Images in Cytology

Seminal Vesicle Carcinoma Presenting with Malignant Ascites

Ekkehard Hewer, MD[1,*], Yara Banz, MD[1], Urspeter Knecht, MD[2], Matthias S. Dettmer, MD[1], Erik Vassella, PharmD[1]

1: Institute of Pathology, University of Bern, Bern, Switzerland
2: Department of Radiology and Neuroradiology, Spital Emmental, Burgdorf, Switzerland.

Running head: Seminal Vesicle Carcinoma

*Correspondence to:
Ekkehard Hewer
Institute of Pathology
University of Bern
Murtenstrasse 31
3008 Bern
Switzerland
ekkehard.hewer@pathology.unibe.ch
Tel +41 31 632 9951
Fax +41 31 632 9938
ORCID: 0000-0002-9128-0364

Keywords: Ascites – Cytopathology – Seminal vesicles – Adenocarcinoma

Word count: 599

Conflicts of interest: None

Disclosure of funding: None

A 92-year-old male with a history of right hemicolectomy for colonic adenocarcinoma two years prior presented with abdominal distension due to ascites. Computed tomography revealed a cystic mass in the region of the seminal vesicles (Figure 1A). 3000 ml of ascitic fluid was submitted for cytological analysis. Smears showed three-dimensional epithelial cell clusters with marked variation in nuclear size, pleomorphism, nuclear membrane irregularities and cytoplasmic vacuoles (Figure 1B-E). A papillary growth pattern could be appreciated both on smears and in the cell block. Immunocytochemical stainings performed on the cell block showed positivity for CK7, CA-125 and PAX8, while the tumor cells were negative for CDX2, GATA3, PSA, TTF1 and Calretinin. DNA mismatch repair enzymes MLH1, PMS2, MSH2 and MSH6 were intact. p53 showed a wildtype staining pattern with variably intense immunoreactivity in a minority of malignant cells (not shown). Molecular studies (Oncomine Comprehensive Panel v3 (DNA), Thermo Fisher Scientific) revealed an *EGFR* amplification (15 copies), which was accompanied by EGFR overexpression immunohistochemically. Furthermore, a *SMARCB1* gene variant (c.1060_1061insG) was detected, which was bioinformatically predicted to be deleterious, but did not result in loss of expression as assessed by INI-1 immunohistochemistry (not shown).

By comparison, the histological specimen of the colonic adenocarcinoma, available at our institute for re-evaluation, expressed CDX2, showed loss of expression of MLH1 and PMS2 and was positive for V600E-mutant BRAF (not shown), indicating a sporadic microsatellite-instable colon carcinoma.

Given that secondary involvement of the seminal vesicles by other malignancies, especially by prostatic adenocarcinoma, is much more common than primary carcinoma, the bar for establishing the latter diagnosis is high.

In the present case, immunostainings ruled out both recurrent colonic adenocarcinoma and prostatic adenocarcinoma. Expression of PAX8 – consistent with an origin from Müllerian epithelium[1,2] – and CA-125 supported a diagnosis of primary adenocarcinoma of the seminal vesicles[3], as did the imaging finding of a mass localized in the seminal vesicles.

While the extent of nuclear pleomorphism and co-expression of CA-125 and PAX8 resembled features of high-grade serous carcinomas in females, p53 immunostaining showed a wildtype pattern. Furthermore, the distinct papillary architecture – which is considered an important diagnostic feature in histology – speaks against seminal vesicle adenocarcinoma representing a mere male counterpart of high-grade serous carcinoma. Further studies will be required to assess whether or not the *EGFR* amplification and the presumably pathogenic *SMARCB1* mutation found in the present case are characteristic of seminal vesicle adenocarcinoma in general.

The seminal vesicles are notable for very low frequency of malignant transformation The largest published pathological series of carcinomas of the seminal vesicles comprises just four

cases[4]. To our knowledge, this is the first documentation of both morphologic features of seminal vesicle carcinoma in cytology and underlying molecular alterations.

Several factors were important to reach the diagnosis of a primary adenocarcinoma of the seminal vesicles in the present case: (1) the clinical context of a mass in the region of the seminal vesicles, (2) the exclusion of recurrent colonic adenocarcinoma by direct comparison of morphology and immunophenotype and (3) the characteristic co-expression of PAX8 and CA-125. We conclude from our findings, that the combination of marked nuclear pleomorphism and papillary growth pattern should raise the suspicion of seminal vesicle adenocarcinoma in ascites or possibly a fine needle aspiration specimen from a male patient. Once seminal vesicle adenocarcinoma has entered the differential diagnosis, PAX8 and CA-125 will be the most important positive markers to support this diagnosis.

