Original Article

Spermatocytic seminoma: a 21 years’ retrospective study in a tertiary care hospital in Pakistan

Saroona Haroon, Muhammad Usman Tariq, Saira Fatima, Naila Kayani

Section of Histopathology, Department of Pathology and Microbiology, Aga Khan University, Pakistan

Received August 17, 2013; Accepted September 21, 2013; Epub October 15, 2013; Published November 1, 2013

Abstract: Background: Spermatocytic seminoma is a rare testicular germ cell tumor of old men. Accounting for 1-4% of all seminomas, spermatocytic seminomas have distinct pathogenesis, histological features, immunohistochemical profile and comparatively benign clinical behavior which distinguishes them from other germ cell tumors, especially classic seminoma. Aims: The purposes of our study were to assess the patient demographics, pathological features and to evaluate the utility of CD 117 immunostain along with other immunohistochemical stains in distinguishing Spermatocytic seminomas from classic seminomas. Material and methods: All spermatocytic seminomas patients diagnosed during 1992 to 2013 at Section of Histopathology, Department of Pathology and Microbiology, Aga Khan University hospital were included. Patient characteristics, histological details and follow-up data of few patients were available. CD 117 expression was determined by immunohistochemistry. Results: Total 16 cases of Spermatocytic seminomas were reviewed. Median age was 60 years and average tumor size was 10.4 cms. Microscopically, all of the 16 cases showed presence of edema and absence of lymphocytic infiltrate and intratubular germ cell neoplasia. Cytoplasmic glycogen was negative in all 13 cases, PLAP immunostain was negative in all 12 cases, while CD 117 was positive in all 8 cases, where applied. Conclusion: CD 117 is of limited utility in differentiating the spermatocytic seminoma from classic seminoma as it is expressed in significant number of spermatocytic seminomas. However, different histological features, PAS special stain and PLAP immunostain are significantly helpful in distinguishing these two entities.

Keywords: Testicular tumour, spermatocytic seminoma, germ cell neoplasm, classic seminoma

Background

The testicular tumors have been classified into 3 discrete subclasses by World Health Organization. Clinical topographics such as age of presentation, histology and genetic characteristics are the basis for these sub-classifications [1]. The incidence of more common subtypes such as classic seminoma and yolk sac tumors has been on an increase for past few years in Pakistan [2]; however the patterns of occurrence and clinical features of less common type i.e. spermatocytic seminoma have not been dealt with yet. Spermatocytic seminoma (SS) is a very uncommon testicular neoplasm which presents as a slow growing mass. This tumour has no known counterpart in ovary in females or any other site in males [3, 4]. Spermatocytic seminoma occurs infrequently in young patients with the usual age of presentation after 50 years. Most of the time, it presents as a painless testicular mass. Right testis is more commonly involved and in contrast to classic seminoma there is no relation with cryptorchidism or intraepithelial neoplasia. It behaves in benign fashion and metastasis is extremely rare so that orchiectomy is usually sufficient therapeutic management with long term follow up [5, 6].

Microscopically, 3 distinct cell types are found along with lack of cytoplasmic glycogen. In addition to these features, in strong contrast to classic seminoma there is scant to absent lymphocytic infiltrate [4].

There have been few case reports of sarcomas arising in SS which results in more aggressive treatments. It is imperative to differentiate this neoplasm from its frequent mimics, such as classic seminoma, lymphoma and embryonal carcinoma, because of less aggressive treat-
21 years’ experience of spermatocytic seminoma

Table 1. Summary of clinical and histological features of Spermatocytic Seminoma (n=16)

