# Lymphomas

Learning objectives

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# :Hodgkin's disease(HL)

8-Hodg

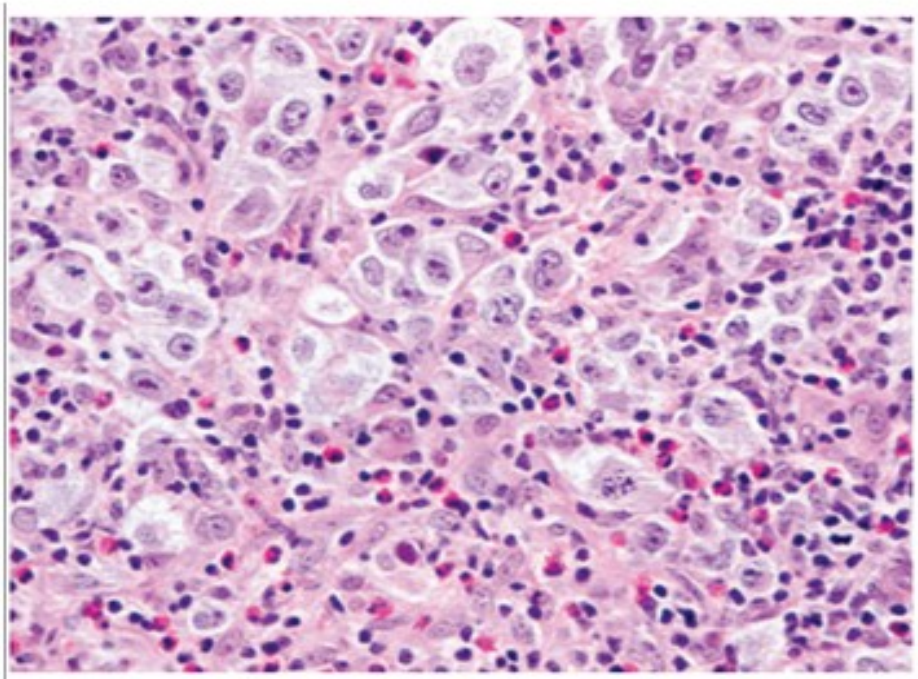

**FIGURE 197-1 Nodular sclerosing Hodgkin's lymphoma.** This figure shows a typical case of classic nodular sclerosing Hodgkin's lymphoma with many lacunar cells, occasional diagnostic Reed-Sternberg cells, and the characteristic background of lymphocytes and eosinophils. *(Photomicrograph courtesy of Randy D. Gascoyne, MD, British Columbia Cancer Agency.)*

Histologically the hall mark of hodgkins disease is the presence of reed-sternberg cells, which are large malignant lymphoid cells of B-cell origin.

These cells are often present in small numbers surrounded by normal T-cells, plasma cells and eosinophils.

According to the appearance of reed-sternberg cells and surrounding reactive cells, hodgkins disease classified into:

A-Nodular lymphocyte – predominant HL.

B. Classical HL

1- Lymphocyte – rich.

2- Nodular seclerosing (peak during young age and seen commonly in women).

3- Mixed cellularity (Peak in olderly).

4- Lymphocyte depleted (rare).

# Epidemiology:

1- Incidence about 4 new cases/ 100.000 population/ year.

2- Slight male excess (1.5:1).

3- First peak of disease in 20-35 and second peak in 50-70 age group.

## Risk factors:

1- Inherited immuno deficiency disease (klinefelters syndrome, ataxia telengectesia).

2- Acquired immunodeficiency diseases (HIV-I, hypogamma-globulinemia).

3- Auto immune disease (sjogren's syndrome, celiac disease, RA and SLE).

4-Chemical and drugs (phenytoin).

5-Infection such as (EB virus, HTLV-I, HIV, HCV, H. pylori, human herpes virus. 8).

## Clinical features:

1- Painless rubbery lymphadenopathy, usually in the neck or supraclavicular fossa, the lymph nodes may fluctuate in size.

2- Asymptomatic large mediastinal masses or may cause dry cough and some breathlessness.

3-Hepatosplenomegally may be present (not always indicate disease).

4-Extranodular involvement such as bone, brain, skin involvement is rare.

## Investigation:

1- Full blood count: may be completely normal, anaemia may be present together with lymphopenia which is a bad prognostic feature. Eosinophilia or neutrophilia may be present.

2- ESR may be raised.

3- Liver function may be abnormal in the absence of disease or during hepatic involvement. An obstructive pattern may be caused by nodes at the portahepatis.

4- LDH may be raised which is a bad prognostic factor.

5- CXR.

6- Renal function test should be normal prior to therapy.

7- CT to chest and abdomen which may replace Laparotomy (bulky disease greater than 10 cm in a single node is an adverse prognostic feature).

8-Lymph node biopsy (surgically or needle biopsy).

Staging of hodgkin's disease (Ann Arbor Staging):

1- Stage I: involvement of a single lymph node region or extralymphatic site.

2- Stage II: involvement of two or more lymph nodes regions or an extralymphatic site and lymph node regions on the same site of the diaphragm (above or below).

3- Stage III: involvement of lymph node regions on both sides of the diaphragm with or without localized extralymphatic involvement or involvement of the spleen or both.

4- Stage IV: diffuse involvement of one or more extralymphatic tissue example liver or bone marrow.

Any of these stages may not be associated with symptoms (stage A) or associated with symptoms such as weight loss, fever with temperature > 38 C° or recurrent night sweat (stage B).

## Management;

1- Radiotherapy, good results are obtained in localized stage IA or stage IIA. Smoking may increase the risk of lung cancer after lung irradiation. Fertility preserved after radiotherapy.

