Pseudo–"solid pseudopapillary neoplasms" of the testis: in reality Sertoli cell tumors

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Dear Editor,

We read with interest and concern two reports published in HUMAN PATHOLOGY [1,2] concerning testicular neoplasms that were felt to be "testicular analogues" of the well-known "solid pseudopapillary neoplasm" (SPN) of the pancreas, albeit in one of the 2 papers the authors preferred to designate the tumors as *primary signet ring stromal tumors* of the testis [1]. Although we acknowledge that the pseudopapillae in the SPNs may be limited in amount, their apparent absence, according to the descriptions of the microscopic findings in all of the 14 tumors in these 2 reports, struck us as unusual for a tumor the authors were placing in the SPN category.

The 14 tumors had foci of signet ring–type cells as well as solid, nested and trabecular patterns of growth. They shared many immunohistochemical reactivities with SPNs, including nuclear β-catenin, CD10, CD56 and α-1-antitrypsin in the subset of cases studied by this method. The authors reported they were negative for inhibin (0/12) and calretinin (0/12). Eleven analyzable tumors had exon 3 mutations in the *CTTNB1* gene that encodes β-catenin. In our estimation, these tumors fall within the Sertoli cell tumor, not otherwise specified (NOS) category of testicular tumors and should not be regarded as SPNs.

Signet ring–type cells are a well-recognized feature of Sertoli cell tumor, NOS. They have previously been illustrated in Sertoli cell tumors by authorities in testicular pathology [3-7] (see p. 119, Fig. 5.18 [3]; p. 367, Figure 5.39D [4]; p. 248, fig. 6-20 [5]; p. 790, Fig. 12-79 and p. 791, Fig. 12-83 [6]; p. 716, Fig. 14 [7]), and they are almost certainly due to large fat vacuoles in the cytoplasm. One of us co-authored a large study indicating so, and in that series they were

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seen in 26 of 60 cases (43%) [7]. The reactivity of Sertoli cell tumor, NOS for a variety of antigens, including nuclear β-catenin [8-10] and CD56 [11] is well established, as is their variable positivity for inhibin and calretinin. In 5 series, the rate of inhibin reactivity in Sertoli cell tumors varied from 25% to 90% [12-16], and a recent study showed calretinin reactivity in 43% [16]. Negative staining for inhibin and calretinin, therefore, does not exclude Sertoli cell tumor. We are not aware of studies that have looked for CD10 or α-1-antitrypsin reactivity in testicular Sertoli cell tumors, but ovarian ones are frequently CD10 positive [17]. Additionally Sertoli cell tumors, NOS harbor the same exon 3 mutations in the *CTTNB1* gene [9,18] as described in the testicular tumors considered SPN analogues [1,2]. Our conclusion from these data is that there is long-established overlap in many of the immunohistochemical reactivities and molecular genetic features of testicular Sertoli cell tumors and pancreatic SPNs.

We wish to illustrate 2 recent cases of Sertoli cell tumor that we readily found in our files that showed similar morphological features to those the authors illustrated and that exhibited strong nuclear reactivity for β-catenin (known to correlate with the *CTNNB1* mutation [9]) as well as significant reactivity for both inhibin and calretinin (Figs. 1 and 2). They presented as testicular masses in 43-year-old and 23-year-old men who had negative serum marker studies. In the first case, there was significant hollow tubular/glandular differentiation, a feature that is not seen in SPNs, although this case also showed the nested, trabecular and solid foci the authors emphasized in their descriptions of "SPN analogues." This tumor showed patchy inhibin and calretinin reactivity and diffuse nuclear and cytoplasmic positivity for β-catenin. The second case had solid, nested and trabecular patterns with foci of vacuolated tumors cells (?signet ring cells) and displayed significant nuclear pleomorphism; it prominently invaded paratesticular blood

vessels. It had diffuse inhibin and β-catenin reactivity (calretinin was not performed). It was classified as a malignant Sertoli cell tumor, NOS.

In our opinion, these cases illustrate that Sertoli cell tumors of the testis have overlapping features with those of SPN. They additionally share a mutation of a gene that is altered in a variety of tumors other that Sertoli cell tumor and SPN, illustrating what is becoming increasingly evident concerning the nonspecificity of many molecular genetic changes in tumors. We think it is a mistake to equate such tumors with the solid pseudopapillary tumor of the pancreas, which has a mostly indolent behavior, because it may well lead to undertreatment when, in fact, early aggressive surgical management with retroperitoneal lymph node dissection may be life-saving. Our second case is a prime example of an aggressive Sertoli cell tumor that should not be regarded as a SPN.

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Figure Legends

Fig. 1 Sertoli cell tumor from a 43-year-old man shows (A) solid and trabecular growth with irregular spaces, (B) prominent hollow tubules, (C) patchy inhibin (left) and calretinin (right) positivity, and (D) strong, diffuse nuclear and cytoplasmic reactivity for β-catenin.

Fig. 2 Sertoli cell tumor from a 23-year-old man shows (A) anastomosing solid nests, (B) prominent nuclear pleomorphism with intranuclear cytoplasmic inclusions and vacuolated cytoplasm, (C) conspicuous large vessel invasion in the paratestis, and (D) strong, diffuse cytoplasmic reactivity for inhibin (left) and nuclear and cytoplasmic reactivity for β-catenin (right).

