Aggressive nasal-type natural killer /T-cell lymphoma associated with Epstein Barr Virus presenting as testicular tumor.

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Lymphome agressif T/Natural killer associé au virus Epstein Barr et se présentant comme une tumeur testiculaire.

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RÉSUMÉ

Prérequis: Le lymphome testiculaire est une maladie léthale avec une survie moyenne de 12 à 24 mois. Le lymphome T/Natural killer du testicule, primitif ou secondaire est exceptionnel.

But: Les auteurs rapportent un cas lymphome T/Natural killer du testicule avec étude histopathologique, immunohistochimique et moléculaire et revue de la littérature.

Observation : Nous rapportons un cas lymphome T/Natural killer du testicule chez un homme de 28 ans. L'examen histolopathologique de la biopsie chirurgicale a montré un lymphome à grandes cellules avec angioinvasion et immunomarquage positif pour CD3 (cytoplasmique), CD2, CD8, CD43, CD45, CD45Ro, CD56, "T-cell intracellular antigen-1", perforine, Mib1 et granzyme. L' hybridation in situ pour la détection de l'ARN messager du virus Epstein-Barr encoded était positive. L'étude par "Polymerase chain reaction" sur tissue fixé a montré l'absence de réarrangement du gène "T-cell receptor". Le stade initial d'Ann Arbor était I (EA). Ce lymphome était réfractaire à la chimiothérapie. Le patient avait développé deux mois plus tard, des métastases ganglionnaires dans les chaines iliaques externes et sus-claviculaires. L'évolution était marquée par le décès du patient 8 mois après.

Conclusion: Cette étude confirme que le lymphome T/Natural killer du testicule mérite d'être distingué des autres lymphomes testiculaires. En effet, ce lymphome tend à survenir chez le sujet jeune, à se propager précocément, à avoir une évolution péjorative et fortement associé au virus "Epstein Barr".

Mots-clés

Lymphome testiculaire - Lymphome T/NK - Histopathologie - Immunohistochimie - Biologie moléculaire.

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SUMMARY

Background: Testicular lymphoma is a lethal disease with a median survival of approximately 12 to 24 months. Nasal-type natural killer / T-cell lymphoma of the testis is exceptional whether as a primary or secondary tumor.

Aim: The authors report on the comprehensive histopathologic,immunohistochemical and molecular analysis of a case of primary testicular nasal type NK/T cell lymphoma and review the features of previously reported cases.

Observation : We report a case of primary nasal-type natural killer / T-cell lymphoma of testis in a 28-year-old male. The histopathological examination of the surgical specimen, showed a large lymphoma cells with angioinvasion expressing CD3ε (cytoplasmic), CD2, CD8, CD43, CD45, CD45Ro, CD56, T-cell intracellular antigen-1, perforine, Mib1 and granzyme. In situ hybridation for Epstein-Barr-virus -encoded mRNA was positive. Polymerase chain reaction study of formalin-fixed tissue showed lack of T-cell receptor gene rearrangements. The initial stage was I (EA) of Ann Arbor. This lymphoma was refractory to chemotherapy. The patient developed lymph node metastases in the out iliac and in the susclavicular region two months later. He died of disease after eight months.

Conclusion: This study confirms that testicular NK/T-cell lymphoma deserves to be distinguished from the other testicular lymphomas. In fact, this lymphoma tends to occur at young age, to disseminate early, to have an aggressive course, and is strongly associated with EBV.

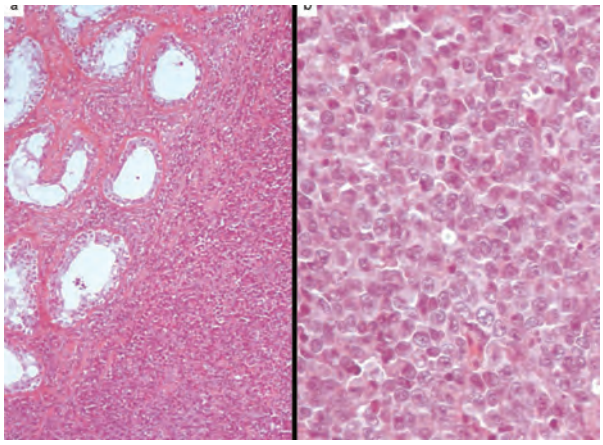
Key-words

Testicular lymphomas - NK/T-cell Lymphoma - Histopathology - Immunohistochemistry - Molecular biology.

T/NK cell lymphomas are exceptional in the testis. These lymphomas are highly aggressive lymphomas of NK- or T-cell lineage with predominant extranodal presentation and are divided into nasal and nasal-type (extra-nasal). The great majority of NK/T cell lymphomas occurs in the nasal or nasopharyngeal region and they are more common among orientals [1,2].

We report the case of a 28-year-old man presenting with a painful testicular mass noted for six weeks. The patient received surgical testicular and epididymal biopsies. Histologic examination of the specimens revealed a diffuse proliferation of malignant round cells within the interstitium of the testicular parenchyma. These cells infiltrated around the seminiferous and epididymal tubules and presented in a discohesive pattern (figure 1a). The tumor cells were large with round nuclei which frequently showed irregular foldings and granular chromatin. The cytoplasm was moderate in amount and often pale. Mitotic figures were easy to find. Karryorrhexis was usually proeminent without zonal tumor cell death (figure 1b).

