Lymphoid Neoplasms — Types and Staging

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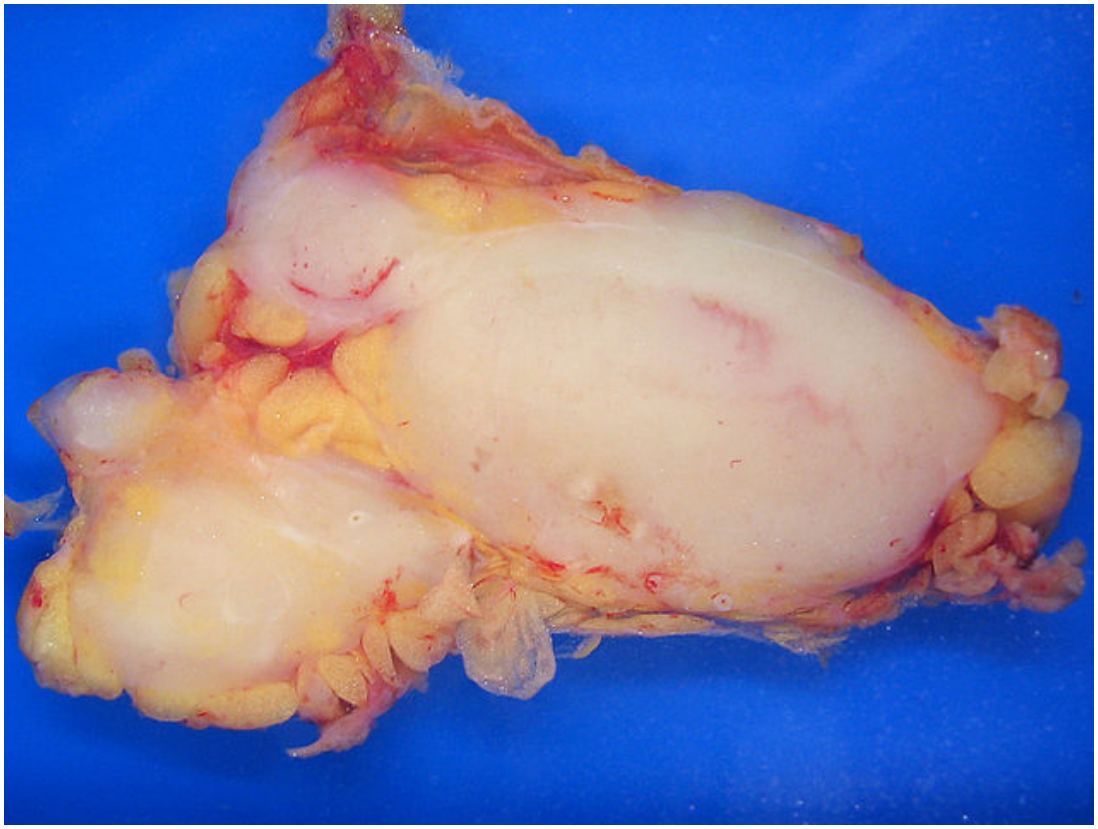
Lymphoid neoplasms are divided into two main groups: Hodgkin and Non-Hodgkin Lymphomas. The former ones are the most curable due to the specific pathogenesis of the ailment and recent advance in the methods of treatment (5 years survival for the patients with favorable prognosis 98 % and 85 % with a less benign one). The malignant cells form in the lymphatic system; mainly, they are represented by white blood cells, namely, immature B-lymphocytes. HL may take place in any part of the lymphatic system. This disease was described by Dr. Thomas Hodgkin in 1832 as a type of cancer of the lymph nodes.



Introduction

Hodgkin lymphoma (HL), previously called Hodgkin disease, is a cancer of B-cells that has unique clinicopathologic features and histological composition, hence separated from other lymphomas. It contains pathognomonic Reed-Sternberg cells, having a mirror image (owl’s eye) nuclei, within an inflammatory background.

Epidemiology

Hodgkin lymphoma makes up around 10% of all lymphomas. Its incidence in Europe and the United States is around 2-3 cases per 100,000 persons. The incidence of Hodgkin lymphoma has a bimodal distribution with the first peak in young adults (15-30 years) and the second peak in older adults (>55 years). It is also more common in males except for the nodular sclerosing subtype, which is more common in young females. The Epstein-Barr virus infection also increases the probability of contracting HL.

