CLINICAL IMAGE

Unexpected cause of anemia: metastasis of neuroendocrine tumor to the bone marrow

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In 2012, a 39-year-old male patient underwent a stereotactic biopsy of his right frontal lobe and was diagnosed with oligoastrocytoma grade II. He received 6 cycles of the procarbazine, lomustine, and vincristine regimen, but magnetic resonance imaging (MRI) revealed tumor progression in the primary location. He underwent brain surgery in January 2013, but 6 months later, a repeated MRI showed further tumor progression with infiltrates within the ethmoidal and frontal sinuses. In September 2013, he received image-guided radiotherapy at a total dose of 45 Grey. A complete blood count (CBC) showed no abnormalities. The brain mass seemed to be unaltered on MRI performed in January 2014, but a complete blood count test revealed severe anemia (hemoglobin, 6.3 g/dl) and mild thrombocytopenia (platelet count, 87×10⁹/l). During his stay in the hematology unit, all common causes of anemia and thrombocytopenia were excluded. A bone marrow examination showed the aggregates of polymorphic, partly spindle-shaped cells with abundant eosinophilic cytoplasm that were located in organoid nests surrounded by scant fibrovascular stroma (FIGURE 1A). Moreover, nuclear chromatin was typical for a neuroendocrine tumor (so called

"salt and pepper"). These cells were found to be CD45-negative but CD56- and CD57-positive on flow cytometry. The results of a broad panel of immunohistochemical tests were typical for neuroendocrine tumor with positive CD56 and synaptophysin staining (FIGURE 1BC). The Ki-67 index was 80%. Unexpectedly, brain tumor markers (glial fibrillary acidic protein and neurofilament) were found to be negative. Extensive clinical and imaging workup did not show the primary site of neuroendocrine tumor. An archived material obtained from an initial brain biopsy was then verified by 3 independent neuropathologists but the primary diagnosis of glioma was maintained. The patient received several cycles of palliative chemotherapy consisting of cisplatine and vepeside but no effects were observed.

A neuroendocrine tumor in the bone marrow continues to be an extremely rare finding. There are only single reports of carcinoid tumors with bone marrow metastases.^{1,2} Carcinoid tumor cells were also found in the bone marrow on autopsy.³ Two other patients were reported to have bone marrow infiltrates by neuroendocrine tumor with an unknown primary site.^{4,5} Bone marrow infiltration by neuroendocrine tumor preceded by

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FIGURE 1 A – an aggregate of polymorphic cells in the May–Grünwald–Giemsa stain of the marrow aspirate, $\times 100$; B – cells showing strong positivity for CD56, $\times 40$; C – cells showing strong positivity for synaptophysin, $\times 40$

glioma has never been reported before. It is unknown whether the prior therapy for brain cancer contributed to the development of the tumor in our patient. This case underlines the importance of bone marrow biopsy in the diagnosis of nonhematological disorders.

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