

Case 15

A 62 year old white male presented with an inguinal lymph node swelling for 6 weeks duration. He denied fevers, chills or sweats, but admitted to a 20 pound weight loss over the last two months without any change in appetite. The patient denied HIV risk factors. Physical examination was notable for normal vital signs. Lymphadenopathy was apparent in the inguinal, axillary and cervical areas. The lymph nodes were hard, non-tender, and fixed. There were no petichiae,¹ rashes or bruises. There was organomegaly.² There were no localizing signs of infection. Hemocult exam was negative. Laboratory examination was notable for a Hgb of 8.0 gm/dl, WBC of 2,000/ μ l, and platelet count of 80,000/ μ l (pancytopenia). Coomb's test (direct and indirect)³ were negative and the reticulocyte count was 0.5% (low, given anemia). A PPD was negative and an HIV test was negative. A CT scan of the chest, abdomen and pelvis revealed generalized adenopathy including the retroperitoneum (**Fig. 1**). An excisional biopsy of an

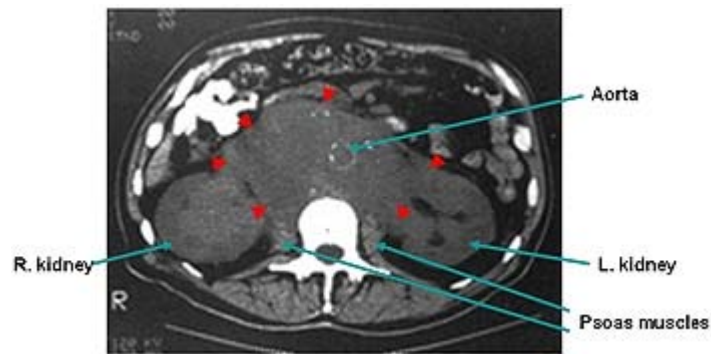


Fig. 1. Abdominal CT demonstrating evidence of massive lymphadenopathy (delimited by arrowheads) encasing abdominal aorta.

enlarged superficial lymph node was diagnostic of a diffuse large cell lymphoma (**Fig. 2**). Special stains were consistent with a B cell lymphoma. The patient was started on 6-cycles of CHOP chemotherapy⁴ and Rituximab. The patient developed mild tachycardia and rashes with

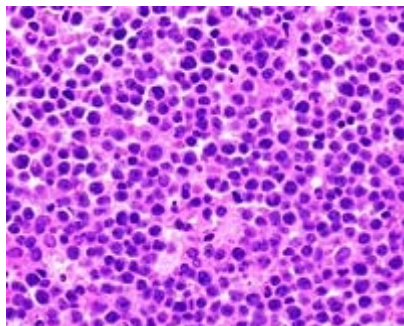


Fig. 2. Hematoxylin and Eosin stain of inguinal node biopsy. Note diffuse effacement of lymph node architecture by infiltrate of large cells with eccentric nuclei and deeply basophilic cytoplasm.

the third infusion that responded well to benedryl. Although his Hepatitis B serologies were consistent with past history of Hepatitis B, his liver function tests were normal during Rituximab therapy. The lymph node enlargement resolved and a CT scan done after the 4th cycle demonstrated near complete resolution of the abdominal lymphadenopathy. The patient's CBC⁵ normalized and follow-up CT scan after the 6th cycle demonstrated no evidence of disease. However the peripheral B cell count remained low for more than one year. Total serum levels of IgG remained normal throughout.

One year later, the patient presented with recurrent lymphadenopathy. Repeat lymph node biopsy was consistent with recurrent disease. The patient was enrolled in a clinical trial (using historical controls) designed to test the efficacy of an anti-idiotypic vaccine. The vaccine had three components: A, An immunogen consisting of a protein sequence derived from the patient's tumor-derived idiotype fused to an irrelevant protein; B, concurrent administration of subcutaneous GM-CSF, as an adjuvant; C, concurrent administration of an antibody that depleted regulatory T cells (Tregs). The patient demonstrated evidence of clinical remission.

¹punctate erythemaous macules indicative of thrombocytopenia or platelet dysfunction

²enlarged liver and spleen

³tests of antibody-mediated hemolysis

⁴cyclophosphamide, doxorubicin, vincristine, prednisone

⁵Complete Blood Count (includes WBC, Hgb, Hct, and platelet count)

Questions for Case 15

1. Why were normal peripheral blood B cells reduced for months despite normal antibody levels?
2. Which immune cells and receptors were likely to have mediated tumor shrinkage in the first few days/weeks after treatment?
3. What was the likely mechanism of pancytopenia in this case?
4. Why was it important to know the Hepatitis B serology and liver function tests during treatment with Rituximab?
5. Why is efficacy increased and toxicity decreased, in general, with humanized, rather than mouse antibodies?
6. How might treatment with Rituximab be useful for the treatment of autoimmunity?
7. What is the immunological basis for the vaccine used?
8. Why do many patients with malignancies fail to mount an effective immune response against the tumors?