

Olfactory neuroblastoma

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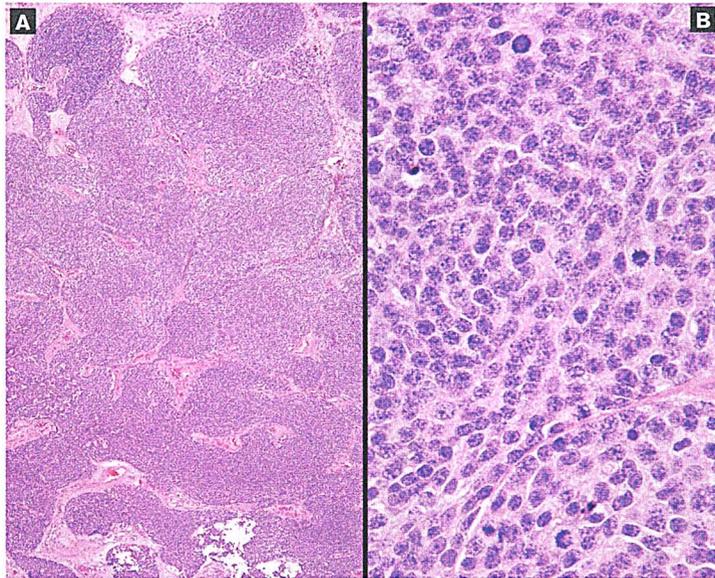


Figure 1. A: These tumor lobules are easy to identify. They are separated by a vascularized stroma. B: The “small, round, blue-cell” neoplasm has scant cytoplasm surrounding variably hyperchromatic nuclei with an even distribution of granular nuclear chromatin. Mitotic figures are noted.

Olfactory neuroblastoma (esthesioneuroblastoma) is an uncommon malignant neuroectodermal nasal tumor that accounts for approximately 5% of all malignant neoplasms. Olfactory neuroblastomas are thought to arise from the specialized sensory neuroepithelial (neuroectodermal) olfactory cells that are normally found in the upper part of the nasal cavity, usually including the cribriform plate of the ethmoid sinus. These tumors affect both sexes equally. A bimodal age distribution (the 2nd and 6th decades of life) has been documented, although patients of all ages can be affected. Patients present with nonspecific symptoms of nasal obstruction (70% of cases) and epistaxis (50%); less common symptoms include headache, pain, visual disturbances, and anosmia (<5%). Owing to the nonspecific nature of the presenting symptoms, patients often have a long history prior to diagnosis.

One of the characteristic radiographic findings of olfac-

tory neuroblastoma is a dumbbell-shaped mass that extends across the cribriform plate; erosion of the cribriform plate, lamina papyracea, and/or fovea ethmoidalis may also be seen. T1-weighted magnetic resonance imaging with gadolinium contrast will show marked enhancement. For practical purposes, all olfactory neuroblastomas involve the cribriform plate to some degree or other. Even though the bulk of a tumor may lie intracranially, it is still attached to the cribriform plate.

Microscopically, one of the most reliable histologic features is a lobular architecture (figure 1, A). Circumscribed lobules or nests are made up of “primitive” neuroblastoma cells, usually below an intact mucosa and in a vascularized fibrous stroma. The tumor cells are small, round, and blue; they are slightly larger than mature lymphocytes; and they have a high nucleus-to-cytoplasm ratio. The cells are often arranged in a syncytial pattern, with a tangle of neuronal

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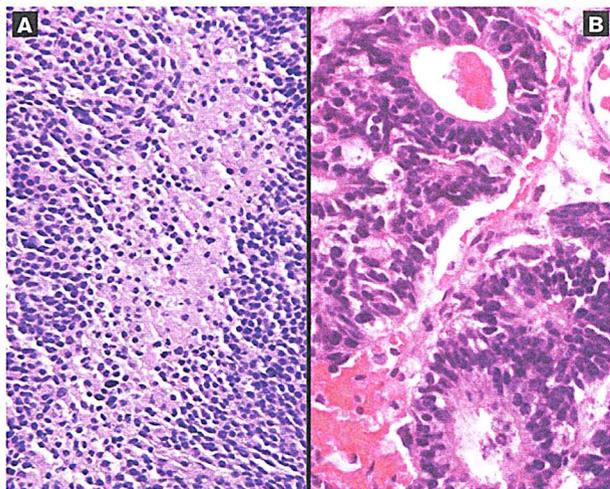


Figure 2. **A:** Image of a pseudorosette shows a cuff of neoplastic cells surrounding an edematous neurofibrillary matrix. **B:** A true rosette has a well-defined lumen.

processes forming the background. The nuclei are small and uniform with an even distribution of granular nuclear chromatin (figure 1, B). Nucleoli are inconspicuous. For the most part, nuclear pleomorphism, increased mitotic figures (>2 per high-power field), and necrosis are uncommon.

