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Seminar article

State of the art in germ cell tumor imaging

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Abstract

Germ cell tumors (GCTs) are the most common tumors of the testis and arise from germinal epithelium cells in the seminiferous tubules. All GCTs show malignant behavior and frequently metastasize. The diagnosis of GCTs depends on the clinical manifestations, laboratory parameters, preoperative imaging features, and tissue biomarkers. Ultrasonography and Doppler ultrasonography are the primary imaging modalities used to evaluate testicular masses. Sonoelastography is a diagnostic tool that can measure the stiffness of tissue and may differentiate between benign and malignant tumors of testis. Magnetic resonance imaging of the scrotum may be used as an additional tool, which may provide additional information owing to its high soft tissue contrast discrimination capability. Computed tomography of the thorax and abdomen and positron emission tomography/computed tomography are used for staging of the disease and for follow-up after treatment.

Keywords: Germ cell tumor; Testis cancer; Ultrasonography; Computed tomography; Magnetic resonance imaging

Introduction

Germ cell tumors (GCTs) arise most frequently in the gonads and GCTs of the testis are a heterogeneous group of neoplasms that originate from the primordial germ cells. Other rare sites of GCTs are the pineal gland, neurohypophysis, mediastinum, and the retroperitoneum. Primordial germ cells can be sequestered in these sites during their intrauterine migration and extragonadal GCTs arise from these demigrated primordial germ cells [1].

Testicular malignant tumors are the most common tumors in males between 15 and 34 years of age and they account for 1% of all malignancies in men [2]. The GCTs account for approximately 95% of all testicular neoplasms [3]. A substantial increase in their incidence has been reported over the past 3 decades, with a current estimated incidence rate of 6.6 cases per 100,000 persons per year [4]. GCTs of the testis can be classified as seminomas and nonseminomatous tumors. According to the National Cancer Data Base, most testicular GCTs are seminomas (56%) [5]. Nonseminomatous GCTs are divided into 4 subgroups: embryonal carcinomas (ECs), yolk sac tumors (YSTs), teratomas, and choriocarcinomas [1]. The major risk factors for developing testicular GCTs include an undescended testis, testicular dysgenesis, family history, and a previously diagnosed testicular GCT [2]. Testicular microlithiasis is a relatively rare condition that occurs owing to accumulation of hydroxyapatite crystals within the lumens of the seminiferous tubules [6]. On ultrasonography (US), these crystals are clearly seen as scattering or clustering, punctate, nonshadowing, echogenic foci (less than 3 mm) (Fig. 1) [7,8]. Testicular microlithiasis is a common condition in the general population and the role of microlithiasis in cancer risk is controversial. According to the guidelines of the European Society of Urogenital Radiology scrotal imaging subcommittee, testicular microlithiasis may appear in 2 different radiologic forms: 5 or more microliths in the entire testis, or 5 or more microliths in a local area of the testis [8]. The first form is commonly a simple and benign condition. The latter form expresses clustering microliths in the testis. Especially, the condition with more than 10 scattered clustering microlithiasis areas in the testis is associated with an increased risk of developing testicular cancer and these areas may contain carcinoma in situ foci [8]. The first form is a simpler and more benign condition. The latter form expresses clustering microliths in the testis. Especially, the form with more than 10 scattered clustering microlithiasis areas in testis is

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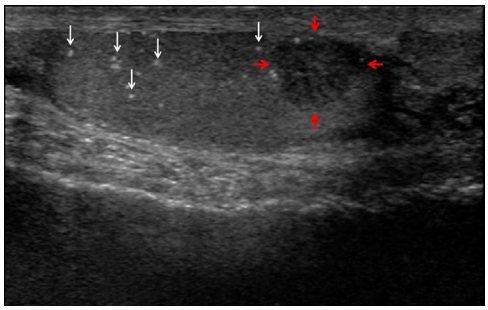

Fig. 1. US scan in a 22-year-old man with left scrotal mass (red arrows) and incidental finding of microlithiasis. US of the left testis shows multiple punctuate nonshadowing echogenicities compatible with microlithiasis (white arrows). (Color version of figure is available online.)

associated with an increased risk of developing testicular cancer and these areas may contain carcinoma in situ foci [8].

The most common clinical finding of testicular GCTs is a testicular mass causing testicular enlargement or pain [4]. Another clinical finding of testicular GCTs is back pain secondary to metastatic spread of the disease to the iliac or retroperitoneal lymph nodes at diagnosis.

