UNDIFFERENTIATED CARCINOMA OF THE EPIDIDYMIS

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SUMMARY – Epididymal tumors are uncommon and usually benign, with only 25% of them being malignant. Undifferentiated epididymal carcinoma in particular is extremely rare. We report on a 54-year-old male patient presented with right testicular pain and scrotal mass for the last 6 months. Laboratory investigations were unremarkable but epididymal biopsy result was epididymal undifferentiated carcinoma. Inguinal radical orchidectomy was performed and pathological examination of the surgical specimen confirmed the presence of undifferentiated carcinoma. Then, adjuvant chemoradiotherapy (four cycles of cisplatin-etoposide chemotherapy and radiotherapy) was administered. After four months, lung metastases were detected and three doses ifosfamide-Adriamycin chemotherapy were given, but the patient died due to the disease progression. Reports of epididymal undifferentiated carcinoma are extremely rare and the present report emphasizes the need of including epididymal undifferentiated carcinoma in the differential diagnosis of an epididymal mass.

Key words: *Epididymis; Undifferentiated carcinomas; Metastasis*

Introduction

Sakaguchi first described a benign epididymal neoplasm in 1916, which was later named "adenomatoid tumor" by Golden and Ash[1]. Epididymal tumors are uncommon and approximately 75% of all epididymal tumors are benign; 60% to 78% of these benign neoplasms are adenoid tumors. Papillary cystadenomas, leiomyomas, lipomas, and lymphangiomas are among other benign tumors[1,2]. Only 25% of all epididymal tumors are malignant including fibrosarcomas, rhabdomyosarcomas, squamous cell carcinomas, teratomas and other neoplasms of germ cell origin, carcinomas, adenocarcinomas, lymphomas, and undifferentiated carcinomas[1,3-5]. Undifferentiated epididymal carcinoma is extremely rare and to the best of our knowledge, this report presents the 25th case in the world literature.

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Received September 2, 2008, accepted August 25, 2011

Case Report

A 54-year-old male patient presented with complaints of right testicular pain and scrotal mass for the last 6 months. He did not have a history of genitourinary infection or trauma. On initial physical examination, the right epididymis was painful and abnormally enlarged. All laboratory investigations were unremarkable including blood count, blood chemistry, and tumor markers. Right caput epididymis was very thick on scrotal ultrasonography (USG), resembling chronic epididymitis. The patient was prescribed antibiotic therapy, but his complaints did not improve.

One month later, a 28x21 mm epididymal mass was found on scrotal USG. Orchidectomy was performed and pathological examination revealed epididymal undifferentiated carcinoma. No metastasis was found on thoracic and abdominopelvic computerized tomography examination, and inguinal radical orchidectomy was performed. The orchidectomy specimen consisted of a 3x2x2 cm nodular lesion in the epididymis, in the upper part of the testis. The

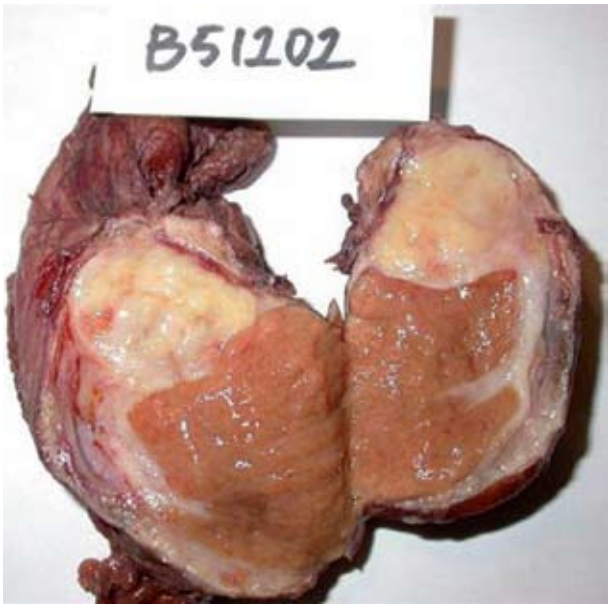

Fig. 1. Solid, gray-white tumor tissue in the epididymis compressing the testis.

