Acute transverse myelitis and autoimmune pancytopenia after unrelated hematopoietic cell transplantation

Immune-mediated reactions in allogeneic hematopoietic cell transplantation (HCT) may affect the nervous system causing myasthenia gravis, polyneuropathy and inflammatory demyelinating polyneuropathy and the hematopoietic system causing autoimmune cytopenias. We report a case of simultaneous acute transverse myelitis (ATM) and autoimmune pancytopenia (AIP) after an unrelated HCT successfully treated with immunosuppressive therapy.

A 21-year old male was diagnosed as having refractory anemia with excess of blasts and monosomy 7 in September 1996. He was referred to our institution in July 1997 for unrelated HLA-identical HCT. Conditioning was achieved with cyclophosphamide (60 mg/kg/day × 2 days) and unfractionated total body irradiation (1200 cGy). Graft-versus-host disease (GVHD) prophylaxis consisted of cyclosporin A (CyA) and a short course of three doses of methotrexate. Trilineage engraftment was achieved on day +25. Acute grade ++ skin GVHD (clinical I) was observed on day +30 and limited cutaneous chronic GVHD on day +120: both resolved with steroid treatment. Throughout this period hematologic parameters were within the normal range and the CyA was progressively tapered off.

In the 10th month after HCT and while receiving treatment with only CyA, the patient presented with fever, mucocutaneous purura, jaundice and choriola. Physical examination revealed pallor, jaundice, hemorrhagic ulcerations on the oral mucosa and petechiae on the lower limbs. There were no evidence of chronic GVHD. Hematologic studies showed severe pancytopenia (hemoglobin: 99 g/L, white cell count 1.9 × 10⁹/L, platelets 8 × 10⁹/L) and a reticulocyte count of 18%. Serum biochemical investigation demonstrated hemolysis: bilirubin: 0.02 g/L, LDH 50 U/L, haptoglobin 0.084 g/L. The direct Coombs’ test and indirect antiplatelet antibody test were positive. An antineutrophil antibody test was not conclusive. The remaining biochemical parameters were within the normal range and all other autoantibodies tested were negative. Bone marrow aspirate and trephine revealed normocellularity and erythroid hyperplasia without dysplastic features. Cytogenetic analysis showed a normal 46,XY karyotype and chimerism studies revealed complete donor hematopoiesis. Multiple microbiological cultures, virological studies (CMV, Epstein-Barr, herpes simplex, varicella zoster, HIV-1, hepatitis B and C, parvovirus B19 and HTLV-1) and VDRL serology were negative.

Over the following days the patient developed paraparesis and sphincter control loss, without upper limb or cranial nerve symptoms. Neurological examination revealed weakness of the lower limbs with preserved tendon reflexes, and sensory loss below T7 including a decrease in proprioceptive sensation. Neurophysiologic studies showed no peripheral nerve damage and normal somatosensory responses in the upper limbs. Somatosensory evoked potentials from the lower limbs were, however, of low amplitude and very slow. Cerebrospinal fluid studies were normal. Magnetic resonance imaging showed a hyperintense intramedullary lesion in T2-weighted images at the level of the T7 vertebral body (Figure 1).

Table 1. Cases of autoimmune pancytopenia (AIP) reported in the literature. Case 4* only bicytopenia (anemia + thrombocytopenia).

Delayed immune reconstitution, T-cell depletion, thymic damage, chronic GVHD and CyA therapy are well-known causes of multifactorial immune dysregulation after an HCT.

True autoimmune diseases after HCT are uncommon. Autoimmune thyroiditis, myasthenia gravis and isolated monocytopenias are the most frequently described. AIP is exceptional and only three cases before this have been reported.

As far as concerns the etiology of the pancytopenia, histologic, cytogenetic and chimerism bone marrow studies excluded graft rejection, poor engraftment, bone marrow aplasia by CMV or drugs and relapse as being responsible. The evidence in favor of an autoimmune origin includes the positive direct Coombs’ and indirect anti-platelet tests as well as the rapid response to immunosuppressive therapy.

Immune-mediated reactions may also affect the nervous system causing myasthenia gravis, polymyositis and inflammatory demyelinating polyneuropathy. ATM, to our knowledge, has been reported after HCT in only two patients. We think it is possible to speculate that these patients had an autoimmune basis to their ATM as their clinical course paralleled the pancytopenia and they had an excellent response to steroids.

In summary, AIP is a life-threatening late complication of HCT frequently associated with other autoimmune phenomena. Preliminary analysis suggests a higher incidence of neurological pathologies in these cases (Table 1).

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