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Primary testicular Non-Hodgkin's lymphoma: A case report

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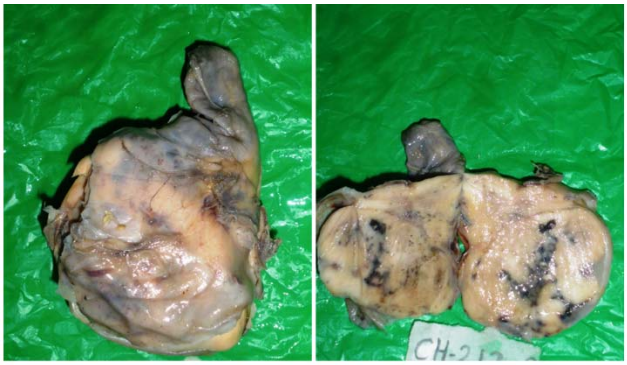
Abstract
Non-Hodgkin's Lymphoma (NHL) of the testis is an uncommon extranodal presentation accounting for 1% of all NHL, 2% of extranodal lymphoma, and 5% of all testicular tumours. There are various subtypes of primary Non-hodgkins lymphoma of testis including diffuse large B-cell lymphoma (DLBCL), Burkitt's lymphoma, follicular lymphoma and B-cell lymphoma. Differential diagnosis of testicular lymphoma is made with seminoma of classic or spermatocytic type, embryonal carcinoma, viral and granulomatous orchitis. Orchidectomy with adjunctive chemotherapy or radiotherapy is the treatment. It is important to identify primary testicular DLBCL correctly and distinguish it from other entities because of differences in therapy, management, and prognosis. We hereby present a case of a 76 year old man who presented with bilateral testicular enlargement with dragging pain and abdominal discomfort since 1 month. FNAC was done followed by right sided orchidectomy and was sent for histopathological study. Immunohistochemistry was done which showed LCA and CD 20 positivity and negative for CD 3. A final diagnosis of diffuse large B-cell lymphoma was made.

Keywords: Non-Hodgkin's lymphoma, DLBCL, LCA, CD20

Introduction
Non-Hodgkin's Lymphoma (NHL) of the testis is an uncommon extranodal presentation accounting for 1% of all NHL, 2% of extranodal lymphoma, and 5% of all testicular tumours. The disease typically presents in patients aged 60 to 80yrs. Right and left sided testicular involvement is equal in frequency. 6–35% of testicular lymphoma s will have bilateral involvement. These patients usually present with abdominal lymphadenopathy and may show involvement of CNS, lung, skin, bone, adrenals, liver, GIT [1].
Histopathologically, 80-90% of primary lymphoma of testis are of diffuse large B cell type and show tendency to disseminate systemically.

Case report
A 76 year old man presented with bilateral testicular enlargement with dragging pain and abdominal discomfort since 1 month. On examination there was bilateral testicular enlargement with right more than left, firm to cystic in consistency and nontender. USG and CT scan showed features of bilateral testicular tumour with distorted contour and heterogenous echotexture. Reactionary fluid collection was seen in tunica vaginalis bilaterally with pre and para aortic lymphadenopathy and multiple space occupying lesions in the liver. FNAC was done and reported as? NHL/? Germ cell tumor. Right sided orchidectomy was done and sent for histopathological study.
Grossly the testes measured 12 x 9 x 5.5cm.Cut-open of capsule drained serous sanguineous fluid. Cut-section showed grey-white homogenous tumour with nodularity involving the entire testis. Spermatic cord and epididymis was unremarkable.



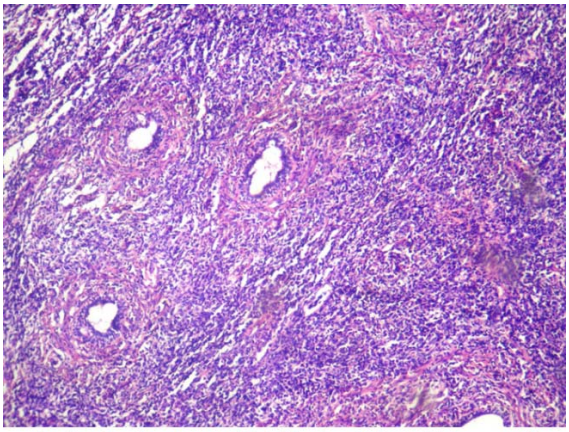
Right orchidectomy specimen, covered by capsule with surface showing bosselations. Cut section showing grey white nodular tumor with areas of hemorrhage

