Hodgkin's disease

From: Manfred Schwab <M.Schwab@DKFZ-Heidelberg.de>
To: <oma@ets.it>
Sent: Wednesday, February 09, 2000 9:08 PM
Subject: Cancer Research Enzyclopedia

Dear Dr. Tirelli,
I am currently involved in putting together a Cancer Research Encyclopedia. The core of this will consist of short (3-4 pages) mini-review type essays on a wide range of topics. I am writing to you to explore if you would be willing to contribute an essay on "Hodgkin's disease". On the basis of your expertise in the field I think this would require only minimal effort on your side. For your information I am attaching the current instructions for authors.
Sample chapters are on our homepage

http://claim.springer.de/EncRef/CancerResearch/default.htm

Publication is tentatively scheduled for summer to early autumn 2000.
This is a very important topic, and I would be extremely happy if you would be positive about this.
Hoping to hear from you soon.
With my best regards.,
Manfred Schwab
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DEFINITION: Hodgkin's disease (HD) is unique among the neoplasms derived from lymphoid tissues, i.e. malignant lymphomas. Infact, many characteristics of HD are controversial in particular the epidemiological, virological, genetical, histopathological, immunological, and biological findings. It is now clear that HD is not a single disease with variants, but rather a group of at least two diseases, namely nodular lymphocyte predominant Hodgkin's disease (nLPHD), and classic Hodgkin's disease (cHD).

CHARACTERISTICS (Clinical, molecular and cellular).

While nLPHD is a B-cell neoplasm, it is not clear whether the B-cell derived displastic cells, i.e. the L-H or popcorn cells are monoclonal or polyclonal. Moreover, it is not clear whether nLPHD should be treated in that it shows slow or no progression at all. In contrast cHD contains four histotypes, i.e. NSHD (nodular sclerosis HD), MCHD (mixed cellularity HD), LDHD (lymphocyte depletion HD), and cLRHD (lymphocyte rich HD) that require treatment because otherwise they are fatal.

Immunological and molecular biological studies of cHD at the single cell level suggest that HRS (Hodgkin's and Reed Sternberg) cells in most cases are monoclonal derivatives of late germinal center B-cells, but in few cases are derivatives of cytotoxic T-cells and although less likely of NK-cells. The major event in the pathogenesis of B-cell related cHD is the blockage of apoptotic pathway. Epstein-Barr Virus (EBV) might be involved in the postulated hindrance of the apoptotic pathway, leading to the genesis of classic HRS cells.

The essential elements for diagnosis of HD are the following:

1. lymphomegaly, single or multiple, not painful, often monostational and with variable dimensions in the time;

2. frequent presence of one or two systemic symptoms (fever, night sweats, loss of weight);

3. presence of the Reed-Sternberg cell in the lymphonodal biopsy.

Most characteristically clinical presentation of HD is a young adult discovering a asymptomatically lymphnode swelling. The enlarged lymphglande which is usually not tender occurs most widely in the neck, often sopraclavicolar fossa but it may also be discovered in the mid- or right neck or in the axilla. Another common presentation of the illness is the discovery of an anterior mediastinal mass on the routine chest radiographic examination.

Treatment of patients with HD has been one of the most significant success in twentieth century clinical medicine. This was once uniformally a fatal disease, now is curable in approximately 75% of patients at many major medical centers worldwide. The management of these patients however is often difficult and requires particular attention to details of the staging and treatment program. This is a necessarily procedure in order to obtain excellent results by keeping to a minimum the potential serious toxicities and morbidities of the therapy. Most of the serious effects of the therapy of HD are not evident for at least five-twenty years or more after treatment is completed. These might be described as problem of success, since they require many years of survival, free of HD recurrence to be recognized. As they have become evident, treatment programs have been modified in an effort to reduce their incidence and severity to a minimum. Therefore, the management of patients with HD continues to evolve. Treatment recommendations however, may differ somewhat among physicians and investigators with great experience of treatment of HD.

Therapeutic program for a patient with HD should not be initiate without definitive diagnosis of an experienced hematophatologist. Appropriate diagnostic studies and stage determination should be made before start a therapy. Almost all patients benefit from consultation with both experienced medical oncologist, or hemathologist and radiation oncologist to jointly plan a treatment program, although not all patients require both modalities, chemotherapy and radiation therapy, in their initial management. Generally, the standard recommended treatment for patients with HD depends on the stage of the disease. There are special clinical situations and settings in which the standard approach must be modified, for example in patients with HIV infection. Briefly, patients with stage IA and IIA supradiaphrammatic may be managed with full dose extend field radiation without chemotherapy. Those patients with bulky disease request management with combined chemo- and radiation therapy modality. Patients with stage IA and IIA infradiaphrammatic may be cured with radiation therapy alone. Patients with stages I and IIB are usually treated with chemotherapy alone alone or with a combined modality approach, i.e. chemotherapy and radiation therapy. Patients with

stage IIIA may be treated with a combined modality approach, while those in stage IIIB are generally treated using chemotherapy alone as in a those with stage IV. ABVD (adriamycin, bleomycin, vinblastine and dacarbazine) is the most effective single chemotherapy regimen in HD.

There are a lot of clinical problems that require the intervention of experienced medical oncologists, to dissolve in particular pulmonary infiltrates, epidural cord compression, herpes zooster, postsplenectomy sepsis. Moreover there are clinical problems after therapy including complications and late effects of the therapy, either by from radiation therapy than chemotherapy, for example sterility, second-tumors, coronary heart and lung and artery diseases from radiation therapy, ecc. Recently, in order to avoid these serious long-term side effects, any center try to use combined chemo- and radiation therapy approach with a short but intensive chemotherapy regimen in combination with limited field, low-dose radiation therapy. This approach could be successful, in order to maintain the high rate of cures decreasing the potential serious side-effects in the follow-up. Finally those patients who relapsed or become resistant may be salvaged by high dose chemotherapy with stem cell support. This approach has been shown to be able to cure a fraction of patients who otherwise will die for HD.

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