General indications for radiotherapy:

- Stage I disease.
- Stage IIA disease with three or less areas involved.
- Bulk disease after chemotherapy.
- Serious pressure problem.

2- Chemotherapy. Chemotherapy used in whole patient with B symptoms and in stage II disease with more than three areas involve in addition to stage III and stage IV.

The original MOPP regiemen (nitrogen mustard, vincristine (oncoviene), prednisolon and procarbazine) this drug given on an outpatient basis every 3-4 weeks for a total of 6-8 cycle. Treatment response is assessed clinically and by CT. This type of chemotherapy carries a high risk of inducing permanents infertility in men, myelodysplasia and acute leukaemia  can occur 5-10 years after alkaylating therapy.

ABVD (Doxorubicin, Bleomycin, vinblastine, and Dacarbazine) can be used, this line of treatment have a less severe side effect than the previous medication with a more and long term disease .free survival (about 70%)

**Note**: unusual manifestation of hodgkins disease include  itching, skin disorders such as erythema nodosa and icthysiform atrophy, paraneoplastic cerebellar degeneration, nephritic syndrome, immune haemolytic anaemia and thmorbocytopenia, .hypercalcemia, and painful lymph nodes on alcohol ingestion

**Note**: differential diagnosis of lymph node biopsy finding include inflammatory process, mononucleosis, non hodgkins lymphoma, .other malignancy

## Prognosis:

1- > 90% of stage IA cured by radiotherapy.

2- 70% of stage IIA cured by chemotherapy.

3- Primary failure to chemotherapy may achieve long term survival after high- dose chemotherapy.

4- Failure or relapse after radiotherapy respond well to chemotherapy with an increased risk of long-term toxicity.

5- Relapse within or after year respond to high-dose chemotherapy and autologous stem cell.

## Non hodgkins lymphoma(NHL):

Monoclonal proliferation of lymphoid cells. NHL may be of B-cell origin (70%) or T-cell origin. A large number of classification system reflect the difficulties in its classification. REAL classification has introduced phenotypic, molecular, cytogenetic and morphologic classification of the disease.

Clinical grading as high grade NHL which characterize by high proliferation rate, rapidly produces symptoms, fatal if untreated but potentially curable and low grade NHL which has a low proliferation rate, a symptomatic for many months before presentation with indolent course is not curable by conventional therapy .

# Epidemiology:

1- Incidence 12 new cases/ 100.000 people/ year.

2- Slight male excess.

3- Median age 65-70 years.

4- Aetiology: no single causative abnormality describe, however it may associate with HIV infection, EBV, HHV 8 and HTLV infection, H. pylori infection, chromosomal lesion such as (14:18) and in immune deficiency state or immune suppressed patient during post transplantation.

## Clinical feature:

1- NHL is often widely disseminated at presentation.

2- Lymphoid enlargement may be associated with systemic upset (weight loss, sweats, fever and itching).

3- Hepatosplenomegaly may be present.

4- Extranodal disease is more common especially in T-cell disease.

5- Bone marrow involvement is more common in low grade (50-60%) compared to high grade (10%).

6- Compression syndromes may occur such as superior vena cava obstruction and spinal cord compression.

The same staging system is used for both HD and NHL but NHL is- more likely to be stage III or IV at presentation

## Investigation:

The same investigation as for HD but in addition the following test should be performed:

1- Routine bone marrow aspirate and biopsy.

2- Immune phenotyping of surface antigens to distinguish T and B cell tumors.

3- Immunoglobulin determination (IgG or IgM associated lymphomas) which serve as a markers for treatment response.

4- Serum uric acid level.

5- HIV testing.

Bad prognostic features in NHL (high risk scores):

1- Age ≥ 60 years.

2- Serum LDH level elevated.

3- Poor performance status (concomitant disease).

4- Ann. Arbor stage III or IV (advanced stage).

5- > than one site of extra nodal involvement.

Factors determine line of management:

1- Age of the patient.

2- Concomitant disease.

3- Histological grade.

4- Staging of the disease.

5- HIV status.

6- Patients wishes.

## Management:

Low grade NHL:

1- Asymptomatic patient may not require therapy.

2- Symptomatic patient including systemic symptoms, lymphadenopathy causing discomfort or compression, bone marrow failure are indication for treatment which include:

a- Radiotherapy for localized stage I disease.

b- Chemotherapy: oral therapy with chlorambucil is well tolerated or more intensive intravenous chemotherapy for younger patient (neither therapy will cure patients).

c-Monoclonal antibody therapy: used as a carrier to deliver cytotoxic drugs or radiotherapy or to induce direct tumour cell apoptosis. Clinical response seen in up to 60% of patients it may be used with other standard chemotherapy.

d- Transplantation: Autologus stem cell transplantation are in progress.

## High grade NHL:

These patients need treatment at initial presentation:

a- Chemotherapy > 90% will need I.V combination chemotherapy.

The CHOP regimen (cyclophosphamide, Doxorubian, vincristine and prednisolon) remains the standard therapy.

b- Radiotherapy for stage I without bulky disease, residual site of bulky disease after chemotherapy and for spinal cord or other compression syndromes.

c-Transplantation. Autologus stem cell transplantation may be beneficial at first relapse. Transplantation can be used in lymphoblastic lymphoma which is an aggressive lymphoma which affect predominantly young adult which should be considered after response to initial chemotherapy (relapsed chemosensitive disease).

d- Monoclonal antibody therapy can be used in combination with chemotherapy (rituximab) which increases the complete response rates and improves overall survival.

The combination of R-CHOP is currently recommended for those with stage II or greater diffuse large cell lymphoma as first line therapy.

**Note**: of all cases of NHL, 85% are either high grade diffuse large cell NHL or low-grade follicular NHL. Other forms of NHL, including mantle cell lymphoma and malt lymphoma, are less common.