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Original article

Testicular cancer: The usage of central review for pathology diagnosis of orchiectomy specimens

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Abstract

Background: Radical orchiectomy specimens present a unique set of challenges for pathology assessment owing to their rarity and complexity. This study compares second opinion pathology reports generated at a single, large academic institution to primary reports from outside hospitals.

Methods: A database search was conducted for orchiectomy cases that were sent to our institution for management of testicular cancer from 2014 to 2015. Cases sent for consultation without a finalized diagnosis from the outside hospitals were excluded. A total of 221 consecutive cases were evaluated for comparison of final diagnoses between the outside institution and central pathology review.

Results: This study revealed significant discrepancy involving multiple parameters between original and second opinion pathology reports. Of 221 cases of germ cell tumors assessed, 31% showed some discrepancy of histologic subtype. Overall, reporting of lymphovascular invasion changed in 22% of cases; of those, initially called positive 23% were changed to negative and of those initially called negative 12% were changed to positive. Although the overall discrepancy for spermatic cord invasion was 9%, an initial positive diagnosis was negated 35% of the time. The pathologic stage was altered in 23% of cases, mostly secondary to differences interpreting lymphovascular and spermatic cord invasion.

Conclusion: Pathologists evaluating orchiectomy specimens should be aware of the major pitfalls in classification and staging, many of which may affect patient management.

Keywords: Testis; Germ cell tumor; Orchiectomy; Central pathology review; Pathologic staging; Vascular invasion; Differential diagnosis

1. Introduction

Testicular cancer is the most common solid cancer in young men, and its incidence has been on the rise in both the United States and Europe [1–4]. Over the previous half century, major strides in the management of testicular cancer have been made to the point that what was an often-lethal tumor is now associated with 5-year survival rates up to 97% [2,4–6]. This evolution has shifted the major point of emphasis to minimization of unnecessary treatments to avoid associated toxicities and secondary malignancies, while simultaneously maintaining the impressive cure rates [1,2,7,8]. Sophisticated risk stratification algorithms and management strategies, based on pathology-derived information, have been implemented to achieve this

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goal. Therefore, consistent and accurate pathologic assessment of radical orchiectomy specimens is still important. This study compares the experience at a large academic institution with a uniquely high volume of orchiectomy cases vs. that of other hospitals.

2. Materials and methods

A database search was conducted at Indiana University School of Medicine for radical orchiectomy specimens received from outside institutions that were reviewed at this institution during the 2014 and 2015 calendar years. To be included, a finalized pathology report from the outside institution was required, thus eliminating cases sent for expert consultation. The cases collected for analysis were part of the internal (central) pathology review performed systematically for patients seeking clinical management at this institution and whose pathology was initially assessed elsewhere. Only cases with an outside or internal diagnosis of germ cell tumor (GCT) were included.

The pathology reports from outside institutions, which were scanned into the electronic medical record at the time of accessioning, were reviewed and compared with the reports prospectively generated by in-house expert genitourinary pathologists (J.N.E., D.J.G., M.I., and L.C.) who are specialized in handling genitourinary specimens, including testicular tumors. Difficult cases or cases with major pathology discrepancy were usually shared with a leading testicular pathologist (T.M.U.), to reach consensus. Parameters assessed for comparison included pathologic stage, lymphovascular invasion, hilar invasion, and spermatic cord invasion. Further, the presence or absence of each histologic subtype with corresponding percentages was recorded and compared between the outside and central pathology reports.

3. Results

A total of 221 consecutive, confirmed testicular GCTs fitting the aforementioned criteria were collected. The average patient age at the time of accessioning was 32.3 years, ranging from 15 to 66 years. The mean tumor size was 4.5 cm, with a range of 0.4 to 19 cm.

3.1. Tumors of a single histological type

Outside pathology diagnosed 94 pure GCTs (Table 1), including 55 seminomas, 26 embryonal carcinomas, 10 teratomas, 2 yolk sac tumors, and 1 choriocarcinoma. After review, 7 (7.4%) cases were reclassified as mixed GCTs (MGCTs). The 55 pure seminomas were confirmed; but 4 embryonal carcinomas, 1 teratoma, 1 yolk sac tumor, and 1 choriocarcinoma were reclassified as MGCTs. In addition, a pure teratoma was altered to include a somatic-type malignancy (primitive neuroectodermal tumor), although this was still regarded as being of a single histotype.

3.2. Mixed GCTs

Of 127 cases initially diagnosed as MGCTs, all but 2 were confirmed (Fig. 1). Both discrepant cases were diagnosed internally as pure embryonal carcinomas, whereas the outside institution had included yolk sac tumor in 1 case and seminoma with "probable" yolk sac tumor in the other. The terminology for MGCTs varied and included "mixed germ cell tumor," "nonseminomatous germ cell tumor," and the individual listing of components (e.g., "embryonal carcinoma and yolk sac tumor"). Two cases with multifocal disease treated each focus as an independent and pure GCT; for example, one case diagnosed "pure seminoma and pure embryonal carcinoma."

3.3. Qualitative assessment of subtypes

In every MGCT case, there was an initial attempt to characterize the components, although in 3 cases ambiguous terms ("possible" or "probable") were used in reference to a specific histologic subtype.

Of the 127 cases originally considered as MGCTs, 68 (54%) were congruent with the central pathology report regarding the presence/absence of histologic subtypes. There were 81 classification discrepancies, affecting the remaining 59 cases (46%) (Fig. 1). The histologic subtype with the largest number of discrepancies was yolk sac tumor, accounting for 28 (47%) of the overall errors; most of these (22) being a failure to diagnose the yolk sac component. Among the 47 MGCTs that did not carry a diagnosis of a yolk sac tumor component, 21 (45%) had it added.

Table 1
Cases originally diagnosed as germ cell tumors of a single histologic type that changed to MGCT after central review

Diagnosis	Initial pathology	Central pathology	Specific histotype discrepancies
Seminoma	55	55	
Embryonal carcinoma	26	22	2 cases: minor component yolk sac tumor added 1 case: minor components of teratoma and seminoma added 1 case: minor component seminoma added
Teratoma	10	9	1 case: minor component seminoma added (major component leiomyosarcoma also added)
Yolk sac tumor	2	1	1 case: minor components of embryonal carcinoma and seminoma added
Choriocarcinoma	1	0	1 case: minor component seminoma added
Total	94	87	