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CASE REPORT

A rare case of urothelial carcinoma with syncytiotrophoblastic cell differentiation

Rikke Vilsbøll Milling[a], Isa Charlotte Secher Niemann[b], Henning Nielsen Dominiak[a], Estrid Stæhr Hansen[c], Lone Sunde[d,e] and Jørgen Bjerggaard Jensen[a,f]

[a]Department of Urology, Aarhus University Hospital, Aarhus, Denmark; [b]Department of Gynecology, Aarhus University Hospital, Aarhus, Denmark; [c]Institute of Pathology, Aarhus University Hospital, Aarhus, Denmark; [d]Department of Clinical Genetics, Aarhus and Aalborg University Hospitals, Aarhus/Aalborg, Denmark; [e]Department of Biomedicine, Aarhus University, Aarhus, Denmark; [f]Department of Clinical Medicine, Aarhus University, Aarhus, Denmark

Introduction

The majority of bladder cancers (> 90%) are urothelial carcinomas arising in the urothelium of the bladder. Especially invasive and high-grade tumors are able to differentiate into various morphological subtypes. The subtypes vary in frequency, with syncytiotrophoblastic giant cell tumors being extremely rare. As prognosis and treatment depends on tumor origin, it is important to establish the correct diagnosis to ensure optimal clinical outcome [1].

Case report

A 25-year-old female was referred to the department of urology with unspecific abdominal pain, recurrent cystitis, and gross hematuria for a period of 1.5 years. Laboratory test and physical examinations were normal apart from a plasma human choriogonadotropin (p-hCG) of 43 IU/l. The patient was therefore concurrently referred to the department of gynecology. The patient was 7 months post-partum after a normal pregnancy and birth. The gynecological exam was normal, ruling out an extra uterine pregnancy.

A CT-scan revealed a 2.5 cm calcified process in the bladder, and cystoscopy revealed the tumor fixated to the posterior wall with hyperemia in the mucosa around its base. The tumor was removed transurethrally (TUR), and histopathology revealed a combination of mononuclear giant cells and cells showing morphological resemblance to multinucleated syncytiotrophoblastic cells with eosinophilic cytoplasm, papillary high-malignant cells and areas of necrosis (Figure 1). Immunohistochemically, the giant cells were positive for hCG and PLAP. Furthermore, it contained positive staining for AE1/AE3, p53, CK7 and GATA3, but negative for vimentin and alpha-fetoprotein. The atypical morphology, growth-pattern and clinical presentation for an urothelial carcinoma led to the proposed diagnosis of epithelioid trophoblastic tumor (ETT). Analysis of 16 short tandem repeat (STR) loci was performed on DNA from tumor and blood from the patient, her spouse, and their child. For 13/16 loci, the results were inconsistent with the tumor originating in the most recent pregnancy, and for 9/16 loci the results were inconsistent with the tumor originating from any other pregnancy of the couple. In 16/16 loci the tumor alleles were identical with those in the blood of the patient, indicating that the tumor originated in a somatic cell.

Radical cystectomy including lymph node dissection with preservation of the internal female genitalia was performed with urinary diversion with a pouch ad modum Indiana. Histopathological examination of the specimen revealed a small remnant classic urothelial carcinoma of high malignancy stage T1. No metastases were found in 27 lymph nodes. The patient did not undergo neoadjuvant or adjuvant treatment. hCG levels normalized after TUR and both postoperative courses was uneventful. The final conclusion on histological subtype was urothelial carcinoma with syncytiotrophoblastic cell differentiation.

Discussion and conclusion

Approximately 32 cases of urothelial carcinoma with syncytiotrophoblastic cell differentiation have been reported since its first description. A poor prognosis is described, and almost all cases passed within 1 year of diagnosis. The mean age was 63 years, with a majority of male cases, making this case of a young female extremely rare [2].

In this case, the most distinctive abnormal finding was the production of hCG. Normally, hCG is produced by the placental trophoblastic cells. Thus, in a non-pregnant woman, hCG production should give rise to the suspicion of gestational trophoblastic neoplasms such as choriocarcinomas. Although hCG production appears in other solid tumors, hCG positivity is most often seen in the poorly differentiated high-grade tumors, such as syncytiotrophoblastic differentiations, with staining positivity being correlated to the grade of the tumor [3]. The presence of syncytiotrophoblastic cells seems to be of significance, indicating an inferior prognosis with higher mortality compared to typical high-grade urothelial carcinomas, but the precise impact is unclarified [1].

CONTACT Rikke Vilsbøll Milling rikke-milling@hotmail.com Department of Urology, Aarhus University Hospital, Aarhus, 8000, Denmark

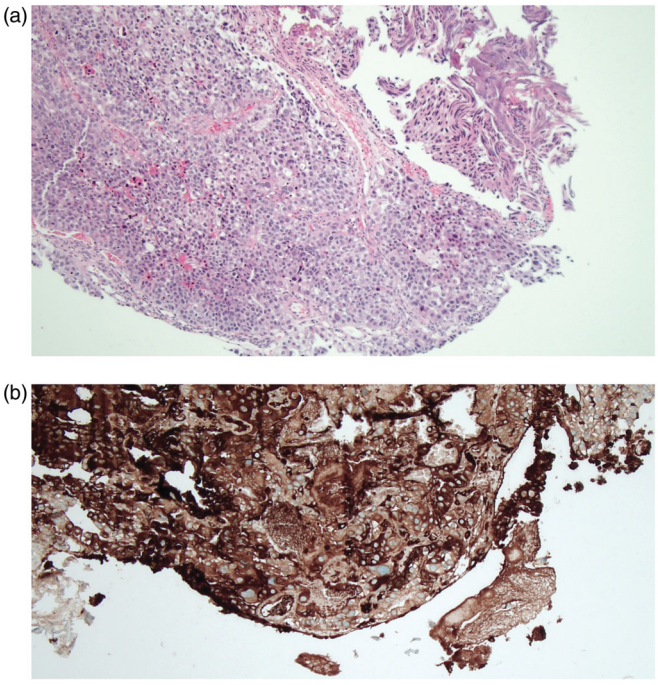

Figure 1. (a) Biopsy from the urothelial carcinoma with syncytiotrophoblastic giant cells stained with hematoxylin and eosin. Multinucleated cells with eosinophilic cytoplasm are shown. (b) Biopsy from the tumor with immunohistochemical staining for hCG.

This specific subtype morphologically mimics ETT. Therefore, immunohistochemical staining methods are often unable to discriminate properly between the two. As ETTs originate in a conceptus, these tumors should show DNA markers originating in the father. While some ETTs originate in a hydatidiform mole, most seem to originate in an inconspicuous full term pregnancy and can present many years after termination of the pregnancy from which it originated [4]. Thus, the DNA marker analysis should not only test if the tumor has markers identical with the most recent pregnancy but also test if the tumor could originate in any type of pregnancy. STR loci are highly polymorphic, and the results from 16 loci allowed us to conclude that the tumor did not originate in the most recent pregnancy. This yielded information otherwise not obtainable from clinical and histological examination, thereby representing a diagnostic tool to separate somatic and gestational neoplasms [5].

Although rare, pattern and morphological recognition of this subtype is important. It ensures usage of suitable diagnostic tools while guaranteeing optimal treatment.

Disclosure statement

No potential conflict of interest was reported by the author(s).

ORCID

Rikke Vilsbøll Milling http://orcid.org/0000-0003-2263-2060
Jørgen Bjerggaard Jensen http://orcid.org/0000-0002-4347-739X

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