Figure 1E).

Based on the above findings, we posited a diagnosis of melanotic variant of choroid plexus papilloma (WHO grade I), along with a comment on the probable origin of the pigment from intratumorally recruited melanocytes.

Although unprecedented with regard to the nature of the host tumor, the plausibility of our observation is nevertheless felt to be supported by the similarities it shares with previously reported examples of the melanocytic colonization paradigm, both in the cutaneous realm and in the CNS. As for the latter, the present case also reinforces the perception that constitutional hyperpigmentation might possibly predispose to melanocytic colonization of tumors evolving within or contiguous to an anatomical compartment physiologically populated by melanocytes [16, 17, 18]. Conversely, profuse transfer of pigment granules from colonizing melanocytes to the cytoplasm of host tumor cells, as seen in our case, has not been a feature in any of the three previously reported me-
ningiomas – although this is an elementary process within the normal epidermal melanin unit [19], and has been observed in the neoplastic epidermis as well [15].

Prior to the present observation, reported examples of pigmented choroid plexus neoplasms – also including one case of carcinoma [20] – indicate that choroid plexus epithelial cells are potentially able to elaborate neuromelanin [10,11] as well as melanosomes [9]. The former pathway has been speculated to result either from inappropriately long persistence or – on the contrary – accelerated senescence of tumor cells. Indeed, so-called “Biondi rings” – a subcellular indicator of both physiological and pathological ageing [21] – have been known to occur in a subset of choroid plexus papillomas [22] and were seen in our case as well. On the other hand, a more generic – rather than mechanistic – argument of divergent differentiation/lineage infidelity has been invoked to account for the presence of true melanosomes. Vague though it may be, this interpretation is nevertheless lent circumstantial evidential support per analogiam by the repeated occurrence of aberrant melanosomes in some non-neural crest-derived CNS tumors in particular gliomas as well [3, 5, 7]. For the sake of completeness, we further remark to have identified at least one case report on ependymoma – a close relative of choroid plexus tumors – containing both melanosomes and neuromelanin [4].

Tentative interpretations of melanocytic colonization tend to point out that several auto- or paracrine growth factors produced by tumors will also promote centripetal migration of neighboring melanocytes [16, and references therein]. Moreover, since all reported cases to date involved a host tumor with epithelial or epithelial-like (i.e., meningothelial meningioma) character, an intrinsic propensity of melanocytes to engage in organoid pairing apt to recapitulate the epidermal melanin unit might be invoked as well [19].

Exceptionally, the colonizing melanocytes themselves may be of neoplastic nature, as exemplified by some sporadic reports on squamous cell carcinoma or basal cell carcinoma amalgamated with melanoma in situ [14]. In our case, the absence of significant melanocytic atypia and detectable mitotic activity rendered such an alternative utterly improbable.

Notwithstanding the arguably limited differential diagnostic scope of our observation, we nevertheless feel prompted to articulate the following points. First, at variance from conventional neoplastic entities consubstantially defined by their melanotic character, the detection of melanin pigment in choroid plexus tumors does not, in itself, appear to determine the behavior of individual cases: neither are melanized choroid plexus tumors intrinsically more aggressive [9, 10, 11, 12], nor does the presence of melanin exclude a diagnosis of choroid plexus carcinoma [20]. Second, the phenomenon of melanocytic colonization reported herein is apt to remind us of the physiological presence of some melanocytes in the choroid plexus stroma: these, in turn, may occasionally be the source of primary intraventricular melanomas [23].

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Conflict of interest

The authors declare that they are not aware of any conflict of interest.

References


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