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References

[1] Michalova K, Michal Jr M, Kazakov DV, et al. Primary signet ring stromal tumor of the testis: a study of 13 cases indicating their phenotypic and genotypic analogy to pancreatic solid pseudopapillary neoplasm. Hum Pathol 2017;67:85-93.
[2] Michal M, Bulimbasic S, Coric M, et al. Pancreatic analogue solid pseudopapillary neoplasm arising in the paratesticular location. The first case report. Hum Pathol 2016;56:52-6.
[3] Young RH, Scully RE. Testicular Tumors. Chicago: ASCP Press; 1990.
[4] Petersen RO, Sesterhenn IA, Davis Jr CJ. Urologic Pathology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2009.
[5] Ulbright TM, Young RH. Tumors of the Testis and Adjacent Structures. AFIP Atlas of Tumor Pathology. Series 4. Silver Spring, MD: American Registry of Pathology; 2013.
[6] Reuter VE, Tickoo SK. Tumors of the testis. In: Amin MB, Grignon DJ, Srigley JR, Eble JN, editors. Urological Pathology. Philadelphia: Lippincott Williams & Wilkins; 2014. p. 749-803.
[7] Young RH, Koelliker DD, Scully RE. Sertoli cell tumors of the testis, not otherwise specified: a clinicopathologic analysis of 60 cases. Am J Surg Pathol 1998;22:709-21.
[8] Zhang C, Ulbright TM. Nuclear localization of beta-catenin in Sertoli cell tumors and other sex cord-stromal tumors of the testis: an immunohistochemical study of 87 cases. Am J Surg Pathol 2015;39:1390-4.
[9] Perrone F, Bertolotti A, Montemurro G, Paolini B, Pierotti MA, Colecchia M. Frequent mutation and nuclear localization of beta-catenin in sertoli cell tumors of the testis. Am J Surg Pathol 2014;38:66-71.
[10] Xiao GQ, Granato RC, Unger PD. Bilateral Sertoli cell tumors of the testis—a likely new extracolonic manifestation of familial adenomatous polyposis. Virchows Arch 2012;461:713-5.
[11] Esber CM, Shabsigh A, Zynger DL. Sclerosing Sertoli cell tumor without expression of typical sex cord stromal tumor markers: case report and literature review. Pathol Res Pract 2012;208:121-5.
[12] Iczkowski KA, Bostwick DG, Roche PC, Cheville JC. Inhibin A is a sensitive and specific marker for testicular sex cord stromal tumors. Mod Pathol 1998;11:774-9.
[13] McCluggage WG, Shanks JH, Whiteside C, Maxwell P, Banerjee SS, Biggart JD. Immunohistochemical study of testicular sex cord–stromal tumors, including staining with anti-inhibin antibody. Am J Surg Pathol 1998;22:615-9.
[14] Kommoss F, Oliva E, Bittinger F, et al. Inhibin-alpha CD99, HEA125, PLAP, and chromogranin immunoreactivity in testicular neoplasms and the androgen insensitivity syndrome. Hum Pathol 2000;31:1055-61.
[15] Comperat E, Tissier F, Boye K, De Pinieux G, Vieillefond A. Non–Leydig sex-cord tumors of the testis. The place of immunohistochemistry in diagnosis and prognosis. A study of twenty cases. Virchows Arch 2004;444:567-71.
[16] Mesa H, Gilles S, Datta MW, et al. Comparative immunomorphology of testicular Sertoli and sertoliform tumors. Hum Pathol 2017;61:181-9.
[17] Oliva E, Garcia-Miralles N, Vu Q, Young RH. CD10 expression in pure stromal and sex cord–stromal tumors of the ovary: an immunohistochemical analysis of 101 cases. Int J Gynecol Pathol 2007;26:359-67.
[18] Colecchia M. Observations on the paper "sclerosing Sertoli cell tumor of the testis: a clinicopathologic study of 20 cases" by Kao et al. Am J Surg Pathol 2014;38:1160.

