NOTE

Aplastic Anemia during Growth Hormone (GH) Treatment in a Girl with Idiopathic GH-Deficiency

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Abstract. We report a 12-year-old girl with aplastic anemia accompanied by chromosome 8 trisomy during growth hormone (GH) therapy. When she was six years old she was diagnosed as idiopathic isolated GH deficiency, and GH therapy (0.175 mg/kg/week) was initiated. At the age 12, she began to exhibit petechiae in both lower limbs. Platelet count was 11,000/μL; serum hemoglobin level 11.8 gr/mL; white blood cell count 3,400/μL, with 37% neutrophils, 58% lymphocytes, 4% monocytes and 1% basophils. Bone marrow examination showed that total nucleated cell count and megakaryocyte were 17,000/μL and 0/μL, respectively, suggesting low formation. In addition, 13% of bone marrow cells contained the 3 signals of chromosome 8 marker (trisomy 8). She was diagnosed as aplastic anemia accompanied with chromosome 8 trisomy. GH therapy was stopped immediately, and simultaneous administration of methylprednisolone and anti-thymocyte globulin was initiated. Platelet count improved with treatment, and the 3-signal chromosome 8 abnormality disappeared from the bone marrow cells. The fact that a hematological adverse effect other than leukemia exists in conjunction with GH therapy warrants further investigation into possible hematological changes occurring during or after GH therapy.

Key words: Growth hormone, GH deficiency, GH treatment, Aplastic anemia

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SEVERAL recent reports have confirmed that growth hormone (GH) treatment does not increase the risk for the incidence of leukemia [1–4]. However, occurrence of leukemia in GH-treated patients [5–8] has prompted us to suspect that GH may have some adverse effects on hematopoietic system. Here, we report a 12-year-old girl with aplastic anemia accompanied by chromosome 8 trisomy during GH therapy.

Case report

A twelve-year-old girl was admitted to our hospital because of petechiae in lower legs. When she was six years old she was referred to another hospital complaining of her short stature (~2.3 SD). Her bone age was evaluated as 4 years using the Greulich-Pyle atlas. Her serum insulin-like growth factor level was 21 ng/mL. Peak GH values induced by L-DOPA, arginine and GH releasing factor were 0.9 ng/mL, 0.7 ng/mL and 9.7 ng/mL, respectively. Other anterior pituitary hormones showed normal responses to the provocation test using CRH, TRH and LHRH. We could not find any abnormalities either in her pituitary gland or pituitary stalk in magnetic resonance imaging of brain. Based on the above results, she was diagnosed as idiopathic isolated GH deficiency, and GH therapy was initiated using recombinant human GH [0.5 U (0.175 mg)/kg/week divided into 7 daily subcutaneous doses].

At age 12, when GH therapy continued for six years, she began to exhibit petechiae in both lower limbs, and was admitted to our hospital. There was no history suggesting viral infection such as sore throat, fever, or
rash. Physical examination showed numerous petechiae on her legs, without hepatosplenomegaly or lymph node swelling. Her serum hemoglobin level was 11.8 gr/mL, and red blood cell count was $4.17 \times 10^6/\mu$L. Platelet count was $11,000/\mu$L and white blood cell count was $3,400/\mu$L with 37% neutrophils, 58% lymphocytes, 4% monocytes and 1% basophils. Bone marrow examination showed that total nucleated cell count and megakaryocyte were $17,000/\mu$L and 0/\muL, respectively, suggesting low formation. Specimen of bone marrow biopsy revealed 13% of bone marrow cells containing the 3 signals of chromosome 8 marker (trisomy 8). However, no blast cells or myeloid dysplastic features suggesting myelodysplastic syndrome (MDS) could be found in her bone marrow specimen.

Based on these data she was diagnosed as aplastic anemia accompanied with chromosome 8 trisomy. GH therapy was stopped immediately, and simultaneous administration of methylprednisolone/anti-thymocyte globulin (ATG) therapy was initiated. Platelet count improved with treatment, and the 3-signal chromosome 8 abnormality disappeared from the bone marrow cells. She has been free from aplastic anemia for about two years.

**Discussion**

Our case is of particular interest because of the occurrence of aplastic anemia during GH treatment. Though MDS during GH treatment is reported [9, 10], our patient is, to our knowledge, the first case of aplastic anemia developed during GH therapy. She was diagnosed as having aplastic anemia because of her thrombocytopenia and typical hypoplastic bone marrow. Trisomy 8, that was found in 13% of her bone marrow cells, has also been known to be found in the bone marrow cells of MDS as well as aplastic anemia [11, 12]. Aplastic anemia should be carefully distinguished from MDS with hypoplastic bone marrow. In our case, the number of bone marrow cells containing trisomy 8 was small, and no myeloid dysplastic features could be observed in bone marrow. These hematological data strongly suggested that she suffered not from MDS but aplastic anemia.

Various drugs, chemicals, toxins, infectious agents, radiation, or immune disorders can result in aplastic anemia [13]. As far as we investigated, we could not find any other causal episodes for her aplastic anemia. In addition, termination of GH therapy resulted in both improvement of thrombocytopenia and disappearance of bone marrow cells containing trisomy 8. These facts suggest that GH might have triggered impairments at the stem-cell level.

While we cannot conclude that her aplastic anemia was induced by GH treatment, the fact that a hematological adverse effect other than leukemia exists in conjunction with GH therapy warrants further investigation into possible hematological changes occurring during or after GH therapy.

**References**


