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Case Report

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SCHIMKE IMMUNE-OSSEOUS DYSPLASIA: A CASE REPORT

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ABSTRACT

The Schimke Immuno-Osseous Dysplasia (SIOD) is an autosomal, recessive and multisystem disease which is rarely seen and to which the biallelic mutation causes in the SMARCAL-1 gene. There are spondyloepiphyseal dysplasia, steroid-resistant nephrotic syndrome, progressive renal failure, T cellular immunodeficiency, bone marrow failure and cerebral infarctions between the typical findings in the SIOD. A patient at the age of 29 and taken to our intensive care unit for following-up by the reason of acute kidney failure will be discussed in this case report.

KEYWORDS: Schimke Immuno-Osseous Dysplasia, Sepsis, Acute Renal Failure.

INTRODUCTION

The Schimke Immuno-Osseous Dysplasia (SIOD) was firstly defined by Schimke in 1971 and is characterized by the spondyloepiphyseal dysplasia, T cellular immunodeficiency and kidney disease progressing with the nephrotic proteinuria.[1] The SIOD's incidence is not clear. However, it is forecasted to be 1 in each 1.000 000 to 3.000 000 live births in the United States of America.[2] The SIOD is an autosomal recessive disorder. There are approximately 50 cases stated in the literature until today. It is not connected with the gender, ethnic origin and geographical location.[3] The prevalent findings in the SIOD contain the spondylo-epiphyseal dysplasia (SED), steroid-resistant nephrotic syndrome (SRNS), progressive kidney failure (FSGS) and T cell immune failure causing the growth and developmental delay. Atherosclerosis, cerebral infarction, transient neurologic attacks (TNA), hypothyroidism and corneal opacity are also connected with the SIOD. The bone marrow failure, autoimmune disease, non-Hodgkin lymphoma, and osteosarcoma had been also stated in these patients previously.[2-4]

CASE REPORT

While a male patient at the age of 29 was investigated in the hematology unit by the reason of thrombocytopenia, he was taken to our intensive care unit by the reason of being a respiratory distress depending on the acute kidney failure and hypervolemia. There was a Schimke syndrome in our patient's history, and his first diagnosis was made while he was 7 years old. The patient, who was not flowed-up, applied to the nephrology polyclinic by the reason of being a swelling in the face and legs while he was 17 years old. The patient was suggested by a further examination by the reason of being a heavy proteinuria; however, the patient left from the follow-up. The patient, who applied to the outside center, was made the chronic kidney disease diagnosis, and the antihypertensive treatment and oral amino acid tablets were suggested.

The patient's brain CT was taken upon having a convulsion in the emergency department after applying to our emergency department by the reason of nausea, vomiting, and nose-bleeding approximately 2 months ago at the latest. The prevalent calcifications (Fahr disease) were observed in the basal ganglion and cerebellum during the CT. The hematoma, which is in a 15x9 mm size and progresses towards the basal ganglion on the left side of the mesencephalon, is present in a smaller size in the precentral gyrus on the right side with the similar appearance. The neurosurgery was consulted for the patient upon being evaluated of the appearance in favor of the hematoma; however, not any interventions were thought for the patient whose platelet value was 10.000. The patient was hospitalized in the neurology intensive care and his follow-ups were started. The hematology was consulted in terms of the thrombocytopenia etiology in the neurology intensive care. A peripheral smear was requested by the hematology. The target cells were present in the peripheral smear, and they were evaluated in line with the mild anisocytosis, mild poikilocytosis, a few schistocytes, and hemogram. The methylprednisolone was suggested as 60 mg IV. The intravenous immunoglobulin was given together with the methylprednisolone. The plasmapheresis was started by

the reason of an increase in the following peripheral smear and schistocytes. The hematoma appearances located on the left half of mesencephalon were prominently regressed in the control Brain CT, and a prominent distention was observed in the hematoma located on the right precentral region. Then, the patient was transferred to the hematology service since his general condition bounced back after the intravenous immunoglobulin, plasmapheresis, and prednol treatments. The patient was consulted by the nephrology since his creatine value increased, and the immunologic markers, immunofixation electrophoresis in the serum and urine, abdomen and thorax imaging, and 24-hour urine examination were suggested. The methylprednisolone treatment of the patient whose tumor markers came within the normal levels was decreased, and the maintenance was continued as 15mg/day. The dialysis support was started for the patient whose progressive increase was determined in the urea-creatine after the 5th day and who had a hypervolemia. The patient was taken to our intensive care unit by the reason of not being regressed of the hypervolemia while he was under the hemodialysis support and being the tachycardia and tachypnea.