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

Dear Editor,

We would like to thank Drs Ulbright and Young for their comments on our articles about pancreatic analog of solid pseudopapillary neoplasm of the testis [1], in which we have described a total of 7 testicular tumors that have the morphologic features, immunohistochemical profile (positivity for β-catenin, cyclin D1, CD10, CD56, NSE, [often] synaptophysin; uniform negativity for inhibin, calretinin, SF-1, and chromogranin), and oncogenic somatic mutation in exon 3 of the *CTNNB1* (β-catenin) gene identical to those seen in solid pseudopapillary neoplasms (SPNs) of the pancreas [2,3].

In addition, in a separate article, we have described 13 signet ring cell testicular tumors that have immunohistochemical profile and β-catenin mutations identical to those encountered in SPN of the pancreas [4]. These 13 testicular tumors were hypothetically likened to pancreatic SPN based on the fact that most pancreatic SPNs (20/22) in our files have a signet ring cell component. We acknowledged that it would need some time to recognize that these 13 signet ring cell tumors of the testis and SPN of the pancreas likely represent the same entity in different anatomic sites.

Drs Ulbright and Young, on the contrary, point out that all these testicular tumors should be classified as Sertoli cell tumors, not otherwise specified (NOS) [1]. They consider the latter a well-established tumor based on the fact that 5 other groups of pathologists thought that this entity exists (their references [3–7]). We have, however, never found a single article that would prove that Sertoli cell tumor, NOS, represents a homogeneous entity, and the mere fact that "5 groups of pathologists thinks so" is not solid proof for such a statement.

The World Health Organization classification blue book [5] describes the immunoprofile of Sertoli cell tumors, NOS, as follows: "Inhibin is positive in 50% of these tumors and nuclear β-catenin in 60-70%. Calretinin, SF-1, CD99, Melan A and WT1 are also typically positive." In our opinion, testicular tumors that are inhibin, calretinin, and SF-1 negative and that contain no adenomatous-tubular structures have nothing in common with any known entities bearing the name *sertoli* and should be better called *unclassified testicular tumors*.

But if one poses the question "What do the seven tumors published in our two papers [2,3] and the two testicular tumors reported by Mengoli et al. [6] have in common with pancreatic SPN?" our answer is "everything": morphology, presence of hyaline globules, immunoprofile, and mutation in the exon 3 of the *CTNNB1* gene. What do these 9 tumors [2,3,6,7] have

