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RESEARCH ARTICLE

RECURRENT PSEUDO-OBSTRUCTION OF THE LARGE BOWEL ASSOCIATED WITH SANJAD-SAKATI SYNDROME: A CASE REPORT

Dr. Mohsin Yahya Murshid and Dr. Farrukh Alim Ansari
Department of General Surgery, Hera General Hospital, Makkah, KSA.

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Abstract

Sanjad-Sakati Syndrome, also referred to as Hypoparathyroidism-Retardation-Dysmorphism Syndrome or Middle East Syndrome, was first reported in Saudi Arabia in 1988 and later in a definitive report by (Sanjad et al.) in 1991. It is a rare autosomal recessive condition reported almost exclusively in the Arab population. The condition is characterized by an extensive array of symptoms, including congenital hypoparathyroidism, severe growth and developmental retardation both intrauterine and post-natal, low Intelligence, seizures, and distinctive facial characteristics. We present an incidence of this disease characterized by repeated pseudo-obstruction. Electrolyte and metabolic disturbances, which are the cause of pseudo-obstruction of the intestine in this child, must be evaluated in order to avoid unnecessary surgical intervention, which may prove to be life threatening.

Introduction:-

Sanjad-Sakati syndrome (SSS), also referred to as Hypoparathyroidism-Retardation-Dysmorphism Syndrome (HRDS) or Middle East Syndrome, characterized by an extensive array of symptoms, including congenital hypoparathyroidism, severe growth and developmental retardation both intrauterine and post-natal, low Intelligence, seizures, and distinctive morphological characteristics such as deep-set eyes, micrognathia, thin lips, long philtrum, small maxilla, severely decayed teeth, beaked noses, depressed nasal bridges, large, floppy earlobes, small hands and feet, short stature.**(1)** Other prominent characteristics include immunodeficiency with hyposplenism and defective neutrophil function, **(2)** ocular defects such as microphthalmia, refractory errors, corneal opacities, and nystagmus, Impaired dentation with widespread carries,**(3)** as well as Endocrinopathies include hypothyroidism, cortisol deficiency, hypoglycemia, and hypogonadism**.(4)** Dermatological features such as Calcinosis Cutis has also been reported.**(5)**

Case Report

A 14-year-old girl, 5.5 kg, 60cm in height, known case of SSS, presented to the ER with abdominal distension and constipation. The patient was admitted to the General Surgery unit for further evaluation and management. The patient showed classic morphological and metabolic characteristics of SSS**.**The patient also showed signs of respiratory distress and had a history of recurring respiratory tract infections. Metabolic Abnormalities included Hypoparathyroidism, hypocalcemia, hypothyroidism and Hypokalemia. Patient was being administered L-Thyroxine supplement her Hypothyroidism. Patient was also being given calcium and Vitamin D supplements.

Corresponding Author:- Dr. Mohsin Yahya Murshid
Address**:-** Department of General Surgery Hera General Hospital, Makkah, KSA.

Upper and lower extremities showed small and thin bones. **(Figure 1)** In addition to the multisystemic features of SSS, our patient exhibits an uncommon presentation of constipation and abdominal distension coupled with metabolic abnormalities. **(Figure 2)**The patient had a long history of multiple hospitalizations due to complaint of constipation and abdominal distension since birth and was managed conservatively all throughout. The metabolic abnormalities may not be associated with the GI symptoms in every episode. There had been no definitive association between the metabolic abnormalities and the recurrent episodes of colonic distension and Constipation. One of the probable causes can be Visceral Myopathy as describe by Pal et al. **(6)** The patient did not have any complaints of vomiting and had no history and features of GERD as reported in another patient. (**7)**

Abdominal CT Findings included Small Spleen Size, Reduced Kidney size on the right side and bilateral calcifications suggesting Medullary Nephrocalcinosis. Bilateral Hydronephrosis was also seen. Basal Lung zones showed Ground Glass Veiling and bilateral atelactatic bands.

