

A Case of Chronic EBV-associated NK/T Cell Lymphoma.

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A 19 year old Ecuadorian male was evaluated for fever, 20 pound weight loss, recurrent sore throats and oral thrush 18 months before admission. Immunological evaluation showed lymphopenia, decreased levels of IgG2 and IgG4 with normal IgG1, IgG3, total IgG, IgM and IgA. He also had elevated ALT 1066 and AST 592, Alk Phos 384, and bilirubin (4.2). EBV Capsid IgG 12 (0-0.9), IgM 0.4 (0-0.9); EBVAB early AG 5.3 (0-0.9) and EBNA Ab 1.9 (0-0.9); PCR for EBV DNA: 46000 copies/ml. A pharyngeal biopsy showed chronic inflammation. He was treated with prednisone 60 mg daily. Attempts to decrease the dose of steroids resulted in recrudescence of his sore throats and fever, requiring steroid treatment for one year.

He was admitted 1 year later with worsening nasopharyngeal ulcerations, eyelid swelling, intermittent fever and cervical lymphadenopathy. He had elevated AST 116/ALT 155. His CD3: 58% (404), CD4: 37% (257), CD8: 20% (141), CD4/CD8: 1.8. Differential diagnosis included granulomatous disease of the upper airway (Wegener granulomatosis or Sarcoidosis) infectious or lymphoma). Initial workup showed negative cANCA, pANCA and atypical ANCA, ESR 30. Anti SM Ab, anti mitochondrial Ab, anticardiolipine, anti MPO Ab, anti Prot3 Ab and ACE were all negative. CT of the chest demonstrated an extensive mass along the tracheobronchial tree, multiple lung nodules and splenomegaly. Nasal/epiglottal biopsy and mediastinal mass/carina demonstrated necrotic material. A bone marrow was normal. Liver biopsy showed steatosis, cholestasis, portal inflammation and fibrosis and increased sinusoidal lymphocytes. Serology and cultures were unremarkable. AFB negative. EBV Capsid Ag IgG positive, IgM negative; EBNA IgG 19 (0-19), EBV Ab early AG diffuse and anti RD both 1:80. PCR for EBV 4740 copies. In-situ hybridization for Epstein Barr virus (EBER) was strongly positive in mediastinal mass and liver sinusoidal lymphocytes, consistent with chronic active EBV infection.

Leukemia/lymphoma markers were informed as normal in epiglottal tissue: 42% T cells, 12% B cells (polyclonal Kappa/lambda) and 42%NK cells. Bone marrow had no abnormal phenotype. Review of multiple biopsies showed a lymphocytic infiltrate CD2+,CD3-, CD7+, CD8+, CD16/56+ which was consistent with nasal NK/T-cell lymphoma. Liver biopsy showed chronic active EBV infection.

Since chronic EBV infection with absent EBNA AB has been described in XLP (X-linked lymphoproliferative disease), a possible immunodeficiency secondary to DSHP/SH2D1A/SLAM-associated protein SAP mutation as the causing defect was evaluated. Mutation analysis by PCR and direct sequencing of SH2D1A showed no abnormality. The patient was treated with ganciclovir, IVIG followed by three cycles of CHOP.

Conclusions:

Patients with chronic active EBV may have congenital or acquired immunological defects in CTL response against EBV, frequently developing lymphoproliferative diseases (LPD). Although most EBV-related malignancies are of B cell origin, T/NK cell lymphomas may occur. Our patient presents an unusual form of lymphoma, and also his slow course is remarkable. Treatment with steroids for a long time may have modified his clinical course. As in most cases of EBV-associated LPD, the immunological defect responsible for his inability to clear EBV infection remains unknown.