Two types of rosettes are seen, although in up to only 30% of cases (figure 2). Pseudorosettes (Homer Wright rosettes) are the more common of the two; they are characterized by a delicate neurofibrillary and edematous stroma that forms the center of a palisaded arrangement of cells. True rosettes (Flexner-Wintersteiner rosettes) have a tight, “gland-like” annular arrangement.

Olfactory neuroblastomas are graded I through IV on the basis of the degree of differentiation and the presence or absence of a neural stroma, mitotic figures, and necrosis. Higher-grade tumors are less differentiated, and pseudorosettes and fibrillar stroma are less common. The nuclei become more pleomorphic, chromatin is more coarse, mitotic figures increase, and tumor necrosis is present. The grade correlates with the prognosis, although not as closely as does tumor stage; stage A tumors are limited to the nasal cavity, stage B tumors involve the nasal cavity and paranasal sinuses, and stage C tumors extend beyond these structures. Approximately one-half of all olfactory neuroblastomas are stage C tumors at presentation.

Owing to the “small, round, blue-cell” nature of the neoplasm, the differential diagnosis is quite broad; it includes melanoma, rhabdomyosarcoma, sinonasal undifferentiated carcinoma, lymphoma, Ewing’s sarcoma, pituitary adenoma, plasmacytoma, paraganglioma, and primitive neuroectodermal tumor. Clinical and demographic findings can help make distinctions, as can pertinent immunohis-

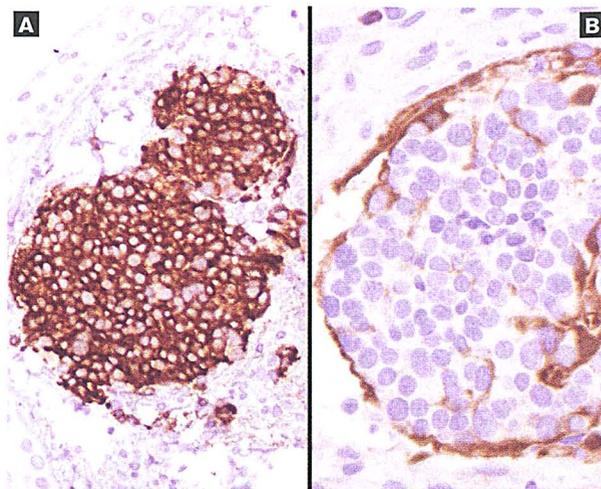


Figure 3. **A:** A lobule of neoplastic cells shows strong, diffuse chromogranin immunoreactivity. **B:** A lobule of neoplastic cells features a sustentacular, peripheral distribution with S-100 protein.

tochemical reactions to synaptophysin, chromogranin, neuron-specific enolase (NSE), neurofilament protein (NFP), S-100 protein, keratin, CD45RB, desmin, CD99, and HMB45. Olfactory neuroblastomas are usually positive with synaptophysin, chromogranin, NSE, NFP, and S-100 protein (sustentacular distribution) (figure 3).

Radical surgical eradication (craniofacial resection) combined with radiotherapy is the gold standard of care. In a few selected cases, endoscopic resection with adjuvant radiation may have merit. Overall 5-year survival ranges from 40 to 80%, depending on the stage and grade. Patients with low-grade tumors have an 80% 5-year survival, while those with high-grade tumors have a 40% survival. As many as 30% of patients will experience a local recurrence following therapy, usually within the first 2 years. Approximately 15% of patients will develop cervical lymph node metastasis, and 10% will develop a distant metastasis at some point during the course of their disease.

Suggested reading

- Dulguerov P, Allal AS, Calcaterra TC. Esthesioneuroblastoma: A meta-analysis and review. *Lancet Oncol* 2001;2:683-90.
- Wenig BM, Dulguerov P, Kapadia SB, et al. Neuroectodermal tumours. In: Barnes EL, Eveson JW, Reichart P, Sidransky D, eds. *Pathology and Genetics of Head and Neck Tumours*. Kleihues P, Sobin LH, series eds. World Health Organization Classification of Tumours. Lyon, France: IARC Press; 2005:65-75.