Figure 1: a: Tumor cells are present around sclerotic seminiferous tubules. b: Higher magnification shows large and medium sized lymphoma cells with irregular nuclear contours fairly dense chromatin and small amount of amphophilic cytoplasm



Angiocentric growth was observed. In some areas, these cells invaded the vessels. Immunohistochemical study demonstrated reactivity with CD3ε (cytoplasmic), CD2, CD8, CD43, CD45, CD45Ro, CD56, T-cell intracellular antigen-1, perforine, Mib1 and granzyme but not CD4, CD5, CD10, CD79a, CD30, CD43, TdT, PAX5 and CD68. Interestingly, there was an aberrant granular immunostaining with panB (CD20). In situ hybridation for Epstein-Barr-virus-encoded mRNA was positive (Figures 2 and 3). Polymerase chain reaction study of formalin-fixed tissue showed lack of T-cell receptor gene rearrangements. The initial stage was I (EA) of Ann Arbor. The patient was initially treated with conventional chemotherapy, the CHOP (cyclophosphamide, adriamycin, vincristine, and prednisolone) regimen. His lymphoma was refractory to chemotherapy and metastases developed in the out iliac and in the supraclavicular lymph nodes and in controlateral testis two months later. A palliative chemotherapy and beam external radiation was performed. The patient died of disease two months later, approximately eight months after the diagnosis of T/NK-cell lymphoma was made.

Figure 2: Malignant cells were immunoreactive for CD3 (cytoplasmic) and CD2 and negative for CD5, and Pax5.

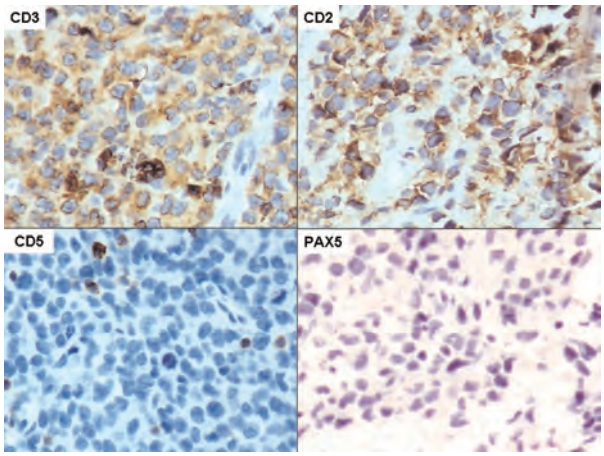
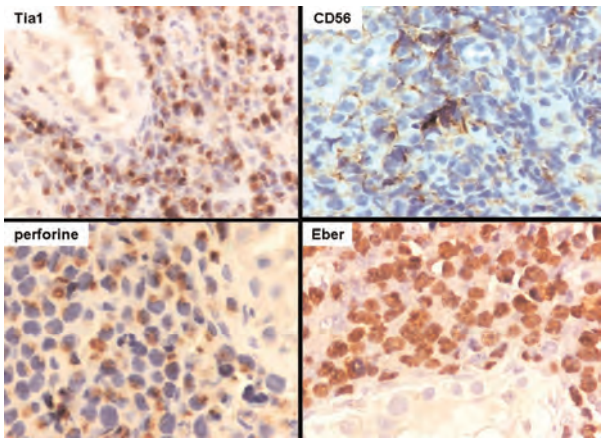


Figure 3: The cells were positive for Tia-1, CD56 and perforine. Large number of lymphoid cells shows positive labelling for EBERs on in situ hybridization.



DISCUSSION

Primary nasal-type natural killer / T-cell lymphoma of the testis is uncommon. Seventeen cases of primary nasal-type natural killer / T-cell lymphoma of the testis were collected [2]. Unlike the other lymphomas of the testis, NK/T-cell lymphoma occurs in young patients. The mean age at presentation with primary testicular disease (stage IE) is 44 years (range: 30-66 years) [2]. Most of the patients are Asian. On histopathological exam, the neoplastic cells infiltrate around seminiferous tubules, cause arrest of spermatogenesis, and tubular hyalinisation. They have polymorphous medium to large angulated nuclei and moderate cytoplasm, with immunologic phenotypes of CD4-, CD8-, variable cytoplasmic CD3 epsilon+, CD56+, cytotoxic proteins (TIA-1, granzyme and perforine) and Epstein-Barr early region

1+, and germ line PCR result for T-cell receptor, which indicated true NK-cell origin [3]. CD56 ("NK-associated antigen") recognizes the neural cell adhesion molecule (NCAM), which exhibits homophilic binding properties. The expression of CD56 in the normal testicular constituents can perhaps explain the tendency for T/NK cell lymphoma to localize in this organ [4]. Their TCR locus is not rearranged (they were called silent peripheral T-cell lymphomas). In fact, 5/9 NK/T-cell lymphoma of the testis which were evaluated for TCR gene rearrangement, had TCR genes in the germline configuration reflecting a true NK-cell origin. The differential diagnosis of primary NK/T lymphoma of the testis with lymph node involvement vs secondary involvement of testis by nodal T/NK-cell lymphoma of nasal type is important since there are differences in treatments as well as clinical staging. Extra-nodal NK/T-cell lymphoma should be distinguished from peripheral T-cell lymphoma since it is associated with poorer prognosis compared with peripheral T-cell. Nasal-type NK/T cell lymphomas often pursued a rapidly progressive course, with additional sites of disease appearing rapidly within weeks to months. Response to multiagent chemotherapy (such as CHOP, BACOP, or ProMACE-CytaBOM) is often poor, even if complete remission could be obtained, relapse develop soon after. [1]. The prognosis of NK/T cell lymphomas is poor: all reported patients died of complications of the disease or the treatment at a medium time of 4 months after diagnosis [2]. Significant prognosis factors in all CD56 + lymphomas are the anatomic site, EBV status, necrosis and the presence of pleomorphic large tumour cells [5]. However, EBV status remains the only independent prognostic factor. More aggressive treatment should be saught for this particular malignancy.

Acknowledgments

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