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Original Contributions

Fourteen-year experience with the intraoperative frozen section examination of testicular lesion in a tertiary university center☆,☆☆

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ABSTRACT

Most testicular tumors are germ cell neoplasias. The number of incidentally detected small-sized, nonpalpable testicular lesions is increasing with the use of high-frequency ultrasound for infertility or trauma. These lesions are benign in 80% of cases and can be treated by organ-sparing surgery on the basis of frozen section examination (FSE). We assess the reliability of FSE in testicular and paratesticular lesions and its possible impact on surgical management. We performed a retrospective review of intraoperative FSE in testicular/paratesticular lesions at Geneva University Hospital during a 14-year period. A total of 170 cases were identified, with 159 testicular and 11 paratesticular lesions. The FSE results, permanent sections, and orchiectomy slides were reviewed and compared. Frozen section examinations were reported to be benign in 9 paratesticular and in 43 testicular lesions, and malignant in 2 paratesticular and 105 testicular lesions. Comparing FSE and final diagnosis, FSE correctly identified all nontumor lesions. There was a failure rate of 3.5% to identify tumor. Specificity was 100%, sensitivity was 95%, positive predictive value was 100%, and negative predictive value was 89%. Frozen section examination is a highly sensitive and specific intraoperative procedure, which allows to differentiate between benign and malignant testicular and paratesticular lesions, with a possibility of organ-sparing surgery when they are benign.

1. Introduction

Approximately 80 men were diagnosed as having testicular cancer, corresponding to 1.4% of all cancers in Geneva (Switzerland) male population between 2005 and 2009 [1]. Most testicular tumors (80%-90%) are germ cell neoplasias diagnosed preoperatively by clinical and imaging findings. Benign testicular lesions are recognized in 10% to 20% of cases [2].

The increased use of high-frequency scrotal ultrasound (US) performed for male infertility or trauma has led to an increase in the number of incidentally detected, small-sized, and nonpalpable testicular lesions, which have been shown to be prevalently (80%) benign, as reported by Giannarini et al [3]. These testicular and paratesticular lesions can be successfully treated by organ-sparing surgery, but it is not always possible to determine by imaging if these masses are benign or malignant. Ultrasound is highly sensitive in detecting small intratesticular masses (96.6%), but its specificity is low (44.4%). There are no sonographic features that definitively differentiate between benign and malignant intratesticular tumors [4,5]. Accurate differentiation between malignant and benign lesions is only possible on the basis of histologic analysis. Intraoperative frozen section examination (FSE) has been effectively used in other organs in order to enable organ-sparing surgery. Few studies have suggested that FSE could be accurate and effective in order to avoid radical orchiectomy. However, there are little large series concerning the reliability of FSE in testicular and paratesticular lesions.

Radical orchiectomy without FSE has been the standard treatment of testicular masses because of the high prevalence of germ cells tumor and the high frequency of intratubular germ cell neoplasia in the remaining testicular tissue [6,7]. However, in patients with bilateral testicular masses and monorchid men, orchiectomy results in androgen deprivation and infertility. These generally young patients must have a long-term androgen substitution and experience psychologic problems of castration that reduce the quality of life [8,9]. The aim of testicular-sparing surgery is to maintain physiologic endocrine function to avoid the need for androgen supplementation and, if possible, fertility [8].

In this retrospective study, we assess the reliability of FSE to characterize testicular and paratesticular lesions and its possible impact on surgical management during a time period of 14 years.

2. Materials and methods

We retrospectively searched in the database of the Division of Clinical Pathology at University Hospitals of Geneva intraoperative FSE in testicular and paratesticular lesions. Between 1998 and 2012, we identified 170 cases comprising 159 testicular and 11 paratesticular lesions,

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in which FSEs were performed. In this series, FSE has been done by general histopathologists. We compare FSE results with final pathology diagnoses. Slides of both the frozen and the permanent sections were available on all patients and were reviewed by 2 experienced uropathologists (J.C.T.I. and P.C.S.) without knowledge of the FSE and final diagnoses. Slides of orchiectomy were also reviewed for histologic confirmation and tumor classification according to the World Health Organization [10]. The size and the laterality of the lesions were determined by reviewing the gross description in the pathology reports. The criteria to predict the malignant nature of Leydig cell tumors included a large size (>5 cm), cytologic atypia, increased mitotic activity, necrosis, and vascular invasion [10]. To simplify the analysis, the cases of Leydig cell tumor were discussed separately.

3. Results

For the 11 paratesticular lesions, the median age of patients was 39 years (range, 7-66 years). Four lesions (36.4%) were in the right side and 7 (63.6%) on the left. The size ranged from 2.7 to 19.5 cm (median, 4.5 cm). Frozen section examinations were reported to be benign in 9 (81.8%) cases and malignant in 2 (18.2%) cases. Of the 9 benign paratesticular FSEs, 1 was reclassified from nontumor tissue to embryonal rhabdomyosarcoma on the final diagnosis and did not result in a radical orchiectomy in the same operating time (Figure A and B).