<table>
<thead>
<tr>
<th>Clinical &amp; histological features</th>
<th>Expression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Range)</td>
<td>35-81 years</td>
</tr>
<tr>
<td></td>
<td>Median 60 years</td>
</tr>
<tr>
<td>Tumor size (Range)</td>
<td>5.5-29.5 cm</td>
</tr>
<tr>
<td></td>
<td>Average 10.4 cm</td>
</tr>
<tr>
<td>Laterality</td>
<td>09 (Right)</td>
</tr>
<tr>
<td></td>
<td>04 (Left)</td>
</tr>
<tr>
<td></td>
<td>01 (Junction)</td>
</tr>
<tr>
<td></td>
<td>02 (Not specified)*</td>
</tr>
<tr>
<td>Capsule</td>
<td>10 (Intact)</td>
</tr>
<tr>
<td></td>
<td>02 (Breached)</td>
</tr>
<tr>
<td></td>
<td>04 (Not assessable)*</td>
</tr>
<tr>
<td>Intratubular germ cell neoplasia</td>
<td>Absent</td>
</tr>
<tr>
<td>Edema</td>
<td>Absent</td>
</tr>
<tr>
<td>Lymphocytic infiltrate</td>
<td>Absent</td>
</tr>
<tr>
<td>Granulomatous reaction</td>
<td>Absent</td>
</tr>
</tbody>
</table>

*Capsule integrity was assessable and the laterality of tumor was not mentioned in the blocks received from outside for second opinion.

Materials and methods

Our Hospital is one of the largest set ups of surgical pathology, with over 50,000 cut-ups per year. We reviewed the surgical pathology database of Aga Khan University Hospital from January 1992 till February 2013 through “Integrated Laboratory Management System (ILMS)” software, after Data Access Committee’s approval of Histopathology section. We retrieved sixteen cases diagnosed as Spermatocytic seminomas; four of the cases were received for histological review and second opinion. Since this was a retrospective study and did not involve actual patients, approval from the Hospital Ethics Committee was not required and confidentiality was maintained. Data was entered on proformas and patients’ demographics, histological and immunohistochemical findings were recorded. Clinical information regarding age, size, laterality and the presenting complaints was available from the pathology reports. Hematoxylin and eosin stained microscopic glass slides were reviewed by two experienced histopathologists and were analyzed for morphological features including three cell population, edema, lymphocytic infiltrate, intratubular germ cell neoplasia, granulomatous reaction and invasion of tunica albuginea and tunica vaginalis. Immunohistochemistry (already been performed using a combination of pressure cooker heating and the standard streptavidin-biotin-peroxidase complex with the use antibodies) and special stains performed on each case were also reviewed.

Results

Total 16 cases of Spermatocytic seminomas and 486 cases of classic seminoma were retrieved in duration of 21 years and reviewed by 2 experienced histopathologists (with minimum of 2 years post fellowship experience). Out of these, 4 cases were received as blocks for 2nd opinion. Age of presentation ranged from 35-81 years with median age of 60 years. Tumors were on right side in 9 cases, left sided in 4 cases and 1 was at the junction of right and left testis. 2 of the blocks received for 2nd opinion were not coded for laterality. Tumor size ranged from 5.5 cm to 29.5 cm with average tumor size of 10.4 cms. Tunica vaginalis was breached in 02 cases. Microscopically, all of the cases showed presence of edema, absence of granulomatous reaction, lymphocytic infiltrate and intratubular germ cell neoplasia (Table 1). Cytoplasmic glycogen was negative in all 13 cases, where applied. Placental alkaline phosphatase (PLAP) immunostain was negative in all 12 cases. LCA immunostain was negative in 12 cases. CD 117 was positive in all 8 cases. CD 30 was negative in all 4 cases and Cytokeratin AE1/AE3 was negative in all 6 cases, where applied (Table 2). Detailed clinical follow up was available in patients from Karachi city only numbering to 4, and all of the patients accessible for follow up were alive and no recurrence or metastasis was found. All of the patients were treated with orchidectomy alone; none received radiotherapy and any further treatment.

