Introduction

Primary extranodal lymphoma of the testis is a lethal disease, second only to primary brain lymphoma; median survival is 12 to 24 months. It accounts for approximately 1% of non-Hodgkin’s lymphomas, 4% of all extranodal non-Hodgkin’s lymphomas, 5% of all testicular malignancies, with an estimated incidence of 0.26/100,000 per year [6,21]. Primary testicular lymphoma (PTL) is essentially an intermediate or high-grade lymphoma, and diffuse large-cell type is the most common one [4]. In contrast to other testicular malignancies, PTL occurs mostly in patients older than 50 years of age [9]. After adequate locoregional and systemic treatment, the central nervous system (CNS) remains the most frequent site of recurrence (up to 30%). Therefore, prophylactic intrathecal (IT) chemotherapy (CT) combined with systemic treatment has been introduced to improve outcome [17]. We review in this chapter some data concerning pathology, staging, prognosis, and finally treatment options for different stage of PTL.

Pathology, staging and prognosis

As for all situations with any suspected tumour in the testes, the primary option remains inguinal orchidectomy for diagnosis and treatment. Orchidectomy is important because it removes the tumour located in the so-called “sanctuary site” with good local control, and provides important information on grade and
pathology subtype [13]. Histologically, 80-90% of primary testicular lymphomas are diffuse large-cell type with B-cell immunophenotype [11]. Complete initial staging work-up is the same as for all other non-Hodgkin’s lymphomas. Cerebrospinal fluid (CSF) examination for malignant cells is recommended due to the high incidence of CNS relapse. Recently, PET or PET-CT is widely used in initial lymphoma staging but few data are available on primary testicular lymphoma [15]. The majority of patients with PTL present stage I or II disease according to Ann-Arbor staging [18]. PTL, like other aggressive extranodal non Hodgkin’s lymphomas, shows a tendency to spread and relapse at several extranodal sites including the CNS, contralateral testis, Waldeyer’s ring, skin, pleura, lung, or soft tissues [5]. The prognosis of PTL is poor even in early stage despite the combination of orchidectomy followed by anthracyclin-based chemotherapy, radiation therapy, and CNS prophylaxis. The majority of patients fail within the first two years following treatment, and mainly in the CNS [2,7].

Treatment options

Given the rarity of PTL, its treatment has not been standardized. Up to now, no prospective trial has been published. Available data are reported by some single institutions and/or by international collaborative groups active in rare diseases [20,22]. The management of PTL depends on stage either at initial diagnosis or after relapse following an adequate initial treatment.

Treatment of early stage I-II

The universally accepted treatment modality for stage I and II aggressive nodal lymphoma is either chemotherapy (cyclophosphamide, doxorubicin, vincristin, prednison; CHOP) combined with rituximab or chemotherapy (CT) followed by radiation therapy (RT) [10,12]. However, an optimal treatment approach has not been defined for extranodal lymphomas. Also no randomized studies have been performed to evaluate the superiority of combined modality treatment to RT or CT alone, especially in testicular lymphoma, where there is an increased incidence of relapse (50-80%) following orchidectomy and RT without chemotherapy [14]. Regarding these results and the patterns of failure, the use of systemic CT combined with prophylactic intrathecal CT has become an important part of the management of early disease. Connors et al. [1], in their study of 15 patients with stage IE and IIE disease, administered (following orchidectomy) a doxorubicin-based CT with testicular RT, and observed 93% actuarial relapse-free survival. However, in a retrospective study by Fonseca et al. [5] including 62 patients, no beneficial effect of combined treatment compared to single modality was observed. In their study, only 10 patients, including 3 with stage I disease, received combined modality treatment. Moreover, only 4 patients received intrathecal-CT, and 2 of these already had leptomeningeal involvement at diagnosis. It is, therefore, difficult to draw a conclusion about the inefficacy of combined treatment. Zouhair et al. evaluated the outcome of a series of 36 patients in a multicentre Rare Cancer Network study [20]. Most patients (80%) had CHOP-CT combined with intrathecal-CT in 17 patients (47%). Testicular RT was delivered to the scrotum alone in 12 patients, or also to the iliac and para-aortic lymph nodes in 8. No relapse was observed in the irradiated volumes. The majority of relapses (12 out of 14) were observed in extranodal sites. Eight patients (22%) had CNS relapse. The 5-year