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Case Report

Burkitt Leukemia in a 5-Year-Old Girl with Williams–Beuren Syndrome: Review of the Literature

Abstract

Williams–Beuren syndrome (WBS) is a rare neurodevelopmental genetic disorder associated with microdeletion at the long arm of chromosome 7 (7q11.23). Few cases have been reported with WBS with hemato oncological malignancies. Herein, we report Burkitt leukemia in a 5 year old girl with WBS. We like to call attention to the management of this rare combination.

Keywords: *Burkitt leukemia, child, Williams–Beuren syndrome*

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Introduction

Williams syndrome is a rare neurodevelopmental disorder, also known as Williams–Beuren syndrome (WBS). WBS is a sporadic genetic disorder that occurs in 1:20000–1:50000. The characteristic features of WBS include dysmorphic face, cardiovascular disease (especially aortic stenosis), mental retardation, hypercalcemia, growth deficiency, high sociability, and friendly personality. Furthermore, children with WBS have characteristic craniofacial features such as periorbital fullness, medial eyebrow flare, stellate iris, flat nasal bridge, strabismus, long philtrum, wide mouth, full cheeks, and lips.[1,2]

Patients with WBS have microdeletion of 25–30 genes in q11.23 regions of chromosome 7. WBS is not considered as a cancer predisposition syndrome.[3] In the medical literature review, single reports of astrocytoma, ovarian mucinous cystadenoma, follicular thyroid carcinoma, Wilms tumor, non-Hodgkin lymphoma, and acute lymphoblastic leukemia (ALL) in association with WBS have been published.[4-6]

Herein, we report on the clinical course and laboratory findings of a patient with WBS who also had Burkitt leukemia.

Case Report

At initial presentation, the patient, a 5-year-old girl with WBS, was referred to our hospital for evaluation of abdominal mass. In her medical history, mother and father were not relatives. She was diagnosed with WBS when she was 4 months old. Aortic valve replacement operation was performed due to supravalvular aortic stenosis when she was 15 months old. She had initial complaints of abdominal swelling, constipation, and fatigue for 4 days. On physical examination at the time of admission, body weight was 15 kg (10–25p), height was 104 cm (25p), and general state was good, and there was no petechiae and purpura. Vital signs were in normal range. The patient showed many of the features such as elfin face, mild mental retardation, swollen eyelids, high palate, epicanthal folds, periorbital fullness, full lower lips, and small mandible. She was also talkative, social, and friendly. There were 10 cm scar over the sternum because of cardiovascular surgery, second-degree murmur, suspected mass in deep palpitation, and no hepatosplenomegaly. Urine analysis was normal. The patient's white blood cell count was 9770/mm^3, hemoglobin level was 11 gr/dL, and platelet count was 522000/mm^3. Peripheral blood smear showed atypical vacuolated lymphoblasts. The patient had elevated lactate dehydrogenase (2561 IU/L), aspartate aminotransferase (203 U/L), and alanine aminotransferase (58 U/L). Serum uric acid, albumin, creatinine, and blood urea nitrogen levels were in normal range. Abdominal ultrasound, computed tomography scan, and magnetic resonance images revealed

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multiple parenchymal nodular mass lesions in the liver and kidneys; abdominal mass lesion in the subhepatic area; para-aortic and mesenteric lymphadenomegaly; and diffuse wall thickening involving terminal ileum, cecum, and ascending colonic segments suggesting of lymphomatous involvement.

Bone marrow aspiration revealed 60% of blasts with many vacuoles and L3 morphology. Immunophenotypical analyses showed that blast expressed CD 10, CD19, CD 20, HLA-DR, and cytoplasmic IgM but were negative for CD14, MPO, CD33, CD13, surface IgM, CD2, CD7, CD11, Glycophorin A, cytoplasmic Tdt, and cytoplasmic CD3. The patient was diagnosed with Burkitt leukemia. The patient was treated as standard risk group ALL with national Turkish BFM protocol.[7] Cytogenetic analyses showed 46, XX.

Abdominal distension resolved after steroid treatment. Chemotherapy course was complicated by sepsis and fungal infection. She was treated with antimicrobial and antifungal drugs. The response of chemotherapy was perfect. She has under outpatient control without any complications, and there is no recurrence for a follow-up period of 7.5 years.

Discussion

Although WBS is not considered a clear cancer predisposing syndrome, the numbers of published cases of malignancies associated with WBS in pediatric adult group have been increasing. The types of malignancies are limited. The most common malignancies are lymphoma and leukemia groups (especially mature B cell originated). In the childhood group, Burkitt lymphoma in six cases, B cell lymphoblastic lymphoma in one, T cell lymphoblastic lymphoma in one, and ALL in one have been reported. In addition to hematological malignancies, two cases of astrocytomas, one case of mucinous cystadenoma of ovary, one case of Wilms tumor, and one case of follicular thyroid carcinoma have been reported in childhood [Table 1].[1,2,4-6,8,9] Culic *et al*.[8] reported a 14-year-old boy with WS and hyperploidic ALL; in this report, the immunological origin of the patient was not given; our presented case is the youngest children with mature B cell leukemia lineage.

Patient with WBS have a higher risk of mortality in normal life compared to normal healthy population. During the treatment of WBS with malignancies have higher risk of morbidity and mortality because of anesthesia, surgery, sedation, and chemotherapy regimen. Especially baseline cardiac examination (blood pressure, electrocardiogram, and echocardiogram) is advised during the pre- and post-treatment period. On the another hand, nephrological evaluation (urinalysis, urinary ultrasound, and Doppler examination) is recommended before the treatment.[1] Our patients did not experience any cardiac problem like arrhythmia. On the other hand, she had hyperglycemia related to chemotherapy protocol including steroid and asparaginase.

