

OSA in a Patient with Mucopolysaccharidosis MPS is (Scheie Syndrome)

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ABSTRACT

A rare case of metabolic disease – mucopolysaccharidosis in a 10 years old child with SDB is being presented. There was history of snoring, irritability and inattentiveness. Though ENT examination revealed retrognathia and a large tongue with bulky pharyngeal walls and pillars, there was no evidence of tonsils or adenoids. Polysomnography done revealed features of significant sleep disordered breathing.

Keywords: MPS : Mucopolysaccharidosis, PSG: polysomnography, OSA: Obstructive sleep apnea, AHI: Apnea hypopnea index.

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Introduction

Mucopolysaccharidosis [1] (MPS) are inherited lysosomal storage diseases which result from the deficiency of specific enzymatic activities and accumulation of partially degraded acid mucopolysaccharides. Mucopolysaccharidosis II was first described by Charles Hunter in 1917. It is an X-linked disorder and results from the deficiency of iduronate sulfatase [2]. Patients of MPS II develop thickening of the tracheal walls secondary to the accumulation of glycosaminoglycans in the cells of the trachea and may lead to obstructive airway disease.

Case history

The patient was a ten-year old boy, eldest of three siblings, having history of recurrent coughs and colds for the past eight years. There was history of snoring since the age

of five years. Over the years the parents noticed that the child was irritable and hyperactive with lacked concentration. It was also noticed that with time the child's sleep was disturbed and the intensity of snoring had aggravated. Since the age five to six years he started developing progressive stiffness in the small joints of the hands and feet besides the knees elbows and shoulders. Deformities of the hands and feet were also noticed. There were no other major illnesses and none of the other siblings had any similar malady. The child was a full time normal delivery. His milestones were delayed but had normal intelligence.

Examination revealed a young boy with coarse features, sparse hair, short stature and short neck. There was proptosis and clouding of the cornea (Fig 1). General physical examination was unremarkable. ENT examination revealed an evidence of retrognathia with a large tongue, high arched palate and bulky pharyngeal walls and pillars leading to anatomically small pharynx [3]. There was no evidence of enlarged adenoids or tonsils. Musculoskeletal system revealed a short stature, broad hands and feet, pes cavus deformity with restriction of movements of the shoulders, elbows and wrists. Thomas tests for hips were positive with mild diminution of muscle power. Cardiovascular system was normal. There was bilateral wheeze on examination of the chest. Hepatosplenomegaly was present. Visual acuity was

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Fig 1: MPS – IS (Scheie Syndrome) showing clouding of cornea, sparse hair, short stature with protuberant abdomen, short neck, retrognathia, long face & high arched palate.

reduced to 6/18 on the right eye and 6/24 on the left eye with moderate increase in ocular tension.

Laboratory parameters including liver and kidney function tests were essentially normal. Urine for mucopolysaccharide spot test (toluidine blue) was positive. Echocardiography revealed thickened aortic valve leaflets with normal LV size and function. Ultrasonography of the abdomen showed enlargement of the liver and spleen to 13.4 cms and 9.2 cms respectively with normal echo patterns. There was evidence of mild ascitis. X rays of the skull, hands & feet, hips and spine were taken (Figure 2). The child could not perform pulmonary function tests. Arterial blood gas analysis showed a PO_2 of 69.6 mm Hg, PCO_2 of 41.2 mm Hg, PH of 7.42 and HCO_3 of 22.6 mmol/l.

The child was subjected to whole night polysomnography which showed an evidence of snoring with intermittent episodes of apneas and hypopneas which were associated with significant desaturation. The minimum saturation noted was of 89%. The apnea, hypopnea index was 3.5 per hour. Scoring was done according to the criteria layed by the American Thoracic Society standards [20] and recommendations of Shimrit et al[17] Fig 3.

Review of literature and Discussion

Mucopolysaccharides consist of glycosaminoglycans attached to a link protein with a hyaluronic acid core. Defective activity of the lysosomal enzymes blocks the

degradation process of mucopolysaccharides, leading to abnormal accumulation of heparan sulfate, dermatan sulfate, and keratan sulfate. The accumulation of these compounds interferes with cell function. These degradation by-products are then secreted and detected in the urine. Their clinical presentations are varied depending on the type of enzyme defect and glycoprotein accumulated [4].