Microscopy

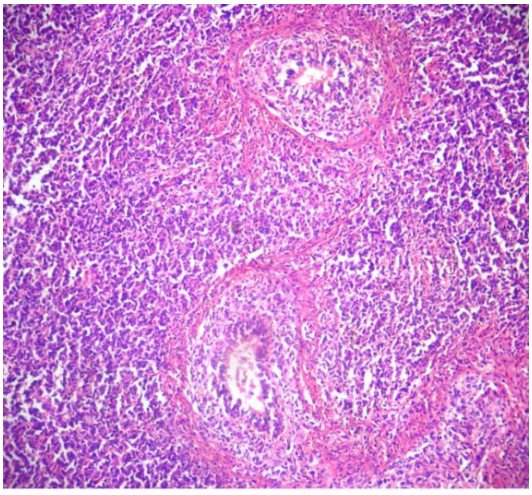
Sections showed discohesive sheets of large monomorphic tumor cells with large, vesicular nucleus, fine to coarse chromatin, prominent nucleoli and scant amphophilic cytoplasm. Tumour cells seen mainly infiltrating the interstitial space and around the seminiferous tubules. The seminiferous tubules appeared normal in most areas with few of them showing atrophic changes and some showing destruction by the infiltrating tumour cells. Epididymis and spermatic cord were normal.

Diagnosis

Features were suggestive of Non-Hodgkin's lymphoma. Immunohistochemistry was advised.



Section showing tumour cells infiltrating the interstitial space and surrounding the seminiferous tubules.(10x)



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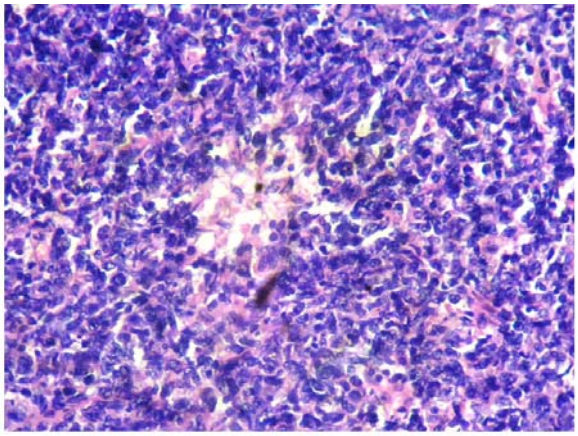
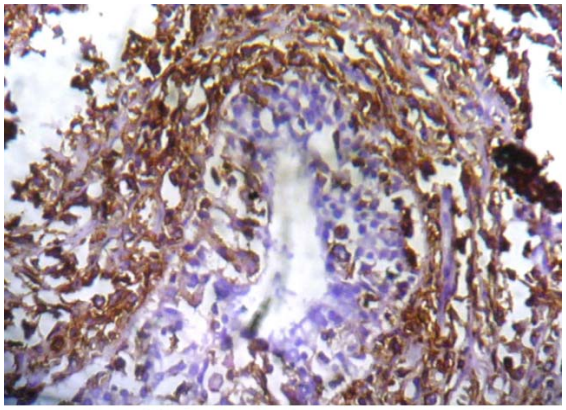


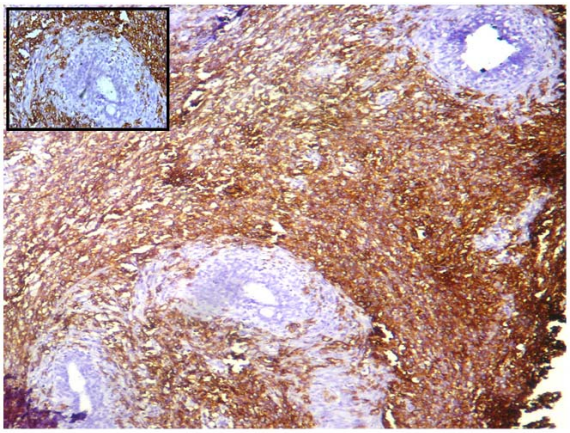
Section showing tumour cells with round nucleus and coarse chromatin and scanty cytoplasm. Destruction of seminiferous tubules seen. (40x)

Immunohistochemistry

Immunopositive for LCA, CD 20 & immunonegative for CD 3. A final diagnosis of diffuse large B-cell lymphoma was made.



Immunopositive for LCA showing tumour cells surrounding seminiferous tubules (40x)



Tumour cells immunopositive for CD20 with sparing of seminiferous tubules. Inset (40x).