Clinical Presentation

The Hodgkin lymphoma most commonly presents with **painless, non-tender, rubbery, lymphadenopathy**, typically involving the neck. These persons often have constitutional symptoms (called B-symptoms) such as:

- Weight loss (unexplained loss of >10% of body weight over the past six months)
- Drenching night sweats.
- Fever of unknown origin.

The fever is often intermittent, more pronounced in the evening and night time, and becomes continuous later on. Less often, few people exhibit a characteristic periodic fever called **Pel-Ebstein fever**, in which fever occurs for 1-2 weeks followed by 1-2 weeks of afebrile periods. Apart from these symptoms, the patient may also present with the following clinical features:

- A cough, shortness of breath, chest pain.
- Skin itchiness (pruritus)
- Back and joint pain
- Hepatosplenomegaly
- Engagement of Waldeyer ring (back of the throat, including the tonsils), occipital or epitrochlear areas
- Superior vena cava syndrome and acute respiratory distress (in cases of massive mediastinal lymphadenopathy)
- Paraneoplastic syndromes, including cerebellar degeneration, neuropathy, Guillain-Barre syndrome or multifocal leukoencephalopathy.

Subtypes

The Hodgkin lymphoma is subdivided into multiple sub-types depending upon the histological characteristics, clinical features, and prognosis.

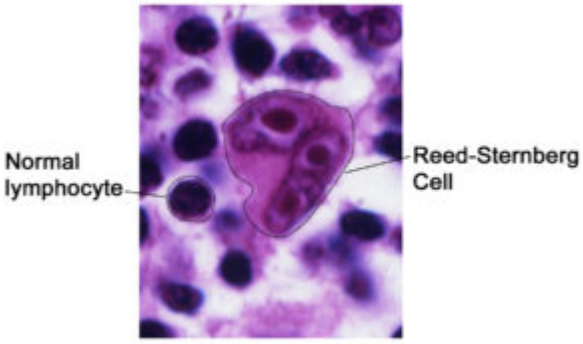
Nodular sclerosis Hodgkin lymphoma	• Most common sub-type • Accounts for 60 to 70 percent of all HL cases • Most commonly diagnosed in young females aged 15 to 34 years • Has nodular growth with scar bands, and rare RS cells • Good prognosis with high cure rates
Mixed cellularity Hodgkin lymphoma	• The second most common sub-type • Accounts for 15 to 30 % of all HL cases • Common in older people and people with immune system disorders, such as HIV/AIDS

Lymphocyte-depleted Hodgkin lymphoma	• Accounts for approx. 4 % of all HL cases • Less number of normal-appearing lymphocytes and high number of RS cells • Poor prognosis as compared to other sub-types
Lymphocyte-rich Hodgkin lymphoma	• Contains a large number of normal-appearing lymphocytes • Very good prognosis

In general, the prognosis of Hodgkin lymphoma is good if there are large numbers of normal-appearing cells and a less number of Reed-Sternberg cells.

Diagnosis

The histologic examination, usually of an excisional lymph node biopsy, is necessary to diagnose Hodgkin lymphoma that demonstrates pathognomonic malignant Reed-Sternberg cells or their variants. These cells contain mirror-image nuclei giving an “owl’s eye” appearance.



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Bone marrow biopsy is indicated in advanced stages of the disease or any abnormality on the complete blood count that is suspicious for bone marrow involvement. Lumbar puncture and magnetic resonance imaging are informative in the cases of CNS involvement

Laboratory studies

- Complete blood counts (in order to detect anemia, lymphopenia, neutrophilia or eosinophilia)
- Erythrocyte sedimentation rate
- Test for HIV, Hepatitis C, and B
- Lactate dehydrogenase
- Serum creatinine
- Alkaline phosphatase

Imaging studies

CT scans of the chest, abdomen, and pelvis (used in order to detect abnormal findings include enlarged lymph nodes, hepatomegaly and/or splenomegaly, lung nodules or infiltrates, and pleural effusions)

Positron emission tomography is informative in diagnostics of initial stages of the disease.

Staging

The clinical staging of Hodgkin lymphoma is done after confirming the diagnosis to measure the extent of the disease, prognosis and guide treatment. Staging in Hodgkin lymphoma is done according to the Ann Arbor staging system which is as follows:

Stage I: Involvement of a single lymph node region (I) or of a single extra-lymphatic organ or site (IE).

Stage II: Involvement of two or more lymph node regions on the same side of the diaphragm alone (II) or with the involvement of limited, contiguous extra-lymphatic organ or tissue (IIE).

