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Diagnosis of the Combination of Immune Thrombocytopenia and Woodhouse-Sakati Syndrome

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Abstract Woodhouse-Sakati Syndrome (WSS) is a rare autosomal recessive syndrome characterized by sensorineural hearing loss, ECG ST-T changes, partial alopecia, hypogonadism, diabetes, and moderate mental retardation. A 23-year-old male patient was admitted to our hospital with complaints of purpura and petechial rashes. His platelet count was 3.04 x 10^9/L and the peripheral blood smear was compatible with this count. No atypical cell was observed. He had mild mental retardation. He had hearing loss since childhood. Physical examination showed widespread petechiae and purpura on bilateral lower extremities. Significant growth retardation was detected and male pattern hair growth was less. In genital examination, bilateral testicles were small; penis length was 1 cm and it was 4 cm when elongated. T negativity was present in precordial derivations of ECG. He was diagnosed Immune thrombocytopenic purpura (ITP) and WSS according to these findings. In addition to ITP treatment with steroids, the combination of testosterone propionate and testosterone phenyl propionatewas also administered to him. Upon we observed that there was an increase in his platelet number, he was discharged from the hospital. WSS is a very rare disease. Different components of the syndrome have been reported in different patients.It is the first time in the literature that ITP is observedtogether with WSS in a male patient.

Keywords: *woodhouse-sakati syndrome, immune thrombocytopenic purpura*

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1. Introduction

Woodhouse-Sakati Syndrome (WSS) was primarily observed by Woodhouse and Sakati in 1983 in 6 patients who were the members of two families from Saudi Arabia. It was reported that WSS is a rare autosomal recessive syndrome which is characterized with partial alopecia, hypogonadism, diabetes, moderate mental retardation with sensorineural hearing loss and electrocardiogram abnormalities (ST-T changes) [1]. Different components of the syndrome were also specified in the following cases [2]. The gene which is responsible for the syndrome is detected on the 2q31.1 chromosome at the DCAF17 localization [3]. Immune thrombocytopenic purpura (ITP) is an acquired disease in which anti-platelet auto-antibodies shorten the life span of platelets. Mild petechiae or even life threatening bleedings can be observed in case of ITP according to the level of thrombocytopenia [4]. In literature, WSS and ITP were observed together only in one female patient in India [5]. We are the second group who reports from Turkish race WSS and ITP together in a patient. However, our study is the first one which shows WSS and ITP together in a male patient.

2. Case

Almost 3 days before, 23 years old male patient was admitted to our hospital since his platelet count was 5 *x* 10^9*/L*and he had widespread purpura and petechial rashes in his lower extremities. According to test results in our hospital, patient had hemoglobin (Hb):13 gr/dl, leukocyte: 4.33 K/uL, neutrophil:1.68 K/uL, lymphocyte:1.77 K/uL, *platelet:3.04 x* 10^9*/L*. The patient was admitted to the hematology service in order to examine both the etiology and the treatment of the thrombocytopenia.A mild mental retardation was detected while taking an anamnesis from the patient. He had no important family history feature. Anamnesis was asked to his relatives and there was no medical history which can explain the etiology of thrombocytopenia. In his physical examination, hisarterial blood pressure was 110/70 mm/Hg, his pulse was 88/min, and his body temperature was 36.8^{0}C.According to his systemic examination, it was observed that the patient had prominent growth retardation according to his age and he did not have the age appropriate hair growth on his skin. There were widespread petechiae and purpura rashes in the bilateral lower extremity. There was no organomegaly according to the abdominal examination. His respiratory