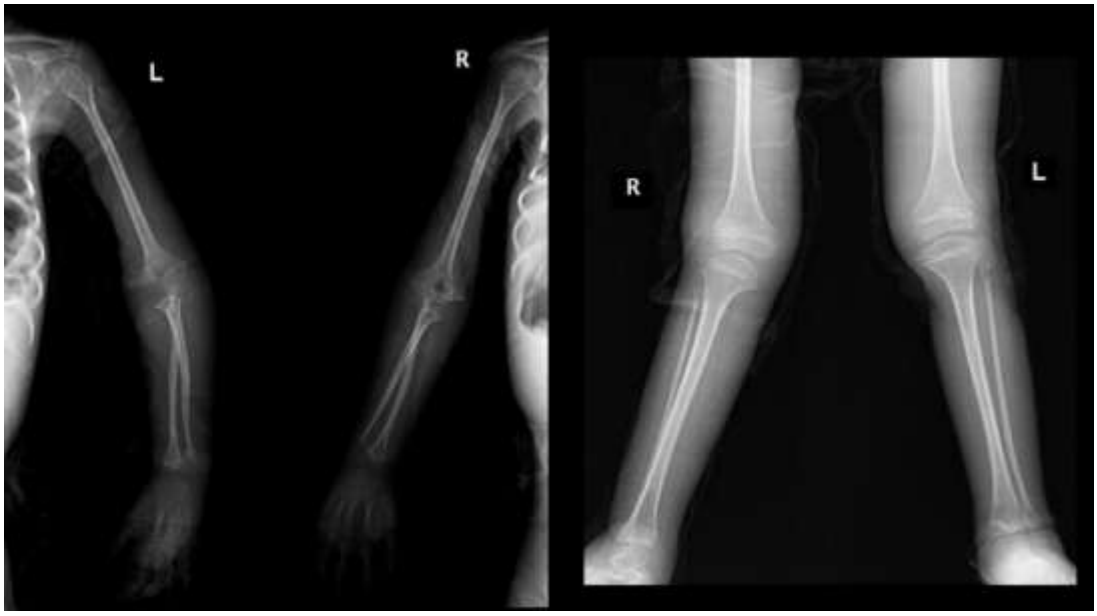

Figure 1:- Peripheral Skletal Features.

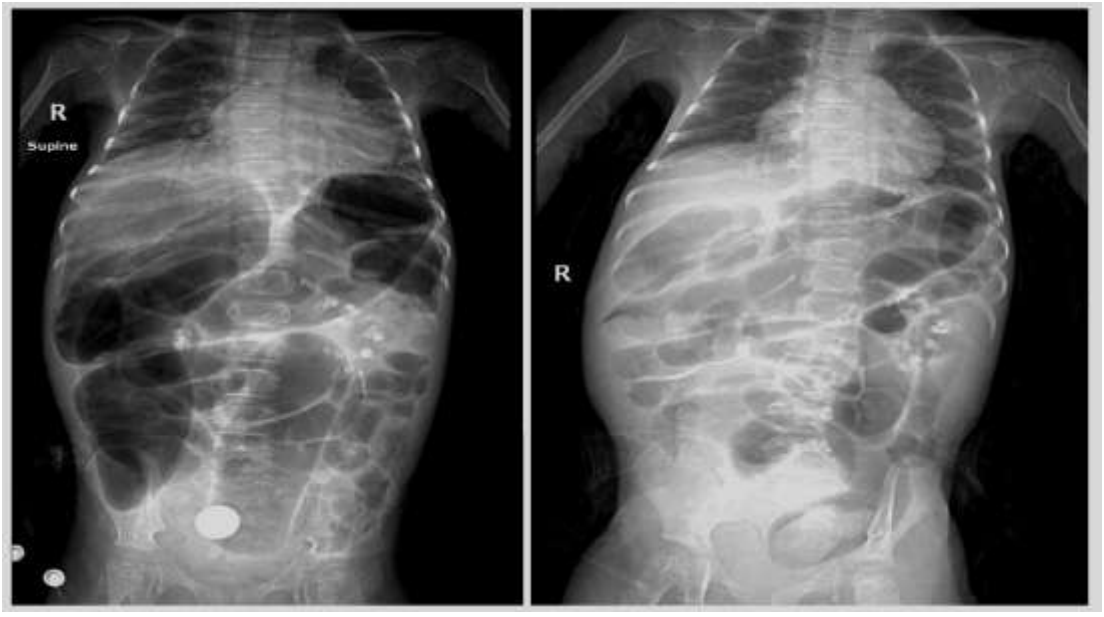

Figure 2:- Abdominal X-ray At presentation (L) and After Conservative Management (R).

The patient was treated conservatively, with IV fluids, continuous monitoring, and correction of electrolyte abnormalities. Correction of hypokalemia, combined with Glycerine suppositories and colonic irrigation, alleviated constipation and reduced abdominal distension.

Discussion:-

SSS is a rare autosomal recessive disease in Arabs caused by consanguineous marriage between heterozygous carriers of chromosome 1q42-q43 mutations that express Tubulin-specific chaperone E (TBCE), also known as "The Bedouin mutation". **(8)** Microtubule assembly requires this protein. All Middle Eastern HRD patients have a homozygous 12-bp deletion in the Tubulin-specific chaperone E (TBCE) gene. **(9)** Since the gene product is practically nonexistent in normal mature parathyroid tissue, TBCE mutations cause hypoparathyroidism through unknown molecular pathways. Some mechanisms include TBCE's role in embryonic parathyroid cell migration and other unidentified functions. **(10)** Autosomal recessive Kenny-Caffey syndrome also results from this homozygous deletion.