Discussion

Spermatocytic seminoma is a rare but distinct and unique testicular germ cell tumor. It accounts for about 1% of all testicular germ cell tumors and about 1.3 to 6.4% of all seminomas. SS was first described by Masson in 1946 and rarely occurs in younger patients [1-3].
21 years’ experience of spermatocytic seminoma

Table 2. Summary of expression of immunohistochemical stains and PAS special stain

<table>
<thead>
<tr>
<th></th>
<th>PLAP</th>
<th>CD 117</th>
<th>LCA</th>
<th>CD 30</th>
<th>Cytokeratin AE1/AE3</th>
<th>PAS</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of cases stained</td>
<td>12</td>
<td>08</td>
<td>12</td>
<td>04</td>
<td>06</td>
<td>13</td>
</tr>
<tr>
<td>No. of positive cases</td>
<td>00</td>
<td>08</td>
<td>00</td>
<td>00</td>
<td>00</td>
<td>00</td>
</tr>
</tbody>
</table>

Figure 1. The gross specimen picture. The gross specimen picture of two cases of spermatocytic seminoma. The cystic change was more prominent in ‘B’.

Figure 2. Low power microscopic picture of tumor. The edematous areas are more prominent towards the periphery of the tumor (Hematoxylin and eosin, 10x).

differs from classic seminoma in a number of ways. It affects elderly white males usually in fifth and sixth decades. However, few cases do occur in classic seminoma age group [4]. Like in our study, 5 patients were of age younger than 50 years. SS presents as a unilateral, painless and slowly enlarging testicular mass but bilaterality has also been reported [5]. There is no association with cryptorchidism, subfertility or gonadal dysgenesis and serum tumor markers are not raised. These tumors exclusively occur in testis and lack extra-testicular or female counterpart [6-8].

Average tumor size is 7 cm with a wide range of 2 to 20 cm [7]. The mean size of our cases was slightly bigger, being 10.4 cm.

Grossly, the tumor is well circumscribed and has diverse appearances of cut surfaces including solid, cystic, lobulated, edematous, mucoid, hemorrhagic or necrotic. In our study, most of the cases exhibited cystic cum solid areas on gross (Figure 1).

Microscopically, tumor is usually well circumscribed and does not extend into paratesticular
tissue. However, lymphovascular and tunica invasion may be seen but testicular capsule is rarely breached. In our study, none of tumour was extending beyond the capsule and tunica vaginalis was not breached in any of case.

Tumor is composed of nodules of non-cohesive tumor cells without intervening stroma. These nodules are separated by prominent edematous areas which impart a pseudoaveolar appearance [9]. We also found that edematous areas which were more prominent towards the capsular margin, giving the tumour lobulated appearance on low power and pseudoalveolar pattern on higher power (Figure 2).

In contrast to classic seminomas, SS lack fibrous septa, lymphocytic infiltrate, granulomatous reaction and intratubular germ cell neoplasia in surrounding testicular parenchyma [10]. These features were also lacking in our cases. The inflammatory was sparse and when present comprised predominantly of plasma cells rather than lymphocytes, as found in classic seminoma cases. Three characteristic cell populations are seen. The predominant medium size (15-20 µm) cells, resembling usual seminoma cells, have denser eosinophilic cytoplasm and more uniform, rounded nuclei with fine granular cytoplasm. The smallest cells (6-8 µm), resembling lymphocytes, have scant cytoplasm and dense hyperchromatic nuclei. The largest cells (80-100 µm), representing primary spermatocyte, appear as scattered mononuclear (occasionally multinucleated) cells with round, oval or indented nuclei with typical spireme-like lacy chromatin. Atypical mitotic figures are also occasionally seen (Figure 3) [10,
One of the variants is anaplastic variant of SS. However, we did not encounter anaplastic variant in our study.

One of the interesting microscopic finding was presence of ghostly cells and tiny eosinophilic globules, which were highlighted by special stain PAS, in 14 of 16 cases reviewed (Figures 4 & 5). Probably these represent degenerative cells and their contents, as this tumor is slow growing as compared to classic seminoma and also the presence of edema causes sparse vascular supply, so the degenerative cells were found in these tumors but not in classic seminoma. However, the ultrastructural nature and diagnostic significance of these cells and eosinophilic bodies needs to be determined and substantiated, which may lead to better understanding of pathogenesis of spermatocytic seminoma.

