American Association of Neuropathologists

Navigating the Border: Skull Base and Head and Neck Pathology for the Practicing Neuropathologist

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Case-Based Questions (please see page 3 for answers)

1.	A 48-year-old man presents with a locally advanced lesion centered within the sinuses and involving the skull base. Histologic examination shows malignant, epithelioid cells with plasmacytoid/rhabdoid morphology, and immunohistochemistry demonstrates positivity for pancytokeratin and p63 (variable). INI1 is lost in neoplastic cells. What is the most likely diagnosis?	
	a.	Atypical teratoid/rhabdoid tumor (AT/RT)
	b.	Rhabdomyosarcoma
	c.	SWI/SNF complex-deficient sinonasal carcinoma

2.	A 66-year-old woman with a 3.6 cm mass of the nasolacrimal duct with orbital and skull base involvement undergoes resection, demonstrating an epithelial neoplasm with complex exophytic and endophytic growth, papillary fronds, monotonous neoplastic cells, and transmigrating neutrophils. In situ hybridization studies are negative for low-risk and high-risk HPV. A consulting head and neck pathologist remarks that some of the features are histologically reminiscent of an inverted sinonasal papilloma; however, there are no goblet cells or ciliated cells. What is the most likely molecular alteration?	
	a.	*DEK*::*AFF2* fusion
	b.	*NUTM1*
	c.	*SMARCA4*

3.	A 53-year-old woman presents with an ethmoid sinus mass that measures 4.1 cm and locally infiltrates the anterior skull base. Molecular testing demonstrates a *PAX3* rearrangement, and the neoplasm was diagnosed as a biphenotypic sinonasal sarcoma. What is the most likely immunohistochemical staining pattern?	
	a.	S100 positive, SMA negative, SOX10 positive
	b.	S100 positive, SMA positive, SOX10 negative
	c.	S100 positive, SMA positive, SOX10 positive

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Correct Answers and Rationales

Question 1 Correct Answer and Rationale: **C: SWI/SNF complex-deficient sinonasal carcinoma**

Rationale: SWI/SNF complex-deficient sinonasal carcinomas may appear basaloid or plasmacytoid/rhabdoid in morphology. INI1 loss, in the context of SMARCB1-deficient carcinomas, and BRG1 loss, in the context of SMARCA4-deficient carcinomas, are demonstrable with immunohistochemistry. Though AT/RTs also feature SMARCB1 or SMARCA4 alterations, the clinical scenario of the tumor arising within the sinuses makes this diagnosis less likely. Rhabdomyosarcomas may demonstrate keratin immunoreactivity; however, they do not demonstrate INI1 loss.

Question 2 Correct Answer and Rationale: **A: *DEK*::*AFF2* fusion**

Rationale: Currently considered a subtype of non-keratinizing squamous cell carcinoma, DEK::AFF2 squamous cell carcinomas demonstrate exophytic and endophytic growth and monotonous, neoplastic cells. Tumor-infiltrating neutrophils are often seen. NUT carcinomas more classically present as sheets of undifferentiated cells, sometimes with abrupt keratinization. SMARCA4-deficient carcinomas tend to have an aggressive appearance with large, anaplastic cells, and such tumors would not be histologically reminiscent of an inverted sinonasal papilloma.

Question 3 Correct Answer and Rationale: **B: S100 positive, SMA positive, SOX10 negative**

Rationale: Biphenotypic sinonasal sarcoma is a spindle cell neoplasm of the sinonasal tract that demonstrates neural and myogenic differentiation and frequently harbors PAX3 gene rearrangements. SMA is positive, consistent with myogenic differentiation, and S100 is positive in the absence of SOX10 staining, a helpful immunohistochemical clue to the diagnosis. S100 and SOX10 positivity in the absence of SMA might suggest a schwannoma. SOX10 positivity is not seen in biphenotypic sinonasal sarcoma.