and cardiac examinations were also normal. In his genital examination, his bilateral testicles were small, penis length was 1 cm and it was 4 cm when elongated, and axillary hair growth was very less (according to the Tanner scale, pubic hair growth was at the stage 3, testicular development was at the stage 2). According to his age, patient had the growth retardation and his weight was 42 kg, his height was 167 cm, his forearm length was 172 cm and his body mass index (BMI) was 15.Patient was using hearing aid for almost the last two years and he had hearing loss since his birth according to his anamnesis taken from his family. Posteroanterior chest X-ray was normal. His leukocyte and hemoglobin levels were normal and his platelet count was 3.040 *x* 10^9*/L*. Since his peripheral blood smear was compatible with this count and since there was no atypical cell, examinations for the etiology of thrombocytopenia were initiated. Intended for infectious factors, toxoplasma, rubella, cytomegalovirus, herpes (TORCH) panel, Epstein Barr virus, and parvovirus IgM were examined and all of them were negative. Antinuclear antibodies, HbsAg, anti-HCV and anti-HCV were negative. Vitamin B12 was 284.6pg/ml (191-663) and folic acid was11.4ng/ml(3.1-17.8).The patient was diagnosed with ITP. Since the patient had thrombocytopenia, hypogonadism, mild to moderate mental retardation, hearing loss, ECG changes, further evaluations were planned in terms of the underlying etiology. Hypogonadism was comprehensively assessed with endocrinology clinic. Patient was examined in terms of follicle stimulating hormone (FSH), luteinizing hormone (LH), total testosterone, free testosterone, growth hormone (GH), insulin-like growth factor-1 (IGF-1), thyroid stimulating hormone (TSH), free T4 (FT4) , adrenocorticotropic hormone (ACTH), cortisol, prolactin, dehydroepiandrosterone sulfate (DHEA-SO4), blood gases, karyotype analysis and fasting blood glucose. In scrotal USG, left testicle size was 16x7x10 mm and right testicle size was 14x7x11 mm.The pituitary magnetic resonance imaging was normal. The karyotype of the patient was normal (46XY). Following parameters were detected in low levels: *FSH:1.25 mIU/ml* (1.5-12.4), *LH:0.324 mIU/ml* (1.7-8.6), *Total testosterone: 0.059 ng/ml*(2.8-8), *free testosterone: 1.37 pg/mL* (5–30). Furthermore, cortisol:22.26 ug/dl, ACTH:28.29 pg/ml(7.2-63.3), *DHEA-SO4: 156.7 µg/dL* (211– 492), *GH :6.74 ng/ml* (0.03 – 2.47), IGF-1 (Somatomedin-C) 276.0ng/ml (116–358),TSH:2.38 µIU/mL (0.27–4.2), prolactin: 6.12 ng/mL (male:4.04-15.2).According to the laboratory examinations, the patient was diagnosed with hypogonadotropic hypogonadism. According to ECG performed by cardiology clinic, patient who had T negativities in precordial derivations (Figure 1), it was detected that the ascending aorta was 2.6 cm, left ventricular ejection fraction was 60%, PAP was 24mm/Hg, and there was a mitral valve prolapse. Patient, who had hearing loss, was examined by the otolaryngology clinic and there was a bilateral sensorineural hearing loss according to the audiometry. According to the literature, patients with other components of this syndrome can be diagnosed as WSS, however genetic evaluation supports the diagnosis. Although our patient could not be evaluated genetically, with the findings such as hipogonadizm, mental retardation, hearing loss, and ECG, the diagnosis of WSS was established (2). Methylprednisolone was administered to the patient due to the ITP diagnosis. In his follow-up, there was no significant increment in his platelet counts and the intravenous immunoglobulin therapy was initiated. The treatment continued till the platelet count reached to 217 *x* 10^9*/L*. According to the recommendations of the endocrinology clinic, it was planned that the patient will receive intramuscular injections of testosterone propionate, testosterone and phenyl propionate in each three weeks. The patient was discharged from the hospital.

