

## Summary of discussion of the experts

The clinical history and gross findings favor a pancreatic primary.

### **Microscopic Features**

This is a high-grade malignant neoplasm, but it is NOT a ductal adenocarcinoma of the pancreas, which is perhaps the foremost/important differential to exclude in terms of the management of this patient.

By overall morphology, this tumor falls into the category of cellular, monotonous, stroma-poor neoplasms for which the differential diagnosis is non-ductal pancreatic neoplasia (neuroendocrine, solid-pseudopapillary neoplasm, acinar, pancreatoblastoma) or secondary tumors. In this case, because of the small-blue-cell appearance, differential diagnoses like desmoplastic small cell tumor and Ewing/PNET would also have to be considered, but the cytology (especially the presence of nucleoli, and relative amount of cytoplasm) are more in favor of a non-ductal pancreatic tumor rather than a secondary/mesenchymal neoplasm.

At low magnification, this solid stroma poor neoplasm appears to be composed of two distinct cell populations and has a pushing border. The cells on the periphery are arranged in nests and sheets and have granular amphophilic cytoplasm with bland oval nuclei, coarse immature chromatin and distinct but small nucleoli. There is abrupt transition to a second population of paler cells with abundant pale bubbly to clear cytoplasm and small pyknotic nuclei. Focal single cell necrosis and occasional mitotic figures are also present.

### **Pertinent Negatives**

No definite acini or prominent nucleoli are present as would be typical of acinar cell carcinoma. No salt and pepper chromatin or rosettes are seen as would be expected in a well differentiated neuroendocrine tumor.

No ill-defined nests typical of solid pseudopapillary neoplasm are seen. Additionally, the chromatin is not typical of solid pseudopapillary neoplasm, which is usually very fine, pale and homogenous.

No cytoplasmic mucin, gland formation or keratinization is seen to favor adeno- or squamous carcinoma.

### **Immunohistochemical Findings**

The strong nuclear staining for beta-catenin could be seen in solid pseudopapillary neoplasm (usually diffuse), acinar cell carcinoma or pancreatoblastoma (usually with a more focal pattern of staining). For the diagnosis of an acinar cell carcinoma and its distinction from other malignancies, acinar markers trypsin, chymotrypsin and BCL10 should be expressed. The lack of trypsin expression in this case excludes that diagnosis. The co-expression of CAM 5.2 and level of Ki-67 argue against solid

pseudopapillary neoplasm, which is usually negative for keratin and has an extremely low Ki67 index (<5% of cases have an index above 3%).

The absence of acinar markers is also a little unusual for pancreatoblastoma, because pancreatoblastoma is believed to be a mostly acinar-lineage neoplasm. However, we have now seen several cases of what we regarded as pancreatoblastomas that lacked acinar markers.

### **Final Diagnosis**

Pancreatoblastoma (2 of 3 experts)

Pancreatic malignant neoplasm, unclassified, with morphologic features suggesting pancreatoblastoma (1 of 3 experts)

### **Expert morphologic takeaways**

- The lymph-node-like appearance on low power (ie, the presence of zones of pallor at the center of nodules resemble germinal centers, in an appearance also described for example in desmoplastic medulloblastomas of the brain) is a characteristic finding in pancreatoblastomas.
- In areas the tumor cells show vague streaming, reminiscent of poorly formed squamoid morules. The second population of pale cells may represent an attempt (albeit, a poor one) at morule formation, which has been reported (PMID: 31581358) in pancreatoblastomas. Indeed, in our experience, the so-called squamoid corpuscles in pancreatoblastoma are seldom really squamoid. They frequently resemble the morules seen in other FAP/beta-catenin related tumors, and these morules are morphologically more meningotheelial-like. Also, in many cases, these morules are subtle, and appear only as pale zones of a distinct population of cells amidst a small-blue-cell proliferation.