Cryptorchidism and Extragonadal Germ Cell Tumor

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Key Words

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Abstract

A patient with an extragonadal germ cell tumor and a history of bilateral cryptorchidism is reported. The rarity of this concurrence in a single patient is discussed. The necessity for thorough investigation of the cryptorchid testes in patients with metastatic germ cell cancer remains essential.

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Introduction

Most male patients with germ cell tumors present with an overt testicular primary, but some 5-10% have an extragonadal presentation. The histogenetic relationship between testicular and extragonadal tumors remains controversial [1, 2]. We present a patient with a germ cell tumor and a history of bilateral cryptorchidism, with documented atrophy and absence of carcinoma in situ in both incompletely descended testes.

Case Report

A 27-year-old man with rapid deterioration of his general condition and a 10-kg weight loss in 6 weeks, was admitted in December 1988. The patient suffered from pain in the chest, abdomen and back, as well as high-grade fever, dyspnea, productive cough and dysphagia. Physical examination revealed hypotension, tachycardia and rales over both lungs. A large midline abdominal mass was palpated. Abnormal laboratory tests included high serum lactate dehydrogenase (LDH) (1,060 U/l), α-fetoprotein (2,390 U/ml), and β-human chorionic gonadotropin (64 mU/ml). Medical imaging techniques disclosed 10-cm diameter masses in both the retroperitoneum and the mediastinum, and multiple pulmonary and bone metastases. Histopathologic examination of tumor tissue obtained at mediastinoscopy-py showed embryonal carcinoma (malignant teratoma undifferentiated). In 1965, the patient had surgical repair of hypospadias. In 1972, a 6-month course of human chorionic gonadotropin (Pregnyl®) for bilateral cryptorchidism resulted in scrotal descent of the right testis, while the left testis could not be located. An elective right testicular biopsy was performed in 1981 because of azoospermia which revealed largely ineffective spermatogenesis. Because of acute pain, the left groin was surgically explored in 1982, and an atrophic testis and epididymis were removed. Review by our pathologists of the surgical
specimens of the right testicular biopsy of 1981 and the left testis and epididymis of 1982, respectively, failed to demonstrate (pre)malignant abnormalities. Clinical examination of the 10-ml volume right testis was unremarkable; ultrasonographic examination showed heterogeneous echogenicity. Inguinal orchiectomy was performed prior to chemotherapy and showed an atrophic testis without residual tubuli. This patient was treated with BOP/VIP (bleomycin, vincristine, cisplatinum/etoposide, ifosfamide, cisplatin) combination chemotherapy after which only a 2.5-cm residual retroperitoneal mass remained [3]. This was surgically removed and showed only fibrotic scar tissue. In August 1994 he remains in complete remission.

Discussion

Extragonadal germ cell tumors (EGCT) present without clinical or ultrasonographic evidence of a testicular primary tumor. Most EGCT are located in the midline structures such as the retroperitoneum (25%), the medias-

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tinum (25%), simultaneous in both these locations (45%) and in the pineal gland (5%) [1]. A primary testicular origin must be excluded by noninvasive investigations and pathological examination is advocated in selected patients. The reported prevalence of cryptorchidism ranges from 0.23 to 1.58% and the prevalence of cryptorchidism in patients with germ cell tumors ranges from 4.3 to 17.5%. The relative risk of testicular cancer developing in patients with cryptorchidism is estimated at 11.25, with a wide range of 5-48 reported [4]. In a recent follow-up study of 224 patients diagnosed with cryptorchidism in the period between 1935 through 1974, 2 malignant testicular neoplasms occurred [5].

The primordial germ cells migrate to the midline structures in the fifth or sixth week of embryonic life and incorporate into the primary sex cords. The EGCT are supposed to originate from germ cells failing this incorporation [1]. Recently, however, this concept has been challenged by observations on carcinoma in situ (CIS) in testicular biopsies of patients supposed to be suffering from EGCT. CIS represents a characteristic pattern of intratu-bular atypical germ cells associated with the development of invasive growth [6]. In patients with a history of cryptorchidism, the presumed incidence of CIS is about 2-3%, but in patients with gonadal dysgenesis it is thought to be much higher [7]. In a prospective study by Daugaard et al. [8], 48 patients with EGCT underwent testicular biopsies. CIS was diagnosed in 42% of the patients with primary retroperitoneal tumors. These observations could mean that patients with EGCT and testicular CIS do have a testicular primary, or that the EGCT and the CIS are independent lesions originating from the same damaging mechanism. In that case, CIS in the testes in association with an EGCT would be identical to having CIS in the contralateral testis in a patient with a testicular primary. Patients with incomplete testicular descent are well known to be at risk for testicular cancer, but this deficient testicular descent is not known to be associated with an increased risk for the development of EGCT. Our patient clearly suffered from bilateral incomplete testicular descent with bilateral testicular atrophy of the germinal epithelium and bilateral absence of CIS. This case suggests an association between maldescending testes and the risk of extragonadal primary germ cell tumors. We consider an occult testicular primary tumor in this patient to be excluded.
In patients with a history of cryptorchidism and clinically and sonographically normal testes, and presenting with metastatic germ cell tumor, the possibility of a testicular primary must however lead to the advice of bilateral testicular biopsies. If CIS is diagnosed, orchiectomy would be the treatment of choice. In patients with bilateral CIS, matters become more complicated. The possibility of residual neoplasia in the testicular sanctuary after chemotherapy should also be included in the decision-making process [9]. This case clearly demonstrates the possibility of a ‘true’ EGCT, in the setting of bilateral cryptorchid testes, with one testis having descended after pharmacological stimulation.

References