Discussion

Malignant lymphoma of testis is rare and accounts for 1% of all NHL and 5% of all testicular tumors. According to National Cancer Data Base study from 1985 to 2004, DLBCL accounted for 77.8%, other B-cell types 21.1% and T-cell type, 1.1% of cases. Most of the malignant testicular lymphomas present with abdominal lymphadenopathy [3].

Primary DLBCL of the testis arises in the testis and is associated neither with lymphoma elsewhere nor with

leukemia. Involvement of the testis by systemic lymphoma/ leukemia defines secondary testicular lymphoma. Primary DLBCL of the test is usually presents in adult patients with a median age in the sixth decade. The most common clinical presentation is a unilateral painless enlargement of the testis, with rapid progression. The history of testicular swelling is generally of weeks to month's duration, but it may be present for several years. In addition to the enlargement of the testis, systemic symptoms such as fever, anorexia, night sweats, and weight loss may be presenting manifestations, and are usually present in 25% to 41% of patients. Involvement of the scrotum and regional retroperitoneal lymph nodes often develops in the course of the disease. Locally there may be a spread to the epididymis, spermatic cord, and scrotal skin, sometimes with sharp scrotal pain [4].

There are various subtypes of primary Non-hodgkins lymphoma of testis including diffuse large B-cell lymphoma, Burkitt's lymphoma, follicular lymphoma and B-cell lymphoma.

Usual light microscopy with H and E stain of all tumours show chiefly intertubular growth pattern without complete destruction of basic architecture. The seminiferous tubules are preserved. Few are atrophic and few are completely obliterated. Spermatogenic arrest, interstitial fibrosis and tubular hyalinization are commonly seen.

Discohesive sheets of tumour cells diffusely penetrate into tissue space producing wide separation of normal structures. The tumour cells are usually medium sized to large lymphoid cells with oval to round vesicular nuclei with fine chromatin. There are multiple small membrane bound nucleoli, the cytoplasm is usually scanty and amphophilic to basophilic [2].

Differential diagnosis of testicular lymphoma is made with seminoma of classic or spermatocytic type, embryonal carcinoma, viral and granulomatous orchitis. Unlike the most lymphoma cells, seminoma cells are uniform, have distinct cell membrane, abundant glycogen rich cytoplasm and rounded flattened central nuclei with one or more prominent nucleoli.

Lymphoma tend to have smaller cells with scant cytoplasm, higher nuclear cytoplasmic ratio. They show diffuse intertubular infiltration with recognizable tubular remnants. Embryonal carcinoma has a characteristic epithelioid appearance that frequently forms glandular, papillary or tubular structure.

Concerning the treatment, retrospective analyses have shown that after locoregional treatment only (orchidectomy and radiation therapy), relapse is high (approximately 50% to 60% of patients) in CNS or in contralateral testis.

Primary testicular lymphoma is predominantly a disease of the elderly. Although multiple lymphoma classifications have been used in the description of testicular lymphoma, the predominant histology is Diffuse Large B-cell Lymphoma (DLBCL). In the largest series involving 3669 cases of testicular NHL registered with National Cancer Data Base (NCDB) from 1985 to 2004, DLBCL accounted for 77.8%. Other B cell types and T cell types were seen in 21.1% and 1.1% cases respectively. In a recent series of 18 cases, immunohistochemical subtyping of testicular DLBCL was attempted and it was found that majority(89%) had non-germinal centre subgroup(CD10/Bcl-6 negative and MUM-1 positive) with high proliferative activity [1].

Testicular Non-Hodgkin's lymphoma has a predilection for spreading to non-contiguous extranodal sites, especially the central nervous system. Advanced stage disease is usually managed with doxorubicin-based chemotherapy. For early stage disease, opinion is divided regarding systemic chemotherapy following orchidectomy. The high incidence of spreading, especially to the central nervous system, leads to advocacy of the use of central nervous system prophylaxis with intrathecal chemotherapy [5].

High inguinal orchidectomy alone was previously performed to treat stage 1E primary NHL of testis, but the 5-year survival rate was as low as 12% and most patients died within 2 years after systemic dissemination. Postoperative radiotherapy was introduced in the 1980's resulting in 5-year survival rates of 64% in stage 1/2 and 17% in stage 3/ 4patients [1].

Conclusion

The most common type of primary testicular lymphoma is diffuse large B-cell type. Treatment is complex and dependent on the initial characteristics of the patient. An orchidectomy, especially in early stage disease, is advantageous because it provides tissue for pathologic evaluation. There is high risk of extranodal relapse even in cases with localized disease at diagnosis. Therefore, an adjunctive chemotherapy or radiotherapy regimen is necessary. It is important to identify primary testicular DLBCL correctly and distinguish it from other entities because of differences in therapy, management, and prognosis.

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