References

1. Ozcan A, Shen SS, Hamilton C, et al. PAX 8 expression in non-neoplastic tissues, primary tumors, and metastatic tumors: a comprehensive immunohistochemical study. *Mod Pathol.* 2011;24(6):751-764.
2. Tong GX, Memeo L, Colarossi C, et al. PAX8 and PAX2 immunostaining facilitates the diagnosis of primary epithelial neoplasms of the male genital tract. *Am J Surg Pathol.* 2011;35(10):1473-1483.
3. Posenato I, Calio A, Segala D, et al. Primary seminal vesicle carcinoma. The usefulness of PAX8 immunohistochemical expression for the differential diagnosis. *Hum Pathol.* 2017;69:123-128.
4. Ormsby AH, Haskell R, Jones D, Goldblum JR. Primary seminal vesicle carcinoma: an immunohistochemical analysis of four cases. *Mod Pathol.* 2000;13(1):46-51.

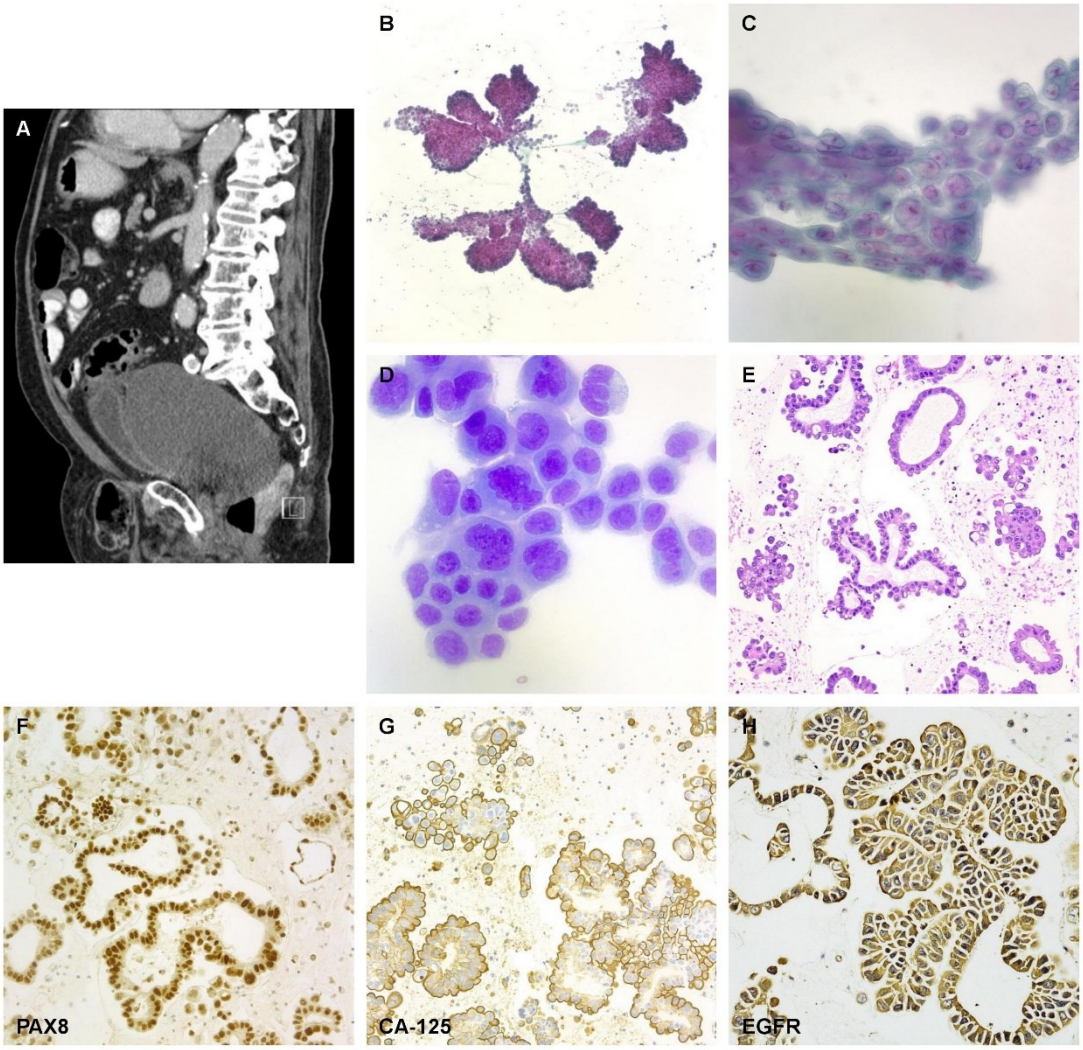

Figure 1. Computed tomography showed a large cystic mass in the region of the seminal vesicles (A). Cytological smears of the ascites showed large, often papillary clusters of epithelial cells (B). There was marked variation in nuclear size, pleomorphism, nuclear membrane irregularities and cytoplasmic vacuoles (C-D). Papillae were also prominent in the cell block (E). Tumor cells were positive for PAX8 (F), CA-125 (G) and EGFR (H). B-C: Papanicolaou staining; D: Modified Romanowsky staining (Hemacolor®). E: Hematoxylin-Eosin staining.