Mucopolysaccharidosis (MPS) can be subclassified according to the type and amount of substance that accumulates, as follows: Hurler syndrome (MPS IH), Hurler-Scheie (MPS I-H/S), Scheie syndrome (MPS IS), Hunter syndrome (MPS II), Sanfilippo syndrome (MPS III), Morquio syndrome (MP IV), Maroteaux-Lamy syndrome (MPS VI), and Sly syndrome (MPS VII).

Patients with MPS have normal development initially. Abnormalities are seen in infancy or sometimes in childhood. Clinical features show evidence of multiple organ system involvement like those of locomotor, cardiovascular, eye, auditory system and CNS involvement. The respiratory system is involved producing obstructive airway disease. It is caused by narrowing of trachea and bronchial airways, thickened vocal cords and redundant tissues in the upper airways. These characteristics can cause problems ranging from sleep apnea to severe respiratory compromise and cor pulmonale including OSA [1,4]. OSA has been reported as a feature of children with MPS.

There are differences in severity of OSA between the different MPS types. In one study [6] conducted to



Fig: 2 X-ray hands and feet showed proximal and distal narrowing of metacarpals. Skull X-ray showed features of increased intracranial tension [copper beaten appearance and sutural diasthesis with flattening of sella (J shaped)]. X-ray hips: showed flattening of the acetabular roof.

measure objectively the degree of OSA in a group of children with a range of MPS syndromes it was found that OSA was present in 24/26 patients, and ranged in severity from mild to severe. OSA was most marked in MPS type IH (Hurler syndrome) followed by types IHS (Hurler—Scheie syndrome) and II (Hunter syndrome) [5]. Frequent arousals and poor sleep quality, not suspected clinically, were noted in several patients.

Taking into account the data from literature [7, 8], the prevalence of sleep apnoea in MPS could be estimated at 40% of patients, which is at least ten times the

prevalence rate in the general population [9]. There are many factors in various types of MPS favouring the development of OSAS, such as craniofacial abnormalities with reduction in the size of the nasopharynx, hypertrophy of the tonsils and the adenoids, macroglossia, thickening of the epiglottis, diffuse infiltration of the soft tissue of the pharynx and the larynx, with hypertrophic tissue obstructing the airway and oedema of the vocal cords, which may even occlude the glottis [10,11]. Tracheomalacia may lead to narrowing of the trachea in the anteroposterior plane [12, 13]. Reduction