For the 159 testicular lesions, the median age of patients was 36 years (range, 1-83 years). The lesion was on the right side in 82 (51.6%) and the left side in 77 (48.4%), including 2 bilateral cases. The size ranged from 0.5 to 12 cm (median, 3.5 cm). Benign and malignant diagnoses on FSE were reported in 43 (29.1%) and 105 (70.9%) cases, respectively. The diagnosis was revised on permanent sections to be malignant in 4 benign FSE cases. In these 4 cases, the FSE/permanent diagnosis was chronic inflammation and fibrosis/regressive seminoma in 1 case, chronic inflammation/seminoma in 2 cases, and chronic inflammation/lymphoma in 1 case (Figure C and D). In one benign FSE, the final diagnosis was a Leydig cell tumor (Figure E and F). At final diagnosis, the testicular tumors accounted for 63 (39.6%) pure seminomas, 32 (20.1%) mixed germ cell tumors, 14 (8.8%) Leydig cell tumors, 7 (4.4%) benign tumors (epidermal cysts), 5 (3.1%) pure embryonic carcinomas, 3 (1.9%) lymphomas, 2 (1.3%) teratomas, 1 (0.6%) "burned-out" seminoma, and 1 (0.6%) mesothelioma. Other testicular lesions (fibrosis, necrosis, hemorrhage, inflammation) accounted for 31 (19.5%) FSEs (Table 1).

Leydig cell tumors are diagnosed on FSE in 11 (6.9%) cases of testicular lesions with a complete concordance at final diagnosis. Three additional Leydig cell tumors were found at permanent examination, with 1 case diagnosed as benign fibrosis on FSE and 2 cases diagnosed as germ cell tumor on FSE.

Altogether, 124 orchiectomies were performed. Two were based on FSE malignant diagnosis in paratesticular lesions with permanent diagnosis of liposarcoma. All the 105 cases with malignant testicular FSE benefited from orchiectomy, with a complete concordance (100%) to malignant or Leydig cell tumor between FSE and final diagnosis. Of the 43 benign testicular lesions diagnosed on FSE, 11 (25.6%) cases resulted in orchiectomy (Table 2). There were 14 (8.8%) Leydig cell tumors, of which 8 (57.1%) cases resulted in orchiectomy. At definitive diagnosis, 5 cases were considered benign Leydig cell tumors with size

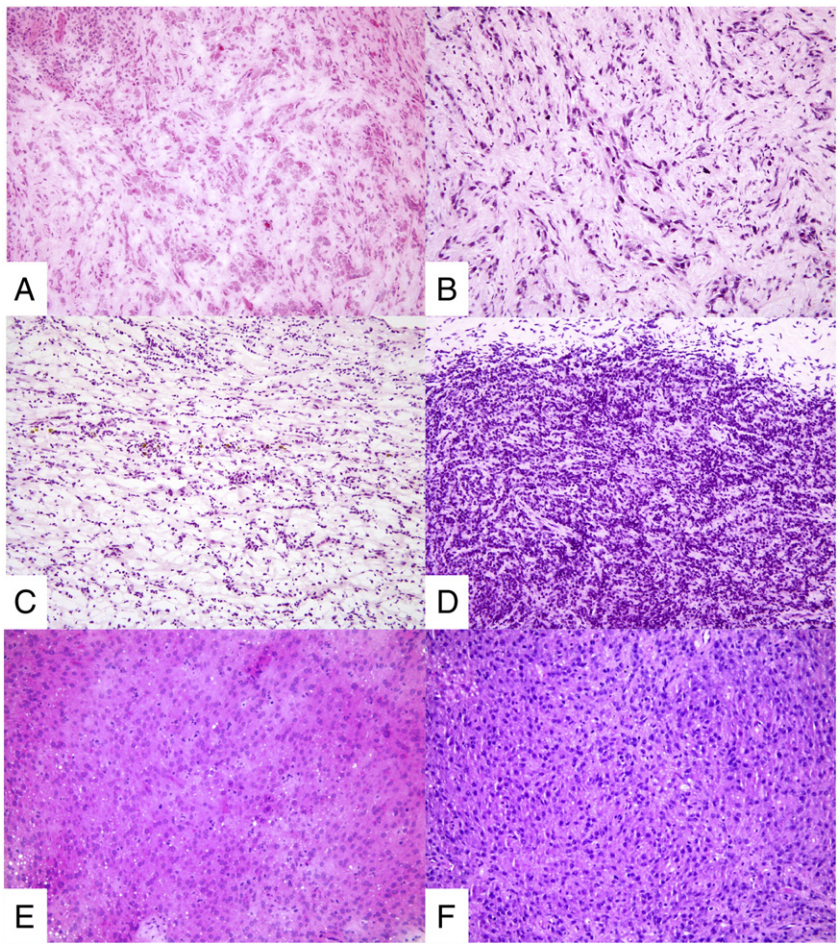

Figure. Examples of nonconcordant FSE/final diagnosis: inflammation at FSE (A) revised to a rhabdomyosarcoma at the final diagnosis (B). Chronic inflammation at FSE (C) revised to a diffuse large B-cell lymphoma (due to sampling by the surgeon; D). Diagnosis as seminoma at FSE (E) revised to benign Leydig cell tumors at the final diagnosis (F).