LYMPHOMAS DUE TO INFECTIOUS ORGANISMS. PATHOGENESIS, PRESENTATION AND THERAPY

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Bacterial as well as viral infections have been suspected in the etiology of lymphomas. Ebstein Barr virus (EBV), Kaposi Sarcoma herpesvirus (human herpesvirus8 – HHV8) and human T-cell lymphotrophic virus (HTLV1) are a well documented cause of lymphoid malignancies in humans and their genomes are found in the tumor cells. EBV, KSHV, HTLV1 contribute to lymphomagenesis by subverting the host cell molecular signaling machinery to deregulate cell growt and survival.

Other viral and bacterial infections are recognized to participate in the processes of lymphomagenesis but their role appears to be indirect. These include hepatitis C virus, helicobacter pylori, campylobacter jejuni, borellia burgdorferi, chlamidia psitaci.

EBV causes non Hodgkin (NHL) and Hodgkin lymphomas wich are more common in individuals with immunodeficiency.

KSHV causes primary effusion lymphomas (PEL) and lymphomas arising from multicentric Castelman's disease.

HTLV1 is the causative agent of adult T-cell leukemia/lymphoma (ATLL).

All herpes viruses (EBV, HHV8) have two main stages: latent and lytic.

During latency, latent herpesviral proteins induce cellular proliferation and protect the cell from interferon and apoptotic signals.

Antiherpesviral drugs are guanosine analogues are phosforilated by viral thymidine kinases, but the viral thymidine kinases are only expressed during lytic infection, but not in latent phase. Thus these compounds do not have any effect on latently infected cells. Attempt have been made to use these antivirals with drugs that can induce lytic replication: valproic acid, bortezomib, gemcitabine and doxorubicine.

In the case of HTLV1 the virus is integrated in the lymphoma cells and viral replication is not part of the oncogenic process, thus antiretrovirals are not usefull for the treatment of ATLL. Viral proteins expressed in specific viral lymphomas would be promising therapeutic targets. Helicobacter pylori has primarly been associated with marginal zone lymphomas including MALT lymphomas and splenic marginal zone lymphomas. The eradication of HP alone can induce complete remissions in gastric MALT lymphomas in more than 77% of cases but the response is slow.

Antibacterial therapy can be succesfull used in combination with chemotherapy even in large B cell gastric lymphomas. Borellia burgdorferi is suspected of causing primary cutaneous marginal zone lymphomas.

Treatment of the B. burgdorferi infection with antibiotics has led to the regression of early stage lymphoma.

Immunoproliferative small intestinal disease (IPSID) can also be successfully treated by eradication of campylobacter jejunii in early stages. Another bacterial infection suspected of involvement in ocular adnexal MALT lymphomas is Chlamydia psitaci. In small sample of cases treated with antibiotics the regression of lymphoma was reported.

Hepatitis C virus (HCV) is associated with development of hepatocellular carcinoma. Its role in development of B-cell lymphoma is more controversial. Prospective study of patients with marginal zone lymphoma associated with HCV has shown complete response in majority of patients concomitant with antiviral response.

Patients without anti HCV response failed to respond to this regimen.