



Unresolved tachycardia in a 14 year old with acute lymphoblastic leukemia patient

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Case

A 14-year-old male patient presented to our emergency department with complaints of bruises on the feet and gingival bleeding. Hepatomegaly and diffuse ecchymoses and petechiae were present on physical examination. Laboratory findings were as follows: WBC: 307 800/mm³, hemoglobin: 7.9 g/dL, platelet count: 46 000/mm³. Abundant blasts were observed on the peripheral smear and bone marrow examination. Central nervous system involvement was present at the time of diagnosis. Phenotyping revealed a diagnosis of T-cell acute lymphoblastic leukemia (ALL). Translocation studies revealed negative t(9;22), t(4;11), t(12;21) and (1;19). With these findings the patient was classified into the moderate risk group according to the modified BFM-95 risk classification. TRALL-BFM-2000 protokol induction treatment was started. On the 8th day, no blast was observed on the peripheral blood smear. On the 15th day, 4% blast was found on bone marrow examination,

but the patient was classified into the high-risk group, since minimal residual disease was found to be 31.39% (normal value: <1x10⁻⁴) as a result of flow cytometry. On the 33rd day, 4% blast was observed on bone marrow examination.

Sinus tachycardia observed in the patient from the first days of induction treatment was initially associated with anemia, but apical heart rates were intermittently found to be 100-140/min, although hemoglobin values were kept in the normal limits with transfusions. Familial history did not include any known thyroid disease or autoimmune disease. No murmur was heard and peripheral pulses were palpable on physical examination. Thyroid examination was found to be normal. Antibiotic treatment was given because of febrile neutropenia. Tachycardia did not resolve in the period when the patients had no fever and infection. Electrocardiography did not reveal any pathology except for sinus tachycardia. Telecardiography, echocardiography and cardiac enzymes were found to be normal.

Diagnosis: primary hyperthyroidism

Thyroid function tests were ordered in terms of thyroid pathology. Free T3 (4.76 pg/ml) and free T4 (2.15 pg/ml) levels were found to be high and TSH level was found to be low (0.6 mIU/L). Anti-thyroglobulin (14.81 IU/mL n=0-40), anti-thyroid peroxidase (7.72 IU/mL n=0-35) and TSH receptor (0.45 IU/mL n=0-1.1) autoantibodies were found to be negative. Thyroid ultrasonography and Doppler ultrasonography were found to be normal. Since the peripheral blood and bone marrow were in remission in this period and no pathology was found on thyroid ultrasonography and Doppler ultrasonography, biopsy was not considered necessary in terms of thyroid involvement. The patient was evaluated as primary hyperthyroidism and propranolol and methimazole treatment was started. Thyroid function tests repeated in the first month of treatment were found to be normal. His complaint did not recur and tachycardia resolved in the follow-up.

Discussion

Acute lymphoblastic leukemia is the cause of approximately 25-30% of childhood cancers and 75% of childhood leukemias. Tachycardia may occur because of different causes during treatment of leukemia. Although infection, fluid loss and anemia are frequently found as the cause, thyroid pathologies should also be considered in the etiology. Hyperthyroidism is a disease which should be considered primarily in the differential diagnosis of tachycardia in individuals who are healthy otherwise. Tachycardia due to increased sympathetic activity is frequently observed in hyperthyroidism.

Different thyroid pathologies may accompany leukemia; hypothyroidism and hyperthyroidism due to different causes may be observed in the patients and sick euthyroid syndrome may be found (1,2,3). In the course of severe diseases including leukemia, changes in thyroid hormone levels may occur in the absence of thyroid disease and this is called sick euthyroid syndrome. The most commonly observed among these changes is decreased T3 concentration alone or in combination with decreased T4 concentration (2). It is thought that thyroid hormone levels change with the effect of the tumor, chemotherapy and impairment in the emotional and physical condition in children with cancer, but the mechanism has not been fully elucidated (4,5). These changes in thyroid hormones may be briefly an adaptation of the body to morbidity, but the physiological effects of this condition are not known. In children, the negative effects of low levels of a hormone which has been shown to be important for growth and development and brain development may be observed in

the long-term. In a prospective study performed in children receiving cancer treatment, changes in thyroid hormone levels were found in 90% of the patients (1). In this study, it was shown that the variable which had the greatest effect on hormone change was dexamethasone treatment. It is known that dexamethasone suppresses the release of TSH, T3 and prolactin. Corticosteroids additionally decrease TBG binding capacity and inhibit peripheral transformation of T4 to T3 (6,7,8). Corticosteroids are one of the most important drugs in ALL treatment and are used with high doses for a long period.

Thyroid involvement can be rarely observed in patients with leukemia (9,10,11,12). Thyroid functions generally do not change, but hypothyroidism is observed more frequently and hyperthyroidism has been found in some patients. It is thought that hyperthyroidism develops as a result of rapid release of thyroid hormone into the blood due to destruction of thyroid follicles with malignancy. Ultrasonography, Doppler ultrasonography, computerized tomography and fine needle biopsy are recommended in clinically suspicious patients, even though thyroid function tests are normal.

We found primary hyperthyroidism in our patient who had unresolved tachycardia from the first days of treatment during leukemia treatment. Low thyroid autoantibodies and normal parenchymal appearance on thyroid ultrasonography suggested that autoimmunity was not the cause of hyperthyroidism. The fact that the patient was in remission and thyroid Doppler ultrasonographic examination was normal excluded thyroid involvement for the time being. However, long-term follow-up of this patient will allow better differential diagnosis for autoimmune thyroiditis or thyroid involvement. In this article, we aimed to emphasize that hyperthyroidism should be considered as a cause in presence of tachycardia observed during leukemia treatment, though it is not a frequent cause and to discuss thyroid pathologies in patients with leukemia.

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