incidence

The crude incidence of Hodgkin lymphoma (HL) in the European Union is 2.2, the mortality is 0.7/100,000 cases/year.

diagnosis

Pathological diagnosis should be made according to the World Health Organization classification from a surgical specimen/excisional lymph node biopsy whenever possible providing sufficient material for fresh frozen and formalin-fixed samples.

Classical Hodgkin lymphoma (cHL) includes nodular sclerosing, mixed cellularity, lymphocyte-rich and lymphocyte-depleted subtypes and represents about 95% of all HL cases. It is distinguished from nodular lymphocyte predominant Hodgkin lymphoma (NLPHL), which accounts for about 5% of all HL cases.

staging and risk assessment

Chest X-ray and a computed tomography (CT) scan of neck, chest and abdomen are mandatory as well as bone marrow aspiration and histology.

A positron emission tomography (PET) scan may be considered according to the revised response criteria.

Staging laparotomy is not recommended [II–III, A].

Full blood cell count, erythrocyte sedimentation rate (ESR) and blood chemistry including C-reactive protein, alkaline phosphatase, lactate dehydrogenase, liver enzymes and albumin are obligatory [II–III, A].

Staging is carried out according to the Ann Arbor system in consideration of B-symptoms and the risk factors listed in Table 1. Treatment is chosen according to the categories shown in Table 1 [II–III, A].

treatment plan

CHL, limited stage

Two cycles of adriamycin/bleomycin/vinblastine/dacarbazine (ABVD) are used in combination with 30 Gy involved-field radiotherapy [I, A]. In young adults, chemotherapy-only based regimens result in slightly higher relapse rates but potentially lower long-term toxicity.

CHL, intermediate stage

Four cycles of ABVD are used in combination with 30 Gy involved-field radiotherapy [I, A].

CHL, advanced stage

By default, patients up to age 60 years are treated with either eight cycles of ABVD or eight cycles of bleomycin/etoposide/adriamycin/cyclophosphamide/vincristine/procarbazine/prednisone in escalated dosage (BEACOPPescalated) followed by 30 Gy radiotherapy of residual lymphoma larger than 1.5 cm [I–II, A].

Patients older than 60 years should undergo the ABVD chemotherapy due to higher toxicity in this age group.

relapsed CHL patients

In first relapse, salvage regimens like the standard dexamethasone/high-dose ara-C/cisplatin (DHAP) protocol or the recently established ifosfamide/gemcitabine/vinorelbine/dexamethasone (IGEV) protocol, each followed by high-dose chemotherapy and autologous stem cell transplantation can be regarded as the treatment of choice [I, A].

Reduced intensity conditioning allogeneic stem cell transplantation (RIC-allo) should be considered in young, chemosensitive patients in good general condition relapsing after high-dose chemotherapy with autologous stem cell transplantation [II–III, B].

For palliative setting gemcitabine-based chemotherapy can achieve acceptable remission rates, a satisfying quality of life and prolonged survival. Novel single agents and/or regional radiotherapy may also be considered.
NLPHL, stage IA without risk factors

Thirty Gy involved-field radiotherapy alone is the standard treatment for patients in this category [III, A].

NLPHL, other stages

NLPHL treatment is identical to cHL in all stages except for stage IA without risk factors.

relapsed NLPHL patients

A localised NLPHL relapse should be treated with rituximab alone [III, B]. NLPHL patients with a more advanced relapse require more aggressive salvage therapy in combination with rituximab.

response evaluation

Response evaluation should be done after four cycles and after completion of chemotherapy or chemotherapy/radiotherapy. Physical examination, laboratory analysis and CT scans are mandatory. In studies in advanced stage patients, early PET scan after two or three cycles identified poor risk patients. Based on early PET scan further therapy might be adapted to the patient’s risk profile [II–III, B]. After completed treatment, positive PET scans may reveal persistent disease activity but false positive PET scan must be excluded.

follow-up

History, physical examination and laboratory analysis including full blood cell count, ESR and blood chemistry should be performed every 3 months for the first year, every 6 months until the fourth year and once a year thereafter [V, D].

Additional evaluation of thyroid function (thyroid-stimulating hormone) after radiation of the neck should be carried out at 1, 2 and at least 5 years [III, A]. CT scans and previously pathologic radiographic tests are performed once to confirm remission status. Afterwards they are indicated if suspicious clinical symptoms occur.

Cancer screening should be conducted regularly due to the risk of secondary malignancies.

Table 1. Staging according to the Ann Arbor system in consideration of B-symptoms and the risk factors

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Clinical stage (CS)</th>
<th>IA, IB, IIA</th>
<th>IIB</th>
<th>III A</th>
<th>III B, IVA, IVB</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>L</td>
<td>L</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At least three involved lymph node areas</td>
<td>I</td>
<td>I</td>
<td>A</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>High ESR</td>
<td>I</td>
<td>I</td>
<td>A</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Large mediastinal mass</td>
<td>I</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Extramedullary disease</td>
<td>I</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td></td>
</tr>
</tbody>
</table>

Definitions: ESR, erythrocyte sedimentation rate; L, limited; I, intermediate, A, advanced.

High ESR: >50 mm/h without B-symptoms, >30 mm/h with B-symptoms.

Large mediastinal mass: more than one third of the horizontal chest diameter.

B-symptoms: fever, night sweat, weight loss.

note

Levels of evidence [I–V] and grades of recommendation [A–D] as used by the American Society of Clinical Oncology are given in square brackets. Statements without grading were considered justified standard clinical practice by the experts and the ESMO faculty.

literature