Lecture 8 in hematology by Dr. Alaa F. Alwan

Hodgkin's lymphoma

Hodgkin's lymphoma described by Thomas Hodgkin in 1832. .

EPIDEMIOLOGY

In the United States, three to four new cases of HL are diagnosed in 100,000 people each year. The age distribution frequency is bimodal, with one peak occurring at 15–30 yr, followed by a second peak in older patients. The incidence of HL has increased in recent years. There is a slight male predominance and, in addition, an increased risk of the disease is associated with higher socioeconomic status.

ETIOLOGY

The etiology of HL remains unknown, associated with Epstein-Barr virus .giant Reed-Sternberg cells are pathognomonic for HL,

CLINICAL FEATURES

The typical presentation of HL is an indolent enlargement of a lymph node or of several lymph nodes, most often at the neck and less frequently at the axillae. Although any lymphatic region can be affected, inguinal or femoral lymph nodes are involved in less than 10% of the cases as the only disease localization. A typical manifestation of the disease is a mediastinal enlargement that may cause dyspnea or no symptoms, which is only discovered on a routine chest X-ray. Abdominal lymph nodes and the spleen may be enlarged, causing abdominal discomfort, or may be discovered only during staging procedures. Solid organs like the lung or the liver may be involved, generally indicating disseminated disease, but may also be infiltrated by direct extension from a lymphatic mass. The bone marrow is involved in less than 5% of unselected patients. Involvement of the central nervous system is rare at the time of diagnosis and usually occurs only in late progressive disease. Patients may have B-symptoms, especially in advanced stages (night sweats and unexplained fever, which may be of the Pel-Ebstein type, and weight loss of >10% within 6 mo). An unusual (<2% of cases) but typical symptom is pain in the enlarged lymph nodes or involved tissues felt after the ingestion of alcohol. More often (in about 10% of cases), patients experience nonspecific pruritus.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS, STAGING OF HL

If a suspicious lymph node is larger than 2 cm in diameter or smaller lymph nodes persist for more than 4–6 wk, or if B-symptoms or other signs suggest malignant lymphoma, the lymph node should be biopsied without delay. If no clear diagnosis can be made, the biopsy should be repeated, whenever possible, on a peripheral node.

The differential diagnoses

1. NHL
2. reactive processes, such as toxoplasmosis or virus like infectious mononucleosis.

If the diagnosis is HL, then the exact stage has to be determined (staging) Other staging procedures may also be useful. For example, magnetic resonance tomographies may also detect an enlarged spleen or abdominal lymph nodes. Lymphography is a sensitive, but invasive, method to detect abdominal lymph nodes and has been abandoned by most centers. In some situations, positron emission tomography (PET) using fluorodeoxyglucose has been found useful for the staging and follow-up of patients with HL. PET is sensitive and, in most instances, specific enough to detect involvement by HL.

The Reed-Sternberg cells (large lobulated, multinucleated cells with prominent nucleoli) are generally considered to be a part of the tumor cell population found in the affected tissues along with stroma cells, reactive lymphoid cells, eosinophils, and neutrophils. As already mentioned, Reed-Sternberg cells belong in most cases to the B-cell lineage. Marker analysis reveals them to be positive for CD30, frequently positive for CD15 and for CD25, and negative in most cases for CD45 and for CD20.

CLASSIFICATION

a. *Nodular lymphocyte-predominant HL* 5% (CD 20 positive)
b. *Classical HL:95% (CD15 positive, CD 30 positive)*

1. Lymphocyte-rich HL 5–8%
2. Nodular-sclerosis HL 35–55%
3. Mixed-cellularity HL 20–35%
4. Lymphocytic-depletion HL 3–4%

The frequency of these subtypes differs in different parts of the world. At present, with effective treatments for HL, the subtypes are no longer prognostically relevant. However, some of these types have particular clinical features: nodular sclerosis is more frequent in young women with a large mediastinal mass. The lymphocyte-predominant HL resembles a low-grade, B-cell lymphoma, and can be treated with limited irradiation at least in early stages.

Staging Procedures for Hodgkin's Lymphoma

Clinical examination, Complete laboratory status (including lactate dehydrogenase, complete blood count, ESR , C-reactive protein, alkaline phosphatase), Chest X-ray

CT scan of thorax, abdomen, and neck

Ultrasound of abdomen

Positron emission tomography imaging (PET-CT scan) (in selected circumstances)

Bone marrow biopsy, Liver biopsy (if liver involvement is suspected

Clinical Stages of Hodgkin's Lymphoma
(Ann Arbor Classification 1971, Cotswold Modification 1990)
Stage I : Involvement of one lymphatic area on one side of the diaphragm or of a single extra-lymphatic site (IE)
Stage II : Involvement of two or more lymphatic areas on one side of the diaphragm
Stage III : Lymphatic involvement on both sides of the diaphragm
Stage IV: Diffuse involvement of solid organs(s) or bone marrow and/or lymphatic involvement
The letter A or B is indicated for all stages: A, no general symptoms; B, general symptoms (night sweats, fever, weight loss of >10%;
The letter E indicate localized extra-nodal involvement of a solid organ.
The letter X indicates a mass of >10 cm in diameter or a mediastinal mass less than one-third of the thoracic diameter is

Treatment
Chemotherapy ABVD (A = adriamycine, B= bleomycine, V= vinblastin, D=Dacarbazine)and radiation

LATE EFFECTS OF TREATMENT
1. Hypothyroidism, which may require treatment by thyroid hormones.
2. Cardiovascular disease, radiation pneumonitis and pericarditis.
3. Lung fibrosis from radiation plus bleomycin.
4. Sterility due to radiotherapy (80%).
5. A rare (<0.5%) but serious second cancers e.g acute myelogenous leukemias (increased risk within 3–8 yr), myelodysplastic syndromes, NHLs, and various solid tumors.