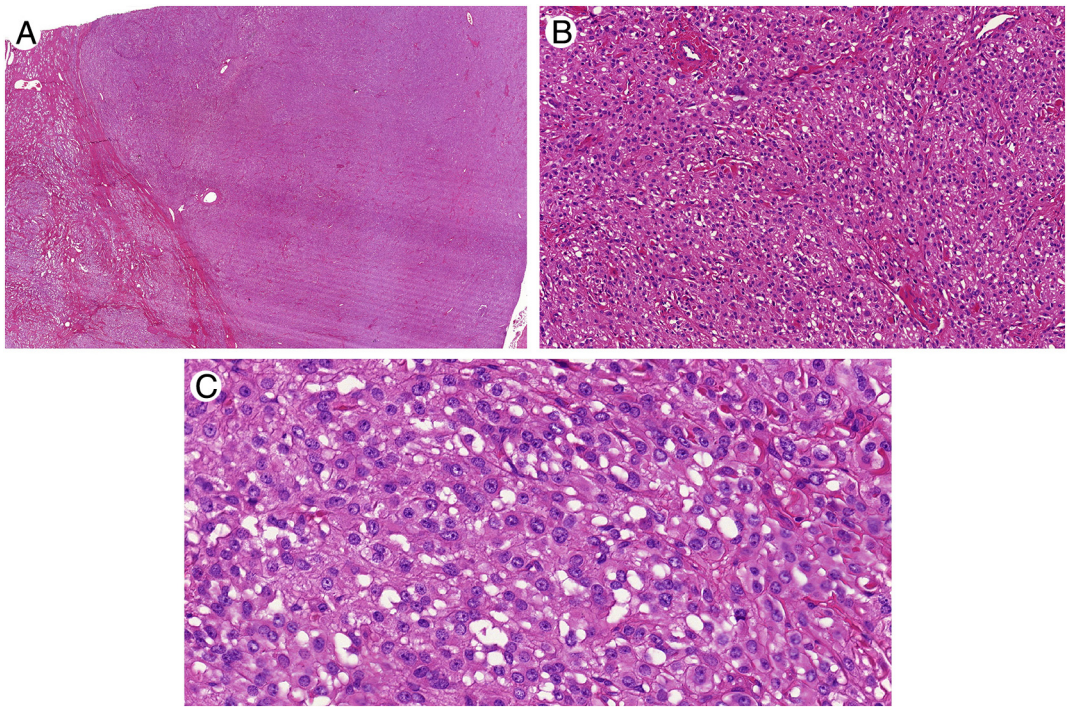

Fig. 1 A-C, Tumor of the testis in a 60-year-old man.

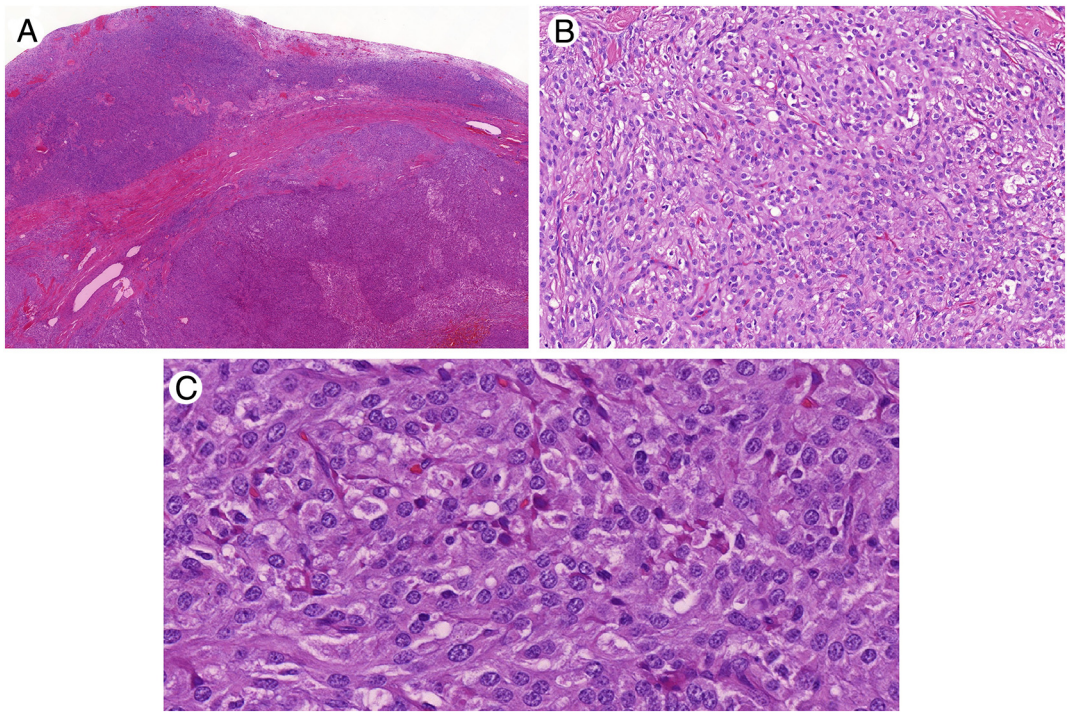

Fig. 2 A-C, Tumor of the ovary in a 53-year-old woman.

in common with any type of Sertoli cell tumor? We think that the answer is "entirely nothing"! Furthermore, why can ovarian tumors identical to these 9 testicular neoplasms be referred to as SPN of the ovary, which is established as a well-defined entity [8-12]? Here is an example. Fig. 1 illustrates a tumor of the testis, whereas Fig. 2 depicts a neoplasm of the ovary. Both tumors look microscopically identical; both lesions manifested the same immunophenotype, with immunoreactivity for β-catenin, cyclin D1, CD10, CD56, NSE, and synaptophysin and negativity for inhibin, calretinin, SF-1, and chromogranin. Both neoplasms revealed a mutation in exon 3 of the *CTNNB1* gene and are indistinguishable from tumors published under the name SPN [2,3,7].

