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Hodgkin lymphoma

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Abstract

Hodgkin lymphoma (HL) is a curable malignancy which shows a bimodal curve in incidence in economically developed countries; there is a putative association with Epstein–Barr virus. The WHO 2008 classification schema recognises two histological types of HL: the nodular lymphocyte predominant and the "classic" HL. The latter encompasses four entities: nodular sclerosis, mixed cellularity, lymphocyte depletion, and lymphocyte-rich. Most patients with HL present with asymptomatic superficial lymphadenopathy. The commonest sites of disease are the cervical, supraclavicular and mediastinal lymph nodes, while sub-diaphragmatic presentations and bone marrow and hepatic involvement are less common. Splenic involvement is usually concomitant with hepatic disease and systemic symptoms; extranodal presentations are quite rare. Systemic symptoms are present in ∼35% of cases. The stage of disease is defined according to the Ann Arbor staging system or its Cotswolds variant, and staging work-up includes physical examination, chest X-rays, chest and abdominal CT scan, and bone marrow biopsy. ^{18}FDG-PET (^{18}fluordeoxyglucose positron emission tomography) plays a central role in staging, response assessment and prognosis definition.

Classic HL usually spreads by contiguity within the lymphatic tissue network, with a late extension to adjacent and distant viscera. Mortality from HL has been progressively decreasing, as confirmed by the most recent 5-year survival figure of 81%. The list of putative prognostic factors in HL has been increasing, but most factors still require prospective validation. Some of these variables are used to stratify early-stage disease into "favourable" and "unfavourable" categories, with "unfavourable early-stage" being intermediate between "favourable early-stage" and "advanced-stage".

ABVD (adriamycin(doxorubicin), bleomycin, vinblastine, dacarbazine) combination chemotherapy followed by involved-field irradiation is the standard treatment for patients with early-stage HL, with a 5-year OS >95%. Several trials assessing less intensive approaches for patients with favourable early-stage HL are ongoing. More intensified combinations, such as the BEACOPP (bleomycin, etoposide, adriamycin, cyclophosphamide, vincristine (Oncovin), procarbazine, prednisone) regimen, are being investigated, usually in patients with unfavourable early-stage HL and interim PET+. ABVD is the standard chemotherapy treatment also for patients with advanced disease. Although some evidence suggests that more intensive combinations provide better disease control, the inevitable increased risk of relevant late toxicity worries investigators. Consequently, there has been a shift towards investigating the innovative strategy of a more aggressive schedule for patients with ^{18}FDG-PET positive results after the first 2 courses of ABVD. High-dose chemotherapy supported by ASCT (autologous stem cell transplantation) is considered the standard of care in patients with HL which has relapsed after, or is refractory to conventional chemoradiotherapy, while allogeneic transplant is a suitable tool for patients with chemorefractory disease and patients failed after ASCT.
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1. General information

1.1. Definition

Hodgkin lymphoma (HL) is one of the few adult malignancies that can be cured in most instances. The salient feature of this lymphoma is the rarity (about 1%) of neoplastic elements in the cell population, whereas the overwhelming majority of cells are non-neoplastic, mostly consisting of T-lymphocytes [1]. Although the clonal B-cell origin of both lymphocyte predominant and "classic" HL was recently demonstrated [2], thus enabling the term 'Hodgkin disease' to be changed to 'Hodgkin lymphoma' [3], the pathogenic mechanisms of this lymphoma are still largely unknown.

1.2. Incidence

HL is an uncommon malignancy, with 7000–7500 new cases diagnosed annually in the United States of America. Most of these patients present with early stage disease. This malignancy displays a bimodal curve in incidence in economically developed countries. In economically underdeveloped countries, the overall incidence of HL is lower than in developed countries, with the exception of children under the age of 15, where a higher incidence is seen. There is only a mild increase in incidence throughout adolescence and young adulthood [4]. A difference in the distribution of histological subgroups occurs as well, since the incidence of nodular sclerosis is lower in underdeveloped countries.

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