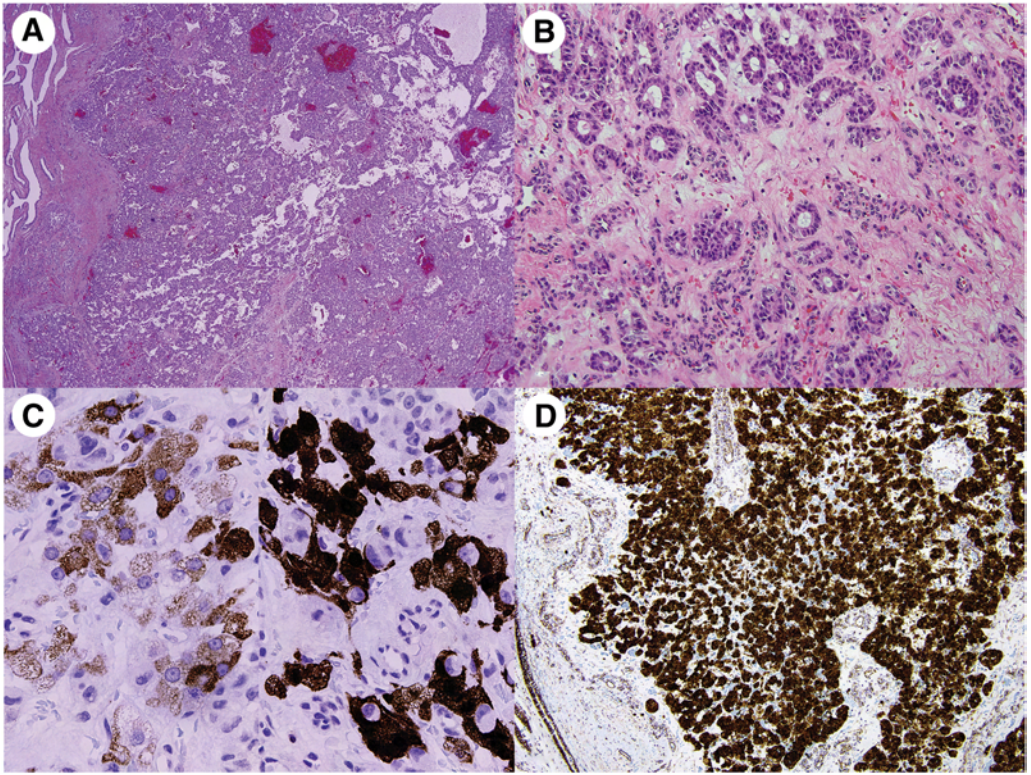

Figure 1

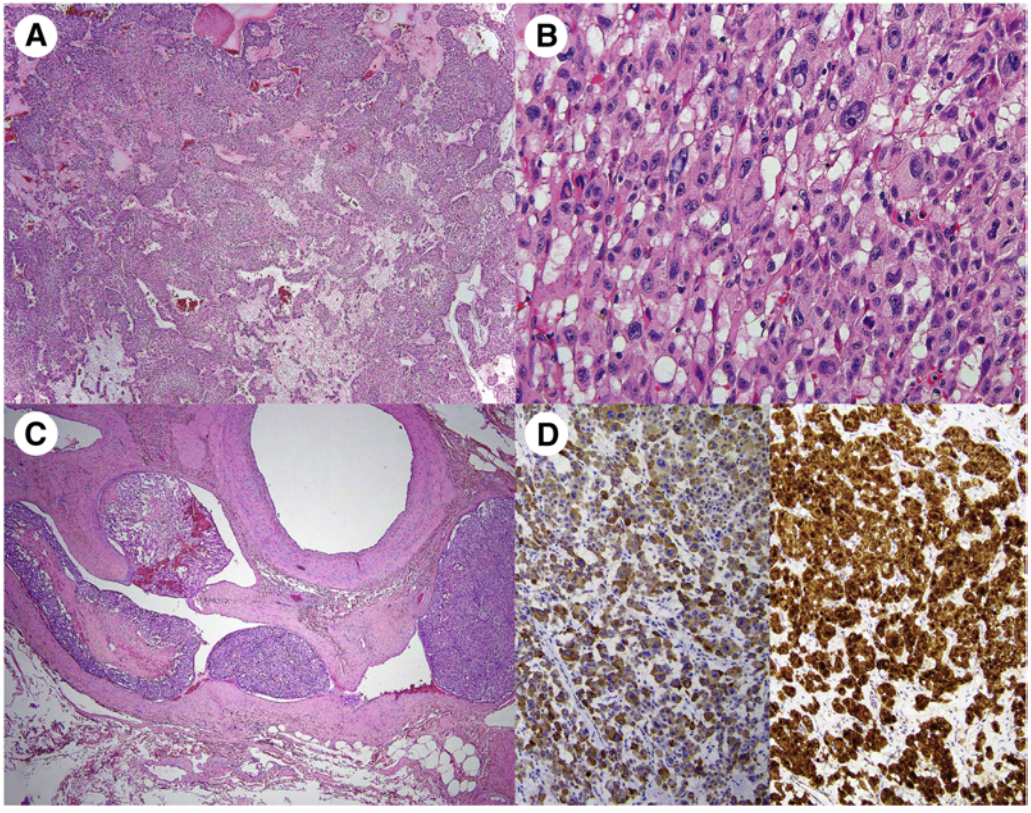

Figure 2