The patient was intubated since his saturation was 75%, respiratory rate was 42, pulse was 148/min, tension was 182/104 and GCS was E2M2V2 when he came. The patient was taken to the emergency hemodialysis. After consulting to the infectious diseases, the antibiotherapy was started (by making the piperacillin-tazobactam nephrologic dose adjustment) for the patient who had the increased procalcitonin and CRP levels and leukocytosis. The Pro-BNP was 35.000, and the daily dialysis was continued. The apheresis, erythrocyte, and fresh frozen plasma support were daily made by consulting to the hematology. The cardiology was consulted for the patient whose general condition progressed as hypertensive and hypervolemia were not healed after thinking that he would have a heart failure. While the EF was measured as 60%, not any severe valve pathologies were determined in the ECHO taken. While the SIFE and IFE requested by the nephrology were normal, the immunologic markers were negative. The tracheostomy was opened by consulting with the thoracic surgery for the patient by the reason of extended intubation. His cultures were repeated and the infectious diseases were consulted since there was an increase in the procalcitonin value and fewer increases in his follow-ups. The patient's antibiotherapy (meropenem and tigecycline) was changed. The infection diseases were consulted again since the fewer increased again and there as an E.coli growth in the blood and respiration cultures on the 7th day of antibiotherapy. His antibiotherapy was changed as the tigecycline and teicoplanin. The patient was consulted again by the thoracic surgery since he had a heavy bleeding from the tracheostomy place on the following days. The tracheo-innominate was predicted as the artery fistula. The sternotomy and innominate artery repair or grafting operation were suggested by the thoracic surgery; however, the patient relatives did not accept the operation. The patient's bleeding spontaneously stopped by the thrombocyte and fresh frozen plasma replacement. The patient was followed-up by our intensive care unit for totally 46 days. The patient was lost because of the sepsis at the end of 46th day. Our patient's first day, 1st month and last day laboratory values were shown in TABLE-1.

Table-1.

Parameter	Hospitalization	1st Month	Discharge
Urea (mg/dl)	80	197	96
BUN (mg/dl)	37	92	45
Creatinine (mg/dl)	3.99	5.05	2.49
Na (mmol/L)	137	142	138
K (mmol/L)	4.01	4.29	3.77
Ca (mg/dl)	9.22	8.33	9.40
P (mg/dl)	6.36	7.22	3.63
CRP (mg/dl)	5.326	1.408	21.295
WBC/Neutrophile (K/uL)	11.900/10.710	9.410/7.120	36.040/30.730
Hemoglobin (g/dl)	6.7	10.3	8.3
Platelet (K/uL)	10	24	3
APTT/PTZ (second)	25.4/12.4	48.5/11.8	38.6/13.9
İNR	1	0.95	1.12
Fibrinogen (mg/dl)	461	322	442
D-dimer (ng/mL)	435	1789	1085

DISCUSSION

The SIOD's etiology could not be completely understood yet. Although approximately 55 different mutations in the SMARCAL1 gene were defined regarding the SIOD, only 50-60% of the individuals with SIOD had the determinable mutation in this gene.[3] The mutations found in the other undefined genes can lead to the SIOD. The SMARCAL1 gene is found in the 2q35 chromosome and a chromatin found in the multiprotein complexes codes the HepA-related protein (HARP), which acts as a remodeling and is a member of the Sucrose Non-

Fermentable (SNF2) family. This protein takes place in a great variety of biological functions such as the transcription, and DNA replication and DNA repair.[3]