homogeneous, solid, gray-white nodular tumor tissue was invading the epididymis and compressing the testis (Fig. 1). The border of the spermatic cord surgery and the testis was intact. Microscopically, the tumor tissue was pseudoglandular with syncytial epithelial islands composed of cells containing large hyperchromatic nuclei and prominent nucleoli, and there were scattered necrotic foci and frequent mitotic figures in desmoplastic fibrous stroma (Fig. 2). Lymphovascular

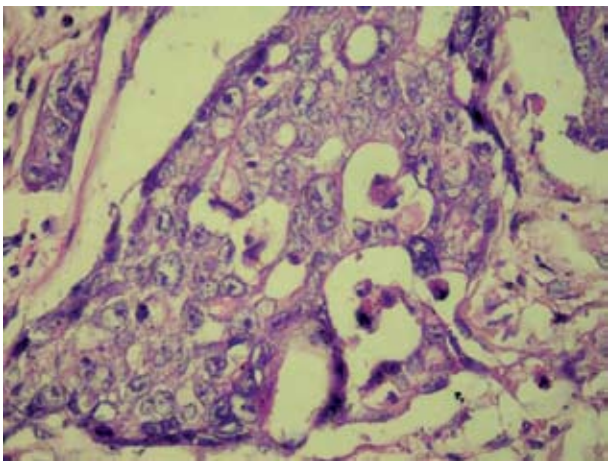

Fig. 2. Tumor tissue was pseudoglandular and had syncytial epithelial islands composed of cells with large hyperchromatic nuclei and prominent nucleoli (H&E, X400).

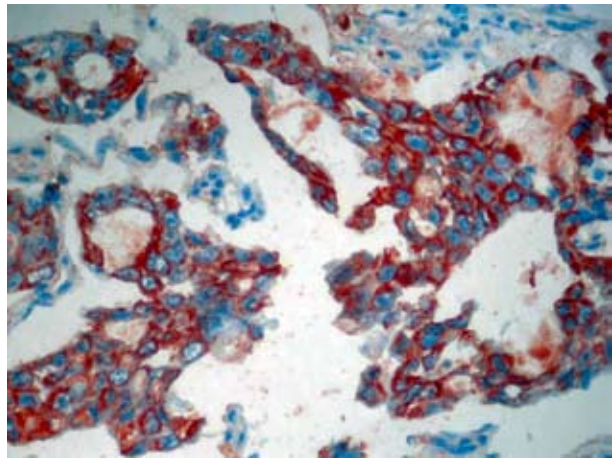

Fig. 3. Immunoreactivity of pan-cytokeratin in tumoral cells (immunoperoxidase, X400).

invasion was observed in tumor stroma. Neoplastic invasion was found between non-neoplastic epididymal ducts, but neoplasia did not originate directly from epididymal ductal epithelium. Therefore, the epididymal tumor was defined as an undifferentiated carcinoma of unknown primary origin.

Tumor cells exhibited a positive staining pattern with pan-cytokeratin (Fig. 3) and CEA; however, they showed a negative staining pattern with PSA, vimentin, S-100, AFP, PLAP, CD30, cytokeratin-7 and 20 (neomarkers).

Adjuvant chemoradiotherapy was administered after the operation (4 cycles of cisplatin-etoposide chemotherapy). The patient was followed up with computerized tomography. Four months later, bilateral multiple metastatic lung nodules were detected. Three cycles of ifosfamide-Adriamycin chemotherapy were administered; however, the patient died three months after the diagnosis of lung metastasis.

Discussion

Primary epididymal carcinoma is an uncommon malignant paratesticular tumor arising from epithelial cells, and it is associated with a very poor prognosis. It has nonspecific clinical characteristics and should be included in the differential diagnosis of intrascrotal masses[4]. Epididymal adenocarcinomas are usually tubular, tubulocystic, or tubulopapillary adenocarcinomas, often with an appreciable content of clear cells. Distinction from metastasis may be difficult and may

depend largely on careful clinical evaluation[5]. Patients older than 50 years are less likely to have a primary malignancy and they mostly have benign epididymal tumors. However, patients between age 20 and 50 are at a higher risk of malignant tumors[1].

