A man in his late 30s presented with testicular pain. On further evaluation, he was found to have a testicular mass, and serum tumor markers that are frequently elevated in germ cell tumors (beta subunit of human chorionic gonadotropin, lactate dehydrogenase, and alpha-fetoprotein) were within normal limits. He underwent radical orchiectomy, which revealed a 4.0 cm cystic mass.

Histopathologic examination of the cystic mass revealed a lesion lined by stratified squamous epithelium without dermal appendages and intraluminal acellular keratinaceous elements (Figure 1A and B). These morphologic features were consistent with an epidermoid cyst. In addition, a 0.5 cm lesion was identified adjacent to the rete testis (Figure 1A and C). This lesion is comprised of nests of cells with eosinophilic cytoplasm and fine speckled chromatin and without appreciable cytologic atypia, mitotic activity, or necrosis. Immunohistochemistry exhibited diffuse positivity for neuroendocrine markers such as synaptophysin (Figure 1D) and chromogranin A, whereas Ki67 immunostain revealed a low proliferative index (<1%). These findings were consistent with a well-differentiated neuroendocrine tumor.

**FIGURE 1.** Well differentiated neuroendocrine tumor and epidermoid cyst (A). Epidermoid cyst (B). Well differentiated neuroendocrine tumor (C) positive for synaptophysin (D).
Which of the following statements regarding testicular epidermoid cyst and well-differentiated neuroendocrine tumor is true?

a. These tumors are associated with germ cell neoplasia in situ (GCNIS).
b. Cytogenetic abnormalities in these tumors include isochromosome 12p/ gain of chromosome 12p.
c. These tumors are unrelated to GCNIS or isochromosome 12p/ gain of chromosome 12p.
d. These tumors are associated with GCNIS, but not isochromosome 12p/ gain of chromosome 12p.

Answer: c. These tumors are unrelated to GCNIS or isochromosome 12p/ gain of chromosome 12p.

Epidermoid cysts are considered part of the spectrum of “prepubertal” germ cell tumors, which are often identified in older (postpubertal) patients. Distinguishing prepubertal teratoma from postpubertal teratoma is important for clinical management, as prepubertal teratoma is benign while postpubertal teratoma is a malignant tumor.

Prepubertal teratoma can exhibit considerable morphologic overlap with postpubertal teratoma, particularly in cases with limited tumor sampling. Ancillary testing can help distinguish these entities, as prepubertal teratomas (such as epidermoid cyst) are unrelated to GCNIS and do not have chromosome 12p abnormalities (type I germ cell tumors).1-4 In contrast, postpubertal teratomas are considered type II germ cell tumors that arise from GCNIS and frequently have chromosome 12p abnormalities.1,3,4 Morphologic evaluation of the background seminiferous tubules and immunohistochemistry for OCT3/4 was negative for GCNIS (Figure 2A and B). In addition, cytogenetic studies were negative for isochromosome 12p/ gain of chromosome 12p, supporting the diagnosis of an epidermoid cyst.

Most of these well-differentiated neuroendocrine tumors have an indolent clinical course. Similar to epidermoid cysts, these tumors are unrelated to GCNIS and do not have chromosome 12p abnormalities. Finally, in some instances, well-differentiated neuroendocrine tumors have been described to occur in association with prepubertal teratomas.4

REFERENCES

FIGURE 2. Seminiferous tubules (A) negative for OCT 3/4 (B).