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Case Report (Pages: 7151-7155)

A Case Report of Schimke Immuno-Osseous Dysplasia: A Rare Autosomal Recessive Disorder

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Abstract

Schimke immune-osseous dysplasia (SIOD) is a rare autosomal recessive disorder presented with specific facial features, skeletal dysplasia, steroid resistance nephrotic syndrome (SRNS) and cellular immune insufficiency. This is a SIOD case reported from Iran. He was 5 years old boy when evaluated for proteinuria and short stature. In appearance, we detected hyperpigmented macules, kyphoscoliosis, and warty lesions. He developed progressive renal failure and steroid resistant nephrotic syndrome, so kidney biopsy was performed and revealed focal and segmental glomerulosclerosis. He didn't respond to prednisolone and Calcineurin inhibitors. He had recurrent lymphopenia with low CD4/CD8 ratio.

However lymphopenia respond to granulocyte colony-stimulating factor (G-CSF), he died with pneumonia and sepsis. Nephrotic syndrome due to focal segmental glomerulosclerosis may be accompanied by syndromes. In Qazvin province, we see autosomal recessive disorders more, because of consanguineous marriages. To the best of our knowledge, this is the fourth case of SIOD to be reported from Iran.

Key Words: Case report, Child, Lymphopenia, Schimke-Immuno-osseous Dysplasia.

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1- INTRODUCTION

Schimke immune-osseous dysplasia (SIOD) characterized by spondylo-epiphyseal dysplasia (SED), steroid-resistant nephrotic syndrome due to focal segmental glomerulosclerosis and T-cell immunodeficiency (1). The other features are hyperpigmented macules, recurrent infections, cerebral ischemia, intellectual delay, hypothyroidism, testicular hypoplasia. Mutations were detected in SMARCAL1 gene at chromosome 2q35. This gene encodes a member of an SNF2 subfamily of proteins that mediate DNA-nucleosome restructuring during gene regulation and DNA replication, recombination, methylation and gene repair.

2- CASE REPORT

We describe an Iranian patient with immuno-osseous dysplasia. He was an eleven-year- old boy. He was second son of healthy consanguineous parents. His parents were cousins. His parents and 15 years old brother were healthy and have normal stature (his mother was 36 years old and 171 cm height, his father was 41 and 182 cm height). His mother had a history of still birth son. He was product of caesarean section at 37 weeks of gestation with birth weight of 1,700 gr, birth length 43 cm, and head circumference 32 cm. He was assessed for short stature at 5 years old, and steroid-resistant nephrotic syndrome was detected. Kidney biopsy revealed focal segmental glomerulosclerosis. He treated with prednisolone, cyclosporin, and mycophenolate for six months. There was partial remission but no response. He received tacrolimus for three months when he was ten, but no decreased in proteinuria. He had short stature, short neck and trunk, kyphoscoliosis, triangular face with round tip nose (**Figure.1**). His neurodevelopment was normal and he did well at school. His height was 113 cm (< 3% percentile), weight 22 kg (< 3% percentile). He admitted with cough, fever and abdominal pain. He was pale and lethargic. . In physical exam, blood pressure was 115/90, heart rate 90 per minute, respiratory distress symptoms and coarse crackles in both lungs. Laboratory findings were as **Table.1**. Bone marrow aspiration performed and sufficient myeloid progenitors were seen, so G-CSF prescribed for 5 days and WBC count reached to 8,000. On the third day of admission, he had fever and respiratory distress. There were patchy infiltrates in para-cardiac regions in chest X-ray (**Figure.2**). Sonography revealed crossed fused ectopia of kidneys right side with increased cortical echogenicity.Chest CT-scan showed upper zone predominance of ground glass opacities in both lungs (**Figure.3**). Unfortunately he died of sepsis and acute respiratory distress syndrome.

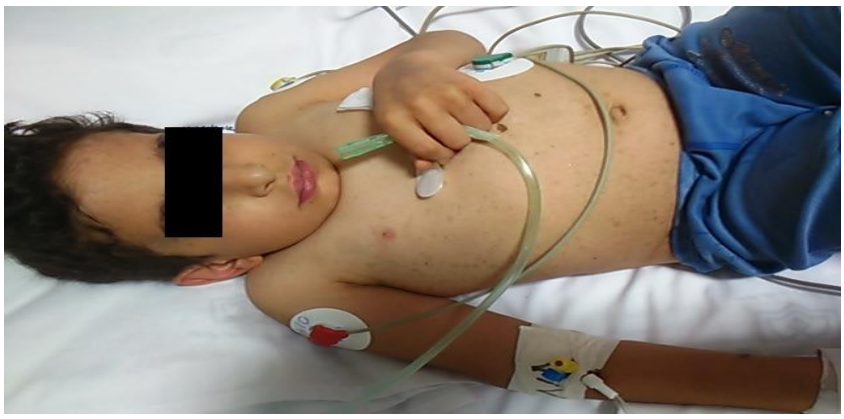

Fig.1: Eleven year old boy with short neck and trunk, triangular face, round tip nose andhyperpigmented macules.

