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Diagnosis of Hodkin's Disease

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1. Introduction

→In Hodgkin's lymphoma ,cells in the lymphatic system grow abnormally and may spread beyond lymphatic system. As Hodgkin's lymphoma progresses it compromises body's ability to fight infection.[1]

→ Hodgkin's lymphoma is characterized by the orderly spread of disease from one lymph node group to another and by the development of systemic symptoms with advanced disease. When Hodgkin's cells are examined microscopically, multinucleated Reed–Sternberg cells (RS cells) are the characteristic histopathology finding.[1]

2. Discussion

Causes

- The cause of Hodgkin's lymphoma is not known. Hodgkin's lymphoma is the most common among the people around 10 to 35 years and 50 to 70 years.[2]
- Past infection with Epstein Barr Virus [EBV] is thought to Contribute to some cares.[2]
- Persons with HIV infection are at high risk.[2]
- It is a disease of Lymph adenomatous system, but one having features'sui generis. It has some resemblances to malignant growth in that the process may extend beyond the lymph nodes in which it originated and invade adjacent tissue and organs, such as the lungs and pleasure and also may produce lesion not unlike metastases in the distant spleen.[3]

Diagnosis

Ultra sound

Lymph nodes were considered pathologic in their longitudinal or transverse maximum dimension exceed 10mm. The spleen was considered pathologic if it was enlarged if it had an inhomogeneous structure or if both factor were present. In normal sieged spleen, any infiltrate of decreased echo in tenety was considered to the suspicious of Hodgkin's involvement.[4]

CT scan

CT scans can show up enlarged lymph nodes in the body. If you have already had a CT scan as part of your tests to diagnose Hodgkin lymphoma you won't need to have another one. But if your lymphoma was diagnosed by biopsy you may need to have a CT scan to see whether you have enlarged lymph glands in other parts of the body. CT scanners take a series of X-rays of part of your body and feed them into a computer to make a detailed picture. You may be asked to drink a liquid called a contrast medium before the scan. This helps to make the gut show up more clearly. But it may cause diarrhea afterwards. There is more about having a CT scan in the cancer tests section.[8]

PET scan

Your doctor might suggest a PET scan to try to tell whether an enlarged lymph node is scar tissue or lymphoma. A lymph node can sometimes be enlarged because of past infections. For a PET scan you have an injection into a vein of a mildly radioactive substance. Cells that are active take up the radioactivity and show up on the scan. Lymph nodes that are swollen due to past infections are not active and do not show up on the scan. Lymphoma cells do take up the radioactivity. [8]. PET scans are also sometimes used during or after lymphoma treatment. If it looks as though there are still enlarged nodes after your treatment, a PET scan may be able to show whether this is left over scar tissue or whether there are still live lymphoma cells there. There is information about having a PET scan in the cancer tests section

PET-CT scan

A PET-CT scan is a combination of a PET scan and a CT scan. It takes CT pictures of the structures of your body. At the same time, a mildly radioactive drug shows up areas of your body where the cells are more active than normal. The scanner combines both of these types of information. This allows your doctor to see any changes in the activity of cells and know exactly where the changes are happening. PET-CT scans are often used during or after your treatment. There is more information about PET-CT scans in the cancer tests section.

BIOPSY

It is the accomplished most satisfactory by the complete removal of a peripheral lymph node. Partial removal of lymph node is hazards because the capsule is released and local spillage and infiltration may occur. Aspiration biopsy is comdemned,it may afford evidence to pathologist that the lession is lymphomatous[6].Laparoscopy is done if the suspious peripheral lymph node do not exist

Lymphangiographic Method

- The radiographic visualization of chest and bones medical survey by physical examination, blood counts and bone marrow study and liver. A minor surgical procedure known as lymphangiography may change the clinical staging of Hodgkin's disease from stage 1 to stage 2
- Using a tiny number .10 polyethylene catheter inserted into an intratatarsal,made visible by a blue dye, a radiograph liquid called Ethiodal is slowly injected by a small lumphoangiogram pump. When the radiographic

procedure reveals a more advanced stage of the disease is diagnosed[7]

Immunologic Markers:

The tumor necrosis factor receptor (TNFR) family member CD30 has been identified as a cell surface antigen expressed on Hodgkin's and Reed Stenberg cells.[9,10] HD tumor cells show constitutive nuclear factor (NF)- B activity as their characteristic feature, suggesting a role for NF- B in the pathogenesis of HL. Development of novel therapies and study of the pathophysiology of this disease requires a reliable tool for the diagnosis of HL derived from both B and T cells. Despite the diversity in clinical manifestations of HL, strong and constitutive NF- B activation is a unique and common characteristic of HL cells in patients [11]. elevated serum levels and expression of IL- 6 with unfavorable prognoses, as well as associating advanced stage and presence of 'B' symptoms with poor survival[.12,13] Although expression of mCD83 by Hodgkin's cells has been reported [14] little is known concerning its expression by other malignant populations.