According to the proposal of Drs Ulbright and Young, one of these identical tumors should be probably classified as testicular Sertoli cell tumor, NOS, whereas the ovarian one should be classified as SPN [8-12], which seems illogical to us.

Although it is difficult to judge from the pictures provided by Drs Ulbright and Young [1], it seems that their Fig. 1B shows distinct tubular structures. Such tubules were not seen in any of our 7 cases of SPN, nor were they evident in any of the signet ring cell tumor of the testis. We therefore think that the tumors illustrated by Drs Ulbright and Young in their letter [1] are different from our cases and, being inhibin and calretinin positive, may indeed be of the Sertolian origin.

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References

[1] Ulbright TM, Young RH. Pseudo–"solid pseudopapillary neoplasms" of the testis: in reality Sertoli cell tumors. Hum Pathol 2018 [in press].
[2] Michal M, Bulimbasic S, Coric M, et al. Pancreatic analogue solid pseudopapillary neoplasm arising in the paratesticular location. The first case report. Hum Pathol 2016;56:52-6.
[3] Michalova K, Michal M, Sedivcova M, et al. Solid pseudopapillary neoplasm (SPN) of the testis: comprehensive mutational analysis of 6 testicular and 8 pancreatic SPNs. Ann Diagn Pathol 2018;35:42-7.
[4] Michalova K, Michal Jr M, Kazakov DV, et al. Primary signet ring stromal tumor of the testis: a study of 13 cases indicating their phenotypic and genotypic analogy to pancreatic solid pseudopapillary neoplasm. Hum Pathol 2017;67:85-93.
[5] Moch H, Humphrey PA, Ulbright TM, Reuter VE, editors. WHO Classification of Tumours of the Urinary System and Male Genital Organs. 4th ed. Lyon: IARC; 2016.
[6] Mengoli MC, Bonetti LR, Intersimone D, Fedeli F, Rossi G. Solid pseudopapillary tumor: a new tumor entity in the testis? Hum Pathol 2017;62:242-3.
[7] Michalova K, Michal M, Hes O, Kazakov DV, Michal M. Solid pseudopapillary tumor: a new tumor entity in the testis? Reply. Hum Pathol 2017;62:243-5.
[8] Deshpande V, Oliva E, Young RH. Solid pseudopapillary neoplasm of the ovary: a report of 3 primary ovarian tumors resembling those of the pancreas. Am J Surg Pathol 2010;34:1514-20.
[9] Syriac S, Kesterson J, Izevbaye I, de Mesy Bentley KL, Lele S, Mhawech-Fauceglia P. Clinically aggressive primary solid pseudopapillary tumor of the ovary in a 45-year-old woman. Ann Diagn Pathol 2012;16:498-503.
[10] Stoll LM, Parvataneni R, Johnson MW, Gui D, Dorigo O, Sullivan P. Solid pseudopapillary neoplasm, pancreas type, presenting as a primary ovarian neoplasm. Hum Pathol 2012;43:1339-43.
[11] Cheuk W, Beavon I, Chui DT, Chan JK. Extrapancreatic solid pseudopapillary neoplasm: report of a case of primary ovarian origin and review of the literature. Int J Gynecol Pathol 2011;30:539-43.
[12] Kominami A, Fujino M, Murakami H, Ito M. β-Catenin mutation in ovarian solid pseudopapillary neoplasm. Pathol Int 2014;64:460-4.