Case Report
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Nelarabine associated myelopathy: is it reversible?

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Introduction

T-cell Acute lymphocytic leukemia (ALL) is associated with central nervous system (CNS) manifestations. Severe and irreversible neurologic toxicity in the dorsal columns has been reported previously secondary to neularabine, a purine analog.[1,2] In the pivotal study of adults with relapsed T-cell leukemias, a dose dependent peripheral neuropathy was the only cited neurologic adverse event.[3] Myelopathy has been increasingly recognized, both in case reports and in a recent phase I study in children, and was found to be irreversible. We describe a case of neularabine-associated myelopathy, which reversed following allogeneic stem cell transplant.

HPI

A twenty-three year-old female with past medical history significant for precursor T-cell ALL presented with bilateral foot drop, loss of sensation in the left lower extremity, and gait ataxia. A bone marrow biopsy performed one month prior to her presentation, showed no evidence of leukemia. Review of symptoms revealed difficulty with ambulation and balance. She denied cognitive or visual deficits, fever, nausea, vomiting, or headaches. She denied recent travel or preceding viral illness.

Physical exam showed absence of vibration sense in the bilateral toes, ankles, and knees. She had decreased sensation to light touch and cold. Her gait was wide based, slow, and unstable. Romberg testing was abnormal. Deep tendon reflexes were diminished throughout. A lumbar puncture was performed to rule out CNS involvement of leukemia. Spinal studies showed clear and colorless fluid, normal protein, two nucleated cells, no red blood cells, normal glucose, and negative gram stain and culture. Oligoclonal bands were not present. Cytology and flow cytometry were negative for leukemic cells.

Laboratory studies were unremarkable, including normal B12, homocysteine, methylmalonic acid and folate levels. HIV and syphilis were negative. Initial MRI with and without contrast revealed a small hyperintense contiguous signal abnormality involving the dorsal columns of the spinal cord from T6-T12. She was initially treated with high dose dexamethasone but her symptoms progressed. She developed progressive bilateral upper extremity weakness, limb ataxia and dystonia. Repeat MRI revealed an enlarging signal in the dorsal columns involving the cervical and the thoracic spine. No spinal expansion was noted. Anti-Hu and Anti-Yo antibodies were not detected in the serum. Repeat bone marrow biopsy was performed, which did not show evidence of ALL. MRI of the brain was normal. As myelopathy progressed, a decision was made to attempt treatment with high dose decadron and plasma exchange with no neurologic improvement.

She eventually was taken to stem cell transplant from a sibling donor. At her clinic follow-up three months following her procedure, her neurologic deficits had resolved. Repeat imaging showed improvement of prior hyperintensities in the dorsal columns.

Discussion

Acute lymphoblastic leukemia is characterized by excessive and abnormal lymphocyte production in the bone marrow, and is known for its rapid progression in the absence of therapy. CNS manifestations are not uncommon and are secondary to both leukemic infiltration or as a side effect of chemotherapy. Dorsal column involvement is a distinctive presentation of myelopathy with marked functional consequences. The differential diagnosis includes drug toxicity, tapering of corticosteroids, nutritional deficiencies, infection, and paraneoplastic syndromes. In this case, that patient did not have improvement, despite reinstitution of corticosteroid therapy. B12, homocysteine, methylmalonic acid, and folate levels were normal. HIV and syphilis testing were negative. Anti-Hu and Anti-Yo antibodies were not detected, making paraneoplastic etiology unlikely. CSF sampling was also unremarkable.

T-cell ALL associated neurologic toxicity has not been previously associated with nucleoside analogs prior to neularabine. Case reports have previously described rapidly worsening transverse myelopathy associated with neularabine. In the initial phase I trial, neularabine had cumulative toxicities of the CNS in the form of hypoesthesias, parasthesias, and peripheral neuropathy.[4] They were dose dependent. All prior case reports involving neularabine toxicity have been irreversible. Our patient had the first reported regression of symptoms of neularabine toxicity following stem cell transplant. More studies and case reports are needed to better identify associated risk factors to allow for better prevention and treatment of a life limiting neurologic toxicity.

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Conflict of interest

The author declares no conflict of interest.

References

1. Papayannidis C, Iacobucci I, Abbenante MC, et al. Complete paraplegia after nelarabine treatment in a T–cell acute lymphoblastic leukemia adult patient. *Am J Hematol*. 2010;85(8):608.

2. Alsdorf W, Schmitz M, Schieferdecker A, et al. Severe and irreversible myelopathyafter concurrent systemic and intrathecal nucleoside analogue treatment for refractory diffuse large B–cell lymphoma: A case report and review of the literature. *Oncol Pharm Pract*. 2016;22(3):523–527.

3. Berg SL, Blaney SM, Devidas M, et al. Phase II study of nelarabine (compound 506U78) in children and young adults with refractory T–cell malignancies: a report from the children's oncology group. *J Clin Oncol*. 2005;23(15):3376–3382.

4. Buie LW, Epstein SS, Lindley CM. Nelarabine: A novel purine anti-metabolite antineoplastic agent. *ClinTher*. 2007;29(9):1887–1899.

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