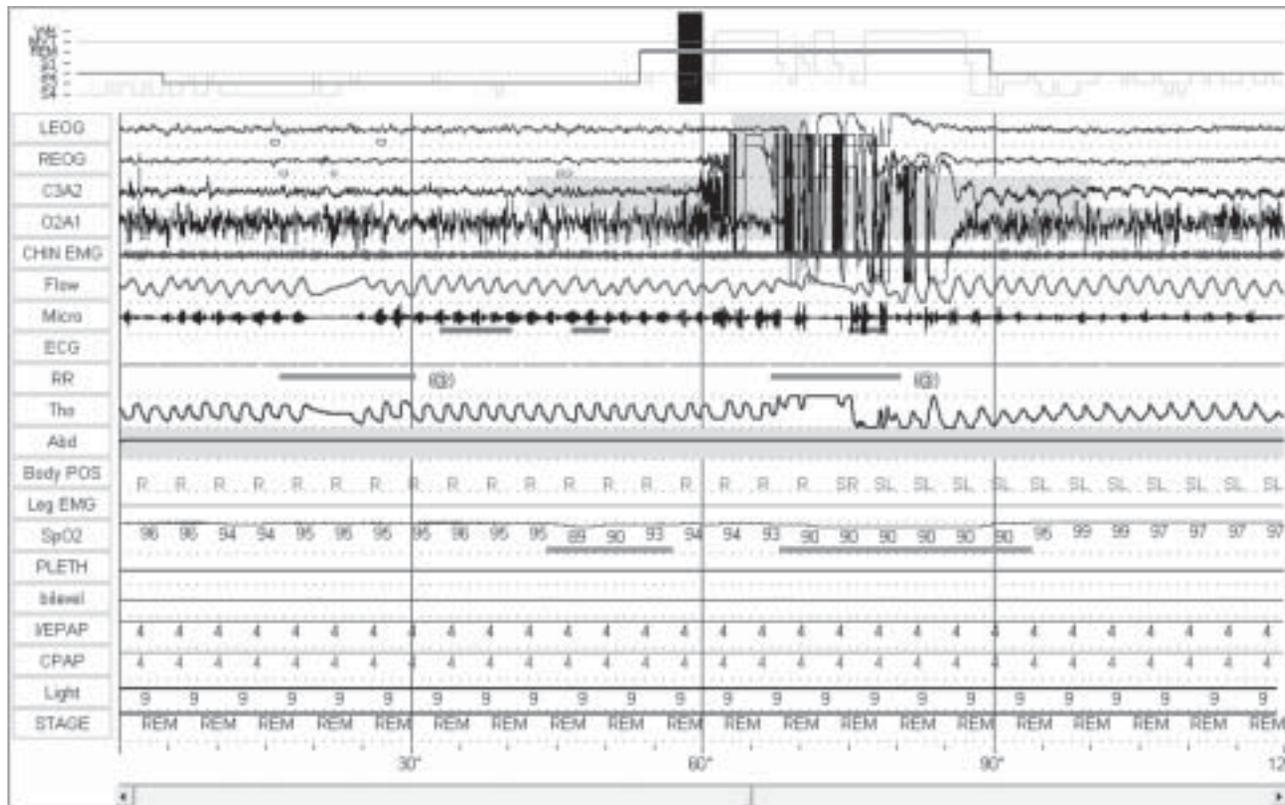


Fig 3: PSG demonstrating snoring, episodes of apneas with arousals and drop in saturation

in lung volumes may also favour the collapse of the UA [14].

Our subject showed several similarities to MPS IS, (Scheie syndrome) one of the mildest forms of MPS. Typically the symptoms had begun to appear around 5 years of age. Like most children with Scheie syndrome he had a fairly normal intelligence with mild learning disabilities. He also had glaucoma, retinal degeneration and clouded corneas with impaired vision. Like in Scheie syndrome he had stiff joints, claw hands, deformed feet, short neck and aortic valve involvement with features of anatomically small pharynx with features of obstructive airway disease. Patients with Scheie syndrome could live till adulthood [1,15].

Assessment of the severity of OSA on clinical history is inadequate. PSG is necessary for evaluation of children with disordered breathing, and to monitor the effects of therapeutic interventions.[15]

Sleep disordered breathing in children may manifest mainly as hypopneas and continuous hypoventilation with only partial cessation of airflow, making it difficult to

diagnose OSA in some children. Our subject demonstrated episodes of apneas and hypopneas of approximately 3.5 AHI/hour. The normal recommended apnea index (AI) in children is less than ≤ 1 /Hr.[17,19]. Episodes of complete airway obstruction are relatively uncommon in children with sleep related upper airway obstruction.[20,16,21,22]. Because complete airway obstruction is relatively uncommon, monitoring carbon dioxide levels (end tidal CO_2 – Pet- CO_2) is recommended with values above 45 mm hg being significant.[17,23]. However, because of technical reasons it could not be done in our subject,

Normal values of nocturnal haemoglobin saturation by various workers are $97.2 \pm 0.8\%$ [17], $97.1 \pm 0.6\%$ [24], $96.0 \pm 2\%$ [18] and 98% with intermittent falls of $>4\%$ [25]. The fall in SpO_2 of up to 89% in our subject with an AHI of 3.5/Hr is suggestive of significant obstructive sleep apnea.

There is data to suggest that even mild SDB and even “primary snoring” are risk factors for neurocognitive defects [26,27,28]. Therefore, in our subject the evidence of significant sleep disordered breathing is likely to be

contributing to the child's neurocognitive defects.

So to conclude, our patient who is a case of MPS I S Scheie syndrome had a significantly narrowed upper airway due to deposition of mucopolysaccharides producing classical clinical & polysomnographic features of obstructive sleep disordered breathing.

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