Table 1: Literature review of hemato-oncological malignancies in children with Williams–Beuren syndrome

Author (year)	Age at diagnosis (year)	Malignancies
Semmekrot *et al*., 1985-1986	5, ?	Astrocytoma
Marles *et al*., 1993	?, female	Mucinous cystadenoma of ovary
Felice *et al*., 1994	29, female	NHL
Culic *et al*., 2002	14, male	Acute lymphoblastic leukemia
Amenta *et al*., 2004	8, male	NHL (Burkitt)
Thornburg *et al*., 2005	5, female	NHL (Burkitt)
Togo *et al*., 2007	5, female	Cutaneous fibrous hamartoma
Urisarri-Ruiz de Cortázar *et al*., 2009	12, male	NHL (T-cell 9)
Onimoe *et al*., 2011	10, female	NHL (Burkitt)
Zhukova and Naqvi, 2013	8, male	NHL (Burkitt)
Chonan *et al*., 2013	3, male	Astrocytoma
Vanhapiha *et al*., 2014	9, ?	NHL (Burkitt) and Ewing sarcoma
Guenat *et al*., 2014	10, male	NHL (B-NHL)
Guenat *et al*., 2014	7, female	NHL (Burkitt)
Velikonja *et al*., 2016	4, ?	Wilms tumor
Chagas *et al*. 2017	12, male	Follicular thyroid carcinoma
This study, 2017	5, female	Burkitt leukemia

NHL – Non-Hodgkin lymphoma; ? – Unknown gender

Chromosome 7 is the most common involved chromosome among the cytogenetic aberrations in the malignancies. Especially, monosomy 7 is a famous genetic predisposition to myelodysplastic syndrome and secondary acute myeloid leukemia. Hasle *et al*.[10] reported the relationship between chromosome 7 and epithelial, hematologic malignancies from the database of Danish cytogenetic registry. They found that five persons with constitutive chromosome 7 abnormality associated cancer including one thyroid carcinoma, three carcinomas of the digestive tract, and one malignant melanoma. There was no identified cancer in the patients with WBS in this study.

There are no large clinic, molecular genetic correlation studies of gen deletions of WBS and development of cancer mechanism. Among the 20 genes that are mapped in affected religion of chromosome 7q11.23, four of these genes are speculated to be responsible for different clinical features of WBS: (1) the *elastin* gene was found to associated with the phenotypical features of WBS such as cardiac features, (2) *LIM-kinase 1* gene abnormalities had been implicated with visual and cognition problems, (3) DNA repair genes such as *BAZ1B, RFC2,* and *GTF2I*

are related with cancer development, (4) *BCL7A, BCL7B* genes which regulates the apoptosis, has been found to be closely related with B cell leukemia and lymphoma.[1,3,9,11] Although the fluorescence *in situ* hybridization aberration of our presented case has been performed, the molecular genetic studies were not done.

Conclusion

Currently, it is not possible to explain the correlation between hemato-oncological malignancies and genetic variation of WBS. It is important to report these cases to literature to call attention to this syndrome for the clinicians.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Zhukova N, Naqvi A. Williams-beuren syndrome and burkitt leukemia. J Pediatr Hematol Oncol 2013;35:e30-2.
2. Vanhapiha N, Knuutila S, Vettenranta K, Lohi O. Burkitt lymphoma and ewing sarcoma in a child with williams syndrome. Pediatr Blood Cancer 2014;61:1877-9.
3. Decimi V, Fazio G, Dell'Acqua F, Maitz S, Galbiati M, Rizzari C, *et al.* Williams syndrome and mature B-leukemia: A random association? Eur J Med Genet 2016;59:634-40.
4. Chagas NB, Maion VH, de Avó LR, Matheucci Júnior E, Moutinho MA, Melo DG, *et al.* Follicular thyroid carcinoma in a male adolescent with williams-beuren syndrome. Clin Dysmorphol 2017;26:44-6.
5. Chonan M, Kanamori M, Kumabe T, Saito R, Watanabe M, Tominaga T, *et al.* Pilomyxoid astrocytoma of the cerebellum with williams syndrome: A case report. Childs Nerv Syst 2013;29:1211-4.
6. Marles SL, Goldberg NA, Chudley AE. Mucinous cystadenoma of ovary in a patient with williams syndrome. Am J Med Genet 1993;46:349.
7. Yuksel Soycan L. BFM-TR ALL 2000: First Turkish multicentric study in the treatment of pediatric acute lymphoblastic leukemia. J Pediatr Hematol Oncol 2007;29:21.
8. Culic V, Culic S, Armanda V, Resic B, Lasan R, Peterlin B, *et al.* Single signal of the williams syndrome chromosome region 1 gene in hyperploidic bone marrow cells of acute lymphoblastic leukemia in a williams syndrome patient. Med Pediatr Oncol 2002;38:205-7.
9. Guenat D, Merla G, Deconinck E, Borg C, Rohrlich PS. DNA damage response defect in williams-beuren syndrome. Int J Mol Med 2017;39:622-8.
10. Hasle H, Olsen JH, Hansen J, Friedrich U, Tommerup N. Occurrence of cancer in a cohort of 183 persons with constitutional chromosome 7 abnormalities. Cancer Genet Cytogenet 1998;105:39-42.
11. Guenat D, Quentin S, Rizzari C, Lundin C, Coliva T, Edery P, *et al.* Constitutional and somatic deletions of the williams-beuren syndrome critical region in non-hodgkin lymphoma. J Hematol Oncol 2014;7:82.