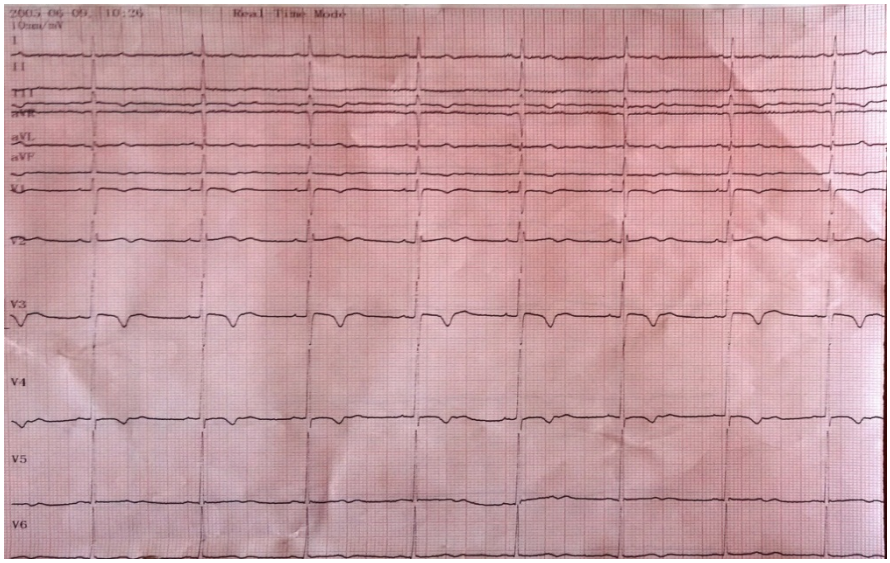

Figure 1.

3. Discussion

Woodhouse-Sakati Syndrome (WSS) is a rare disease which can be observed with alopecia, hypogonadism, diabetes, mental impairment, hearing loss, dystonia (extrapyramidal deficits), ECG abnormalities (ST-T changes). Its pathophysiology is not well known. In some cases, different components of the disease can be observed. It is possible that the diagnosis of the disease can be delayed since hypogonadotropic hypogonadism is not diagnosed until puberty and due to the mild alopecia. Our

study is the second one which reports that WSS and ITP diseases are observed together in one patient.

Various different mutations of WSS have been detected in studies in which cases and different families from different countries were examined.In these patients, nine different mutations have been reported and patients have had different phenotypes although they have the same genetic mutation [2,3,5-13].

In a review written by Agopiantz et al, they assessed clinical characteristics of 72 WSS patients from 29 families. They have summarized that the most common clinical findings such as frontotemporal alopecia, hypogonadism and low IGF-1 levels starts in the childhood. Addition to this triad, intellectual disabilities in different proportions (87%), bilateral hearing loss (76%), cervico-facial diystonia, pain in the extremities (42-89%) and diabetes (66-96%) were also detected in patients [2].

The only case study in which WSS and ITP diseases were reported was performed in 2008. The patient was 20 years old and she was one of the three children of an Indian family. She had sometimes bleeding gums and she was admitted to the hospital due to the recent hematuria complaint. Her platelet count was 11.000/mm^3 and she was diagnosed with ITP according to the comprehensive evaluation of her clinical findings. Oral steroid treatment was initiated. Her mother and father were relatives. According to her anamnesis, she was diagnosed with diabetes mellitus with negative auto-antibodies and insulin and oral antidiabetic drugs were administered to her. She had the first menstrual bleeding in the age of 15 upon the hormonal therapy. She had a progressive alopecia before the age of 3. She had hearing loss in the last three months. Her school performance was lower according to the average and she had a break from school in the eighth grade. In her physical examination, she had hypertelorism, telecanthus, and malocclusion. Additionally, her hairs of the scalp and eyebrows were sparse.She had myopic in her right eye and amblyopia in her left eye. These eye defects were not related to diabetic retinopathy. Additionally, moderate bilateral sensorineural hearing loss was detected. According to her laboratory findings, PLT level was low and there were laboratory test results compatible with gonadotropic hypogonadism. There was no ovary and uterus according to imaging results and there was symmetrical T-wave inversion in anterior derivations according to ECG results [5]. Our patient was male and family members did not have any findings which can be related to the syndrome. Hypogonadotropic hypogonadism was detected in our patient and there were also mental retardation, bilateral sensorineural hearing loss, T negativity in the precordial derivations. His bilateral testicle sizes were small and his secondary sex characteristics were less developed according to his age.

4. Conclusion

We reported a patient who was admitted to the hospital with the complaint of low platelet levels. It is a very rare case that the patient was diagnosed with WSS and ITP together. We support the idea that patients should be comprehensively assessed including examination of all body system instead of evaluating them only according to their complaints. In this way, acquired diseases which may lead to severe clinical problems can be diagnosed earlier and the treatment will not be delayed.

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