Stage III: Involvement of lymph node regions or lymphoid structures on both sides of the diaphragm (III) which may include the spleen (IIIS) or limited, a contiguous extra-lymphatic organ or site (IIIE) or both (IIIES).

Stage IV: Diffuse or disseminated foci of involvement of one or more extra-lymphatic organs or tissues, with or without associated lymphatic involvement.

All stages are sub-classified to indicate the absence (A) or presence (B) of one or more of the constitutional symptoms i.e. significant unexplained fever, night sweats, or unexplained weight loss.

International Prognostic Score

The International Prognostic Score (IPS) is one of the strongest predictors of prognosis for patients with Hodgkin lymphoma. It can be easily calculated in the clinical setting and is based upon the following seven characteristics:

- Male gender
- Age >45 years
- Hemoglobin <10.5 g/dL
- WBC count ≥15,000/mcL
- Absolute lymphocyte count <600/mcL and/or <8% of the total WBC count
- Serum albumin <4 g/dL
- Stage IV disease

In IPS, one point is given for each of the above characteristics and the total score may range from zero (very good prognosis) to seven (poor prognosis).

Management

The treatment of Hodgkin lymphoma depends on its staging, sub-type, general health and age of the patient and complete blood counts. For example, the 5-year survival rate of stage I-A nodular sclerosis HL is >90%, while the 5-year survival rate of stage IV-B lymphocyte depleted HL is <40%. The management options are induction chemotherapy, radiation therapy, salvage chemotherapy, and hematopoietic stem cell transplantation.

Early-stage Hodgkin lymphoma:

- Chemotherapy (two to four cycles of ABVD containing Adriamycin (doxorubicin), bleomycin, vinblastine, and dacarbazine)
- Radiotherapy

Advanced stage Hodgkin lymphoma

- Chemotherapy (ABVD for up to eight cycles)
- Other combinations of chemotherapy:
    - ChlvPP – chlorambucil, vinblastine, procarbazine, and prednisolone
    - Stanford V – mustine, doxorubicin, vinblastine, vincristine, bleomycin, etoposide, and steroids
    - BEACOPP – bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine, and prednisolone
    - GemP – gemcitabine, cisplatin, and prednisolone
    - ESHAP – etoposide, prednisolone, cytarabine, and cisplatin
- Radiotherapy
- Steroids

Recurrent lymphoma or unresponsive to the treatment HL

- Bone marrow/stem cell transplantation
- BEAM chemotherapy

Review Questions

The correct answers can be found below the references.

1. A 23-year-old man presents to you with progressive fatigue and weight loss. He also noticed some swellings in his neck that are painless. He also feels “a frog in the throat” and difficulty with swallowing, which he finds painful. His sibling (sister) 19-year-old has recently undergone treatment for Hodgkin’s lymphoma. His CBC revealed anemia. What is the most probable primary diagnosis for the condition described above?

A. Hodgkin’s lymphoma
B. Non-Hodgkin’s lymphoma
C. Syphilis
D. Infectious mononucleosis
E. Leukemia

2. A 20-year-old woman presents with fever, cough and chest pain for the last 2-3 weeks. On examination, there is cervical and axillary lymphadenopathy. The biopsy of the most enlarged cervical lymph node revealed large binucleate cells, resembling owl’s eye. What is the most probable diagnosis?

A. Syphilis
B. Tuberculosis
C. Flu
D. Hodgkin’s lymphoma
E. Streptococcal pneumonia

3. What viral infection, accompanied by hepatosplenomegaly, may become a predisposing factor for the development of Hodgkin’s lymphoma?

A. Coxacci virus

B. Epstein –Barr
C. Mononucleosis
D. Hepatitis C
E. HIV

References

Adult Hodgkin Lymphoma Treatment (PDQ®)–Patient Version via cancer.gov

LYMPHOMA (a part of the group of tumors of the hematopoietic and lymphoid tissues). Lecture in internal medicine for IV course students via http://dspace.univer.kharkov.ua

Epidemiology and etiology of Hodgkin’s lymphoma via watermark.silverchair.com

Hodgkin Lymphoma via emedicine.medscape.com

Hodgkin Lymphoma Differential Diagnoses via emedicine.medscape.com

Treating Classic Hodgkin Lymphoma, by Stage via cancer.org

Correct answers: 1A, 2D, 3B

Notes