Approximately 25% of all epididymal tumors are malignant, and 8.1% of these malignant neoplasms found in spermatic cord and/or epididymis are metastatic. Primary tumors metastasizing to spermatic cord and epididymis are usually carcinomas originating from the stomach (42.8%) and prostate (28.5%). Rarely, epididymal tumors are the first manifestations of an occult neoplasm (9.5%). The average survival of patients with a metastatic tumor is 9.1 months[6]. Pancreatic carcinoma, renal cell carcinoma, and untreated bladder cancer can also rarely metastasize to the epididymis[7-9].

Undifferentiated epididymal carcinoma is very rare[4,10]. Pathological examination established the diagnosis of undifferentiated epididymal carcinoma in two reported cases operated for an epididymal mass. In one of these cases, metastases to the gallbladder were detected and chemotherapy was not effective[10]. However, in two other previously reported cases with epididymal small cell carcinoma, postoperative chemotherapy was effective[11,12].

PSA and PAP immunoperoxidase staining have been used to differentiate epididymal metastases from prostate carcinoma. A negative PSA stain cannot totally exclude the concomitant presence of a poorly differentiated prostate cancer. Our patient had an unremarkable prostate examination and laboratory results, with no clinical evidence of prostate cancer. The epididymal tumor was not positively stained with PSA or PAP[1].

The management of epididymal malignancies is aided by the pathological diagnosis. Epididymectomy should be performed if palpation of the testicle is normal, without any evidence of epididymal malignancy. Benign tumors are treated with transscrotal excision and epididymectomy. Malignant tumors of the epididymis require more extensive resection and are best performed by an inguinal approach[1].

The best therapeutic approach for these patients is still controversial. However, most authors suggest resection and postoperative chemoradiotherapy as the best therapeutic option[13]. In the present case, we did not perform frozen section for intraoperative diagnosis; nevertheless, intraoperative diagnosis of this tumor can be extremely challenging. It requires immunohistochemical staining and it is not clear whether it may substantially alter surgical decision. Inguinal radical orchidectomy is the most suitable treatment choice for patients with an epididymal mass[1].

Reports of epididymal undifferentiated carcinoma are extremely rare. We report a case of epididymal undifferentiated carcinoma with clinical follow up. Further experience is required to characterize this rare tumor more accurately.

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Sažetak

NEDIFERENCIRANI KARCINOM EPIDIDIMISA

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Tumori epididimisa su rijetki i najčešće dobroćudni te ih je samo 25% zloćudno. Nediferencirani karcinom epididimisa iznimno je rijedak. Opisuje se slučaj 54-godišnjeg muškarca koji je primljen zbog bolova u desnom testisu i tvorbe u skrotumu u posljednjih šest mjeseci. Laboratorijski nalazi bili su normalni, ali je biopsija epididimisa ukazala na nediferencirani karcinom epididimisa. Napravljena je radikalna ingvinalna orhidektomija, a patološko ispitivanje kirurškog uzorka potvrdilo je prisutnost nediferenciranog karcinoma. Tada je bolesniku propisana dodatna kemoradioterapija (četiri ciklusa kemoterapije cisplatin-etoposid i radioterapija). Nakon četiri mjeseca otkrivene su metastaze u plućima, pa je bolesnik primio tri doze kemoterapije ifosfamid-adriamicin, ali je nastupila smrt zbog progresije bolesti. Izvješća o nediferenciranom karcinomu epididimisa iznimno su rijetka, stoga se ovim prikazom slučaja ukazuje na potrebu uključivanja nediferenciranog karcinoma epididimisa u diferencijalnu dijagnostiku novotvorina epididimisa.

Ključne riječi: *Epididimis; Nediferencirani tumori; Metastaze*