Synchronous and metachronous testicular GCTs are rare and their incidence varies from 1% to 5% among all testicular cancers. Bilateral testicular GCTs are extremely rare and are considerably common in patients with seminoma and mixed GCTs (Fig. 2) [9].

Tumor markers have an important role in management of the disease. Alfa-fetoprotein (AFP) and human chorionic gonadotropin (hCG) are the main tumor markers used in the diagnosis, staging, prognosis, and follow-up of GCTs.

Imaging techniques of the scrotum

US is the primary diagnostic tool for evaluating testicular lesions and is highly sensitive for detection of tumors in testicular tissue [10]. Doppler US demonstrates the vascular supply of the normal testis and the vascularity of focal or infiltrative testicular lesions [9]. Testicular US and Doppler US are inexpensive diagnostic tools for the early detection of testicular cancer for boys and men [11]. B-mode sonography and Doppler US examinations of the testis should be performed using broadband high-frequency (5–12 MHz) high-resolution linear array transducer [12]. Scrotal US should be performed with the patient in the supine position with the scrotum elevated [13].

Sonoelastography is a new imaging technique that quantifies the stiffness of tissues [14]. It is an easy and cost-effective method, which provides additional information that may be helpful in differentiating the testicular lesions [14]. Recent studies have shown that real-time sonoelastography has high sensitivity and specificity for differentiating the malignant and benign lesions of the testis [15,16]. On images of sonoelastography, stiff lesions may appear red and soft lesions may appear blue, depending on the producer. Mostly, malignant testicular lesions have heterogeneous color design with more stiffness values on sonoelastography [14–16].

Nonpalpable testicular lesions can be detected incidentally during testicular US for the diagnostic evaluation of scrotal trauma, infertility, scrotal pain, and contra-lateral testicular evaluation [17]. Incidentally detected testicular lesions are usually smaller than 10 mm that are classified as “small” testis lesions. When an incidentally detected testis lesion is smaller than 5 mm, has no vascularity on Doppler US, and the tumor markers are negative, it can be monitored by US every 3 months for the first year [18]. The role of magnetic resonance imaging (MRI) in the differential diagnosis of incidentally detected nonpalpable testicular lesions has not been widely studied yet. Testis-sparing surgery should be the preferred treatment option in patients with small testicular tumors.

MRI is a problem-solving imaging modality when the US findings are inadequate for diagnosis [3]. The location, depth, and shape of a testicular lesion can be identified by MRI. MRI of the scrotum should be performed with a surface coil while the patient is in the supine position. The penis should be taped to the abdominal wall before the MRI examination. Studies have shown that, on MRI, low T2 signal intensity with intratumoral septal enhancement after gadolinium administration is more compatible with seminomas, whereas heterogeneous signal intensity on both T1-weighted images (T1-WIs) and T2- WIs with cystic and necrotic components and a heterogeneous enhancement pattern indicate nonseminomatous testicular tumors [3]. Epidermoid cysts and teratomas are uncommon lesions in testis. They may contain fat tissue on MRI. Teratomas are more heterogeneous lesions on MRI. Epidermoid cysts are usually hyperintense on T2-WI and hypointense on T1-WI. On T2-WIs, epidermoid cysts may contain internal low-signal-intensity concentric rings that are compatible with onion rings sign on US. Epidermoid cysts also show restricted diffusion on diffusion-weighted imaging [19]. Tsili et al. [9], in a study involving 33 patients with testicular lesions, have found that MRI can differentiate benign and malignant intratesticular lesions with 100% sensitivity and 87.5% specificity [3]. In that study, the accuracy of MRI examination in the assessment of local extent of malignant testicular tumors has been found to be 92.8% [3].

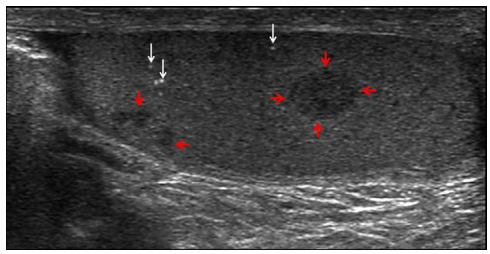

Fig. 2. US scan in a 25-year-old man with multifocal seminoma and incidental finding of microlithiasis (white arrows). Longitudinal US image reveals 2 distant hypoechoic masses in the right testis (red arrows). (Color version of figure is available online.)