SSS consists of a wide variety of features involving CNS, Ophthalmic, Gastrointestinal, Metabolic, Musculoskeletal and Immune System.The most common complication of this disorder is Hypocalcemia due to severe hypoparathyroidism, while hypercalcemia occurs as result of continuous treatment with Calcium and Vitamin D Supplements, which in turn increases the risks of developing Nephrolithiasis and Nephrocalcinosis.Mild congenital anomalies of the kidney and urinary tract, hydronephrosis and once instance of unilateral multicystic dysplastic kidney has also been reported in a single center cohort study.**(11)**

Convulsions are the most common CNS symptom observed in patients with HRDS. It ranged from 63% to 93-100% in three previous cohorts. **(11,12,13)** Hypocalcemia and recurrent episodes of hypoglycemia is the main causative factor for the high prevalence of convulsions in HRD. Other factors causing for severe convulsions include brain anomalies and calcifications. The most commonly seen anomalies are Chari Malformation, Brain Atrophy and Partial agenesis of Corpus Callosum. Basal ganglia calcifications, a known complication of hypoparathyroidism is also a common finding in patients with HRDS ranging from 38% to 51%. **(11,13)**

Intestinal pseudoobstruction is a rare, severe, and disabling condition defined by repeated episodes or chronic symptoms and manifestations of bowel obstruction, including radiological evidence of a dilated colon with air-fluid levels in the absence of a fixed lumen-obstructing lesion. (**14,15)** This complication is serious and potentially lethal. Colonic Pseudo-obstruction is a rare manifestation of HRDS and has only been observed in a handful of previously described cases. **(6,7)** Pal et al. found intact extrinsic and intrinsic neuronal structures, the presence of a normal ICC, and atrophic and fibrotic muscularis propria of the small and large intestines, which suggests primary visceral myopathy as the major etiology of the pseudoobstruction. **(6)**

Constipation and abdominalpainare frequent gastrointestinal disorders. Steatorrhea can also be seen in patients with HRDS due to hypoparathyroidism. **(16)** In previously documented cases, problems such as bile salt-induced diarrhea and progressive respiratory failure **(17)**, superior mesenteric artery syndrome resulting in bowel obstruction **(18)**, gastroesophageal reflux disease, and delayed gastric emptying have also been reported.The uncommon combination of CIPO and SSS increases the risk of increased morbidity due to intestinal failure, TPN cholestasis, recurrent septic episodes, and metabolic consequences, resulting in multiple organ impairment and early death.David et al.**(11)** offer a comprehensive management and follow-up protocol.**(Table 1)**

RECOMMENDATIONS FOR HRD PATIENTS FOLLOW UP AND TREATMENT.
Infectious and immune system:
• Prophylactic antibiotic treatment with amoxicillin • Prompt antibiotic treatment during episodes of febrile illness, including gram negative bacterial coverage, especially when urinary tract abnormalities are present • Anti-Pneumococcal vaccines
Endocrine and metabolic:
• Calcium supplements and active vitamin D analogs to achieve calcium levels slightly below or in the lower range of the reference interval • Annual screening for hypothyroidism and adrenal insufficiency

Gastrointestinal and nutrition:
• A low solute and phosphor diet (e.g., breast milk and SIMILAC 60/40) • Close follow-up of bowel habits and prompt treatment of constipation
Renal:
• Annual ultrasound to screen for Nephrocalcinosis starting at age 1 year
Vision:
• Ophthalmic evaluation during the first months of life to assess treatable vision Impairments (e.g., cataracts) and further follow-up as needed
Hearing:
• An annual hearing screen during childhood to assess both conductive (due to recurrent otitis media) and sensory-neural hearing loss

Table 1:- Recommendations for HRD Patients Follow Up and Treatment (David et al.) 11.

Conclusion:-

SSS has several differential diagnoses, including Di-George syndrome, Kenny-Caffey syndrome, and familial hypoparathyroidism; however, the absence of cardiac lesion, lymphopenia, or skeletal abnormalities can aid to diagnose SSS from other disorders. The treatment consists of calcium and vitamin D supplements, as well as preventative antibacterial treatment, anti-pneumococcal vaccinations, L-Thyroxine and hydrocortisone and L-thyroxin, if indicated. The pathophysiology behind the recurrent obstructive symptoms should be kept in mind while dealing with these cases to avoid unnecessary interventions and to provide appropriate management.

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