The SIOD should be doubted for the patients who have a non-proportional short stature in the physical structure, dysmorphism, hyperpigmented macules, spondylo-epiphyseal dysplasia, progressive steroid-resistant nephropathy and T cell deficiency.[5] There are two types of SIODs including the severe or infantile and mild or juvenile. The symptoms are the early-onset for the patients having a severe form. It is in with the intrauterine growth retardation, nephropathy, neurologic symptoms (such as the transient ischemic attack, seizures, and stroke) and short lifetime.[6] The patients whose symptoms start after 15-16 years old are in the mild form, and the hypothyroidism, recurrent infections, bone marrow failure, and neurologic symptoms are not seen.[7]

The mean life of individuals with SIOD is 11 years. The infection (23%), stroke (13%), pulmonary hypertension and congestive heart failure (13%), kidney failure (11%), organ transplantation complications (9%), lymphoproliferative disease (4%) gastrointestinal complications (4%), respiration failure (4%), bone marrow failure (2%), non-Hodgkin lymphoma (2%), pancreatitis (2%) and other unreported cases (13%) take place within the most important causes of death.[5]

The steroid-resistant nephrotic syndrome (SRNS) (98% of the cases) is frequently seen in the patients with SIOD including the typical kidney pathology and focal segmental glomerulosclerosis and final period kidney disease develops in a short time.[5] However, the minimal change nephrotic syndrome, nephronophthisis, mesangial proliferative glomerulonephritis[8] and membranous nephropathy[9] were also stated. At the present time, the SIOD had increased the life expectancies of children by the reason of recent developments in the transplantation and dialysis. However, the cerebrovascular disease had become an important morbidity and mortality reason.

The SMARCAL1 gene mutation can cause the extensive neurologic findings from the headaches similar to a severe migraine and TNAs to the ischemic incidents. The TNAs are frequently focal and are not the ischemic-origin.[5] On the other hand, the cerebral ischemic incidents occurring by hypertension by the reason of overdose steroid application and disease progression come to existence. While the TNAs or paralyzed patients have generally the diffuse progressive cerebral arteriosclerosis, there are not patients having the isolated migraine headaches. There are symptoms make think atherosclerosis in approximately 50% of the persons with SIOD. The observed vascular changes contain the focal intimal lipid deposition, focal myo-intimal proliferation, macrophage invasion, foam cells, fibrous transformation and calcium depositions.[10-12]

The T cell failure is seen in approximately 80% of the affected individuals and they reflect the clinic as the lymphocytopenia. The B cells are generally normal or can have slightly increased.[5]

The differential diagnosis should be made by glaucoma and Braegger syndrome characterized by (a) the conical epiphyses and chronic kidney disease and kono-renal syndrome being connected with the retinitis pigmentosa and proximal femur abnormality;[13] (b) the nail patella syndrome which affect the nails, skeletal system, kidneys and eyes and is an autosomal dominant disease;[14] (c) the face dysmorphology, mental retardation, extremity anomalies and humoral immunodeficiency together with the nephrotic syndrome[15] for the syndromes taking place in the SIOD's differential diagnosis.

The dialysis and kidney transplantation are the single and effective treatment modalities. The nephropathy replication risk after the transplantation or increase in the rate of incidence of atherosclerosis had not been determined.[8] The optimal immunosuppressive treatment regime had not been solved yet. The development of severe disseminated cutaneous papilloma virus infections or lymphoproliferative disease connected with the Epstein Barr virus had been stated by the traditional immunosuppressive regimes in some SIOD patients.[16]

CONCLUSION

As a consequence, the SIOD should be thought in the children having the growth retardation, steroid-resistant nephrotic syndrome, skeleton abnormalities, and neurologic symptoms. The patients who are doubted to be SIOD should be carefully followed-up for the neurologic symptoms such as the headaches similar to a migraine, seizure and cerebrovascular diseases, mood and memory. Moreover, evaluating the cerebral vascular and preventive vascular intervention in the patients having the cerebrovascular abnormality can help to prevent the early-onset cerebral infarction. They should closely followed-up especially for the proteinuria, hypertension, cellular immunity and opportunistic infections; and the immunosuppressive treatment is required to start for the nephrotic syndrome.

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