Based on morphological features, differential diagnosis (in order of preference) includes classic seminoma, malignant lymphoma and embryonal carcinoma. Immunohistochemical studies successfully discriminate and establish diagnosis [10]. Negativity for Placental alkaline phosphatase (PLAP), OCT ¾ and glycogen rules out classic seminoma, negativity for lymphoid markers rules out malignant lymphoma and negativity for cytokeratin AE1/AE3, CD 30 and OCT ¾ rules out embryonal carcinoma [6, 11-13]. As demonstrated in earlier studies, c-kit (CD 117) was considered of great value because of its negativity in contrast to classic seminoma [3, 15]. However, the recent studies show variable expression of CD 117, even up to complete (100%) positivity [10, 11, 13]. Our study also disregards the value of diagnostic utility of CD 117 in differentiating spermatocytic seminoma from classic seminoma, because in all the cases, where it was applied, it turned out to be strong and diffuse positive in all the 8 cases (Figure 6). In general, the SS cells show focal and/or weak CD 117 positivity. Decaussin reported 7 cases of spermatocytic seminoma in which CD 117 was expressed in all of cases [17]. This finding is conforming to our observation.

VASA, a germ cell marker can be helpful because of its differential expression in these two entities [17]. Another cancer-testis-antigen “NY-ESO-1” is also helpful as it is expressed in normal testis, 50% of spermatocytic seminomas and negative in rest of the germ cell tumors [18].

Ultrastructural features and stage-specific germ cell maturation markers highlight the origin of SS from more differentiated cells of spermatocytic lineage while classic seminomas originating from more primitive cells of similar lineage [15, 19]. Cytogenetically, SS consistently show gain of chromosome 9 in all cases while classic seminomas consistently show gain in chromosome 12 in form of isochromosome 12p [20, 21]. DNA flow cytometric studies demonstrate that SS are diploid, triploid and very few are aneuploid, while classic seminomas are frequently aneuploid, periploid and peripentaploid [14, 22].

SS have anaplastic variant and 6% of SS undergo sarcomatous differentiation [11]. Radiotherapy and adjuvant chemotherapy are the additional treatment modalities for these patients. Active surveillance has been suggested for all patients regardless of the presence or absence of aggressive component microscopically because of the decreased risk of late complications and the ability to achieve better cure rates.

Spermatocytic seminomas rarely metastasize and are treated by orchidectomy [23-25]. Tumors with sarcomatous differentiation have aggressive behavior, metastasis and poor prognosis [26, 27].

Conclusion

Spermatocytic seminoma is a rare germ cell neoplasm in Southern Pakistan, presenting as a large mass at a late age. Among various immunohistochemical markers CD 117 is of limited utility in differentiating the spermatocytic seminoma from classic seminoma as it is expressed in significant number of spermatocytic seminomas. However, different histological features, PAS special stain and PLAP immunostain are significantly helpful in distinguishing these two entities and for definitive diagnosis. Spermatocytic seminoma is a rare testicular tumor, with morphological features that mimic few other neoplastic lesions with different clinical course and management, therefore, requiring the use of ancillary studies for help in differential diagnosis. Negative expression of PLAP immunohistochemical stain and absence
of cytoplasmic glycogen are the most useful diagnostic features to differentiate from classic seminoma. CD-117 is of limited utility in differentiating it from classic seminoma. Negative expression of CD 30 and Cytokeratins immunohistochemical stains help to differentiate from embryonal carcinoma, while LCA immunostain from lymphomas. Eosinophilic globules and ghostly cells are frequent features of spermatocytic seminoma.

Acknowledgements

We thank Mr. Karim Bhojani (Laboratory Assistant) for his assistance in slide and tissue block retrieval.

Disclosure of conflict of interest

None.

Abbreviations

SS, Spermatocytic seminoma; PLAP, Placental alkaline phosphatase; LCA, Leukocyte Common Antigen.

Address correspondence to: Dr. Saroona Haroon, Section of Histopathology, Department of Pathology and Microbiology, Aga Khan University, Pakistan. Tel: 0092-3486-4347; Fax: +92 21 493 4294; E-mail: saroonakm@yahoo.com

References


[22] Talerman A, Fu YS, Okagaki T. Spermatocytic seminoma. Ultrastructural and microspectro-
21 years’ experience of spermatocytic seminoma


