Tibial Adamantinoma: Late Metastasis to the Brain

Most of the tumors that metastasize to the brain are carcinomas (1); sarcomas represent only a very small percentage. Due to improved therapies for aggressive sarcomas with resultant longer posttreatment life spans and the long-recognized propensity of several types of more indolent sarcomas for late metastasis, neuropathologists should anticipate seeing these tumors more frequently. The following case study illustrates this point and documents the occurrence for future reference.

A 52-year-old woman on routine surveillance imaging presented with a left frontal dura-based enhancing lesion thought to be most consistent with meningioma (Fig. 1A). A 3-month follow-up image demonstrated significant growth in this lesion with apparent intraparenchymal extension of an enhancing dura-based mass (Fig. 1B). Her medical history was significant for adamantinoma of the right tibia that had been resected 32 years before, at age 20 years. Given the rapid growth of this lesion and its imaging appearance being more consistent with metastasis, she underwent surgical excision. She also had several presumed pulmonary metastases (data not shown).

Intraoperative resection of the lesion demonstrated that much of the tumor was subarachnoid and intraparenchymal, with only loose, if any, dural attachment. Intraoperative squash preparations showed a hypercellular, monomorphic, spindle-cell neoplasm composed of small to medium cells with mild to moderate atypia and coarse linear eosinophilic cytoplasm (Fig. 1C).

An intraoperative diagnosis of high-grade spindle-cell neoplasm was made; anaplastic meningioma could not be excluded.

Permanent sections confirmed cohesive growth of the tumor and verified the intraoperative impression that the tumor was actually embedded within brain parenchyma and was likely a metastasis (Fig. 1D). The tumor did not have many features that are often seen in primary adamantinomas, such as biphasic growth, basa-lloid appearance, well-defined epithelial structures, and bone formation. The main growth pattern was storiform to fascicular, with bundles of tumor cells approximately 10 to 15 cells wide. Other areas possessed a trabecular to vaguely pseudoglandular growth pattern, with 1-cell-thick cords of tumor cells interconnecting to form a network of rings surrounding a mucinous ground substance. Nuclear chromatin pattern was open, with some stranded chromatin; most nuclei contained 1 or 2 small but distinct, mildly eosinophilic nucleoli (Fig. 1E). The tumor cells had moderate amounts of pale eosinophilic cytoplasm, with cytoplasmic vacuoles giving the cytoplasm a frothy appearance. Inter-cellular borders were not distinct.

Immunohistochemical studies showed that most tumor cells were immunoreactive with antibodies to podoplanin (D2-40) (2), p63 (3), pancytokeratin (AE1/AE3) (4) (Fig. 1F, G, H, respectively), and cytokeratin 19 (4). A minority of tumor cells showed nuclear expression of p53. There was no significant immunostaining for cytokeratin 8/18 (CAM5.2) or cytokeratin 7, as has been reported for adamantinoma of long bones (4). E-cadherin was also strongly immunopositive—a feature that can be seen in adamantinoma (5). Tumor cells were negative for anti-epithelial membrane antigen and antinuclear progesterone receptor antibodies. MIB1 immunohistochemistry showed labeling in up to 20% of tumor cells (Fig. 1I).

Adamantinoma is a very rare primary bone tumor that most commonly presents in young adults during the third and fourth decades of life (6–10). It shows a marked predilection for involving the anterior portion of the tibial metaphysis or coarse linear eosinophilic cytoplasm (Fig. 1C). An intraoperative diagnosis of high-grade spindle-cell neoplasm was made; anaplastic meningioma could not be excluded.

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FIGURE 1. (A) Original magnetic resonance T1 postcontrast image demonstrating a dura-based enhancing nodule believed to be most consistent with meningioma. (B) Magnetic resonance T1 postcontrast image 3 months later demonstrating an intraparenchymal rim enhancing lesion with a central region of hypointensity, with dural enhancement overlying the lesion. (C) Intraoperative squash preparations showing small to medium spindle cells with mild to moderate atypia. (D) Tumor intimately involved with brain parenchyma. (E) Tumor is predominantly composed of densely cellular fascicles of spindle cells with mild atypia. (F) Immunohistochemistry shows expression of podoplanin (D2-40) at varying intensities within the tumor. (G) Diffuse nuclear expression of p63 by tumor cells on immunohistochemistry, without cytoplasmic immunostaining. (H) Tumor cells labeled with pancytokeratin (AE1/AE3) antibodies on immunohistochemistry in a mildly patchy pattern. (I) MIB1 (Ki-67) immunohistochemistry in a more proliferative portion of the tumor labels approximately 20% of tumor cells.
of correctly diagnosing metastases from sarcomas is made more difficult by the fact that many types have multiphasic and/or heterogeneous histologic appearances, and metastatic lesions from such sarcomas often consist of only one such component, as in our case.

The pattern of mucin-filled spaces and pseudoglandular growth in permanent sections, coupled with good clinical history and likelihood of pulmonary metastases, made this case relatively easy to distinguish from anaplastic brain-invasive meningioma in permanent sections. We note in particular, however, that much of the immunohistochemical pattern overlaps between adamantinoma and meningioma. In particular, podoplanin (20, 21) and E-cadherin (22) are usually immunopositive in both tumor types, and nuclear p63 has been (23), which was not with at least some coassociated cytoplasmic immunoreactivity (23), (24), was not present in this case (Fig. 1G). This case provides documentation for anyone in the future who might encounter similar cases.

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