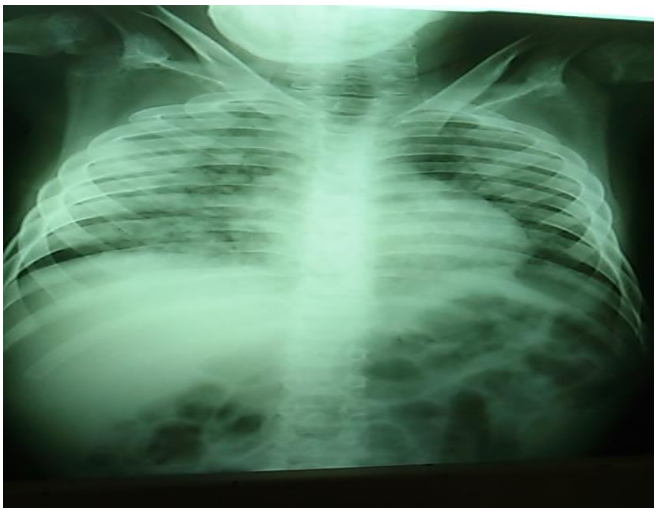

Fig.2: Chest X-ray revealed patchy infiltrates in paracardiac regions predominantly right side.

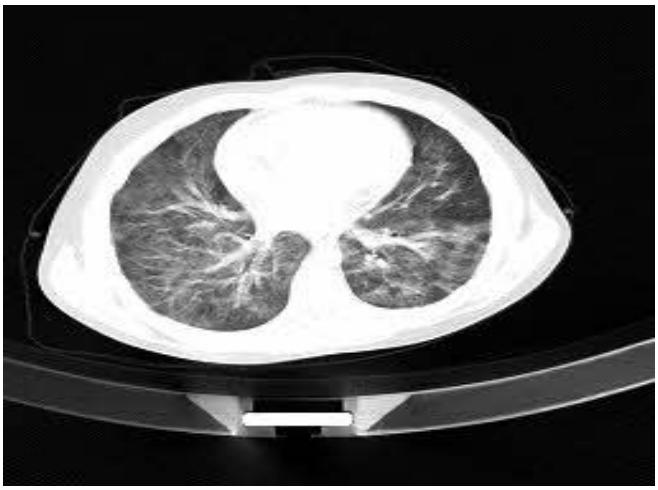

Fig.3: Chest CT-scan showed ground glass opacities in both lungs.

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3- DISCUSSION

We report a rare case of Schimke immune-osseous dysplasia (SIOD) from consanguineous parents from North West of Iran. Schimke immune osseous dysplasia is a multisystem disorder that first described by Schimke et al. as chondroitin-6-sulfate mucopolysaccharidosis with defective cellular immunity and nephrotic syndrome (1). Saraiva et al. reported 25 new cases in 1999(2) and Boerkoel et al. reported 14 cases in 2000(3), and detected mutant chromatin remodeling protein SMARCAL1 in 2002(4). Chewing proposed SMARCAL1 protein regulates proliferation of chondrocytes, lymphocytes, spermatozoa and maintenance of cardiocytes (5). Basiratnia and fallahzadeh reported two cases in South of Iran in 2007 (6). They also reported an 8 years old boy with SIOD and non-Hodgkin lymphoma (7).

The mutations SMARCAL1 (SWI/ SNF1-related, matrix-associated, actin-dependent regulator of chromatin) are responsible for SIOD. New mutations of SMARCAL1 are revealed recently. Santangelo et al. reported in missense change (P. Arg 247 Pro; Point mutation with alternation of arginine 247 residue to proline) and well-known non-sense mutation (P.Glu 848;

Point mutation of glutamine 848 residue) as a mild phenotype (8). Barraza-Garcia et al. identified a new mutation in a six years old SIOD patient with severe symptoms who died of nephropathy. The splicing alternation (point. [Leu 539-Ile 548 deletion]), causes 10 amino acids loss in HARP-ATPase catalytic domain and the RPA-binding domain (HepA-related protein-ATPase is a member of the SNF2 family of ATP-driven molecular motor proteins) (9). Lou et al. assess the longevity of 38 SIOD patients and the cause of death for 22 of them. The patients born after 1990 died of infection, bone marrow failure, and stroke. None of them died primarily of renal failure. The patients with longer survival do not manifest recurrent infections, bone marrow failure, hypothyroidism, and central nervous system symptoms. These patients had two SMARCAL1 alleles with missense mutations, whereas the patients with shorter survival had at least one null allele. They also report a 20- year- old woman with two SMSRCAL1 null alleles and severe symptoms of SIOD (10).

Boerkoelet al. also observed that some missense mutations results in retention of partial SMARCAL1 function and cause milder disease, whereas nonsense, frameshift or splicing mutations causes severe disease (4). In a cohort study, Baradaran-Heravi et al. review five SIOD patients that received bone marrow transplantation, but only one had prolonged recovery. Disorder of DNA repair causes of hypersensitivity to cytotoxic and genotoxic agents in these individuals (11).

4- CONCLUSION

Nephrotic syndrome due to focal segmental glomerulosclerosis may be accompanied by syndromes. In our province (Qazvin) we see autosomal recessive disorders more, because of consanguineous marriages. Three cases were reported from South of Iran, and we report the fourth, from North West of Iran. Cause of death in three patients was sepsis and respiratory distress, so early management of sepsis is important in SIOD.

5- ABBREVIATION

SMSRCAL1: SWI/SNF Related, Matrix Associated, Actin Dependent Regulator of Chromatin, Subfamily A Like 1,

CD4/CD8: Cluster of Differentiation 4/ Cluster of Differentiation 8,

G-CSF: Granulocyte-Colony Stimulating Factor,

SWI/ SNF1: SWItch/ Sucrose Non-Fermentable.

6- CONFLICT OF INTEREST: None.

7- ACKNOWLEDGMENT

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