CD MARKERS:

CD20 is a trans membrane protein involved in the regulation of human B-cell growth and differentiation.[15] It has been suggested that CD20 may function as a calcium channel, thus initiating intracellular signals important for differentiation and cell-cycle progression of B lymphocytes[16] CD20 is detectable on the surface of most mature normal and neoplastic B lymphocytes. In addition, CD20 is detected in the malignant lymphocytic and histiocytic (L&H) cells of almost all HD of nodular lymphocyte predominance (LPHD) type.[17] The neoplastic HRS cells of classical HD also express CD20 with a reported frequency ranging from less than 5% to more than 50% of tumors.[18,19]

ETIOLOGY

The etiology of Hodgkin lymphoma is unknown. Infectious agents, particularly EBV, may be involved in the pathogenesis. In as many as 50% of cases, the tumor cells are EBV-positive; EBV positivity is higher with MCHD (60-70%) than with NSHD (15-30%). Almost 100% of HIV-associated cases are EBV-positive.

An epidemiologic study from Denmark and Sweden showed an increased risk of EBV-positive Hodgkin lymphoma in patients with a self-reported history of infectious mononucleosis (IM) in adolescence.[20]The average incubation time from IM to symptoms of Hodgkin lymphoma was 2.9 years.

Patients with HIV infection have a higher incidence of Hodgkin lymphoma compared with the population without HIV infection. However, Hodgkin lymphoma is not considered an acquired immunodeficiency syndrome (AIDS)-defining neoplasm.

Genetic predisposition may play a role in the pathogenesis of Hodgkin lymphoma. Approximately 1% of patients with Hodgkin lymphoma have a family history of the disease. Siblings of an affected individual have a 3- to 7-fold increased risk for developing Hodgkin lymphoma. This risk is higher in monozygotic twins. Human leukocyte antigen (HLA)-DP alleles are more common in Hodgkin lymphoma.

A study by Chang et al found that routine residential UV radiation exposure may have a protective effect against lymphoma genesis through mechanisms that may be independent of vitamin D.[21]

Pathology:

- The morphology of the Hodgkin's cell is characterized by large nuclei with several indentations and prominent nucleoli; The cytoplasm shows cluster of mitochindria,some lysosomes, short strands of rough surfaced endoplasmic reticulum, polyribosomes and fine micro fibrils
- Hodgkin's cell may be in close contact with surrounding lymphocytes. The contents of lysosomes and finger like cell protrusions have been used as arguments in favor of the histocyte-nature of Hodgkin's cells[25]

Prognosis

Hodgkin's disease is considered one of the most curable forms of cancer, especially if it is diagnosed and treated early. Unlike other cancers, Hodgkin's disease is even potentially curable in late stages Five-year survival rates for patients diagnosed with stage I or stage II Hodgkin's disease are 90 - 95%. With advances in treatment, recent studies indicate that even patients with advanced Hodgkin's disease have 5-year survival rates of 90%, although it is not yet certain if their disease will eventually return. Patients who survive 15 years after treatment are more likely to later die from other causes than from Hodgkin's disease.[22]

Survival rates are poorest for patients who:

- Relapse within a year of treatment
- Do not respond to the first-line therapy and have signs of disease progression

Staging

Ann Arbor staging system with Cotswold modifications for Hodgkin's lymphoma:[23]

a) Stage I: involvement of one lymph-node region or lymphoid structure (e.g. spleen, thymus, Waldeyer's ring).
b) Stage II: two or more lymph-node regions on the same side of the diaphragm.
c) Stage III: lymph nodes on both sides of the diaphragm.
   - Stage III (1): with splenic, hilar, coeliac, or portal nodes.
   - Stage III (2): with Para-aortic, iliac, or mesenteric nodes.
d) Stage IV: involvement of extra nodal site(s) beyond that designated E (see below).
e) Modifying features:
   - A: no symptoms.
   - B: fever, drenching night sweats, weight loss greater than 10% in six months.
   - X: bulky disease: greater than a third widening of mediastinum or greater than 10 cm maximum diameter of nodal mass.

- E: involvement of single, contiguous, or proximal extra nodal site.

Disease is further classified into limited, intermediate or advanced:[24]

a) Limited disease: up to IIB with no risk factors.
b) Intermediate disease: up to IIB with at least three involved lymph-node areas or high ESR (ESR over 50 mm/h without B symptoms, or over 30 mm/h with B symptoms; B symptoms are defined as fever, night sweat, weight loss.
c) Advanced disease:
   - Stage IIB with large mediastinal mass (more than one third of the horizontal chest diameter) or extranodal disease.
   - Any stage III or above.

3. Conclusions

The neoplastic cells of the Hodgkin's disease and the follicular lymphoma that occurred in this patient derived from a common precursor B cell. Its differentiation stage could be identified as that of a germinal center B cell. Thus, transforming events can be more important than the cell of origin in determining a disease entity.

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