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Medicine

"PRADER-WILLI SYNDROME – PRESENTATION OF AN EXCEPTIONAL CASE"

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ABSTRACT We report a case of a 29 year old male patient who presented to us with difficulty in breathing since 3months more since 10 days; cough and fever since 7 days. He also had excessive day time sleepiness, morbid obesity, hypotonia and underdeveloped secondary sexual characters along with features of diabetes mellitus and hypopituitarism. Based on thorough clinical examination and blood investigations, a diagnosis of Prader Willi Syndrome was made.

KEYWORDS : - prader willi syndrome, congenital obesity, methylation studies, bilateral pneumonitis.

INTRODUCTION:

Prader Willi syndrome is the most common congenital disorder leading to obesity[1]. It occurs with an incidence of 1:10,000 to 30,000 births. In the general population approximately 60 people in every 1,000,000 are affected. Prader willi syndrome is a genomic imprinting disorder caused by deficiency of paternally expressed gene or genes on chromosome 15 (15q11.3-q13.3 region). Prader Willi syndrome is characterized by hypotonia, daytime sleepiness, irritable behavior, mental retardation, dysmorphic features, short stature and excessive appetite with progressive obesity. Most patients also have endocrine dysfunction like hypogonadotropic hypogonadism suggesting hypothalamic pituitary dysfunction[4]. Here we report this case of Prader Willi Syndrome due to its rarity.

CASE REPORT:

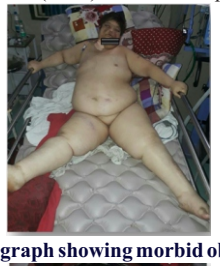
A 29 year old male patient was referred to us from private hospital for difficulty in breathing, cough and fever. Breathlessness was not relieved on taking rest, cough was non-productive and his fever was low grade. There was no associated history of chest pain, hemoptysis, pedal edema or noisy breathing. He was a known case of Diabetes and Hypertension on treatment since 6 years of age. He had never attended school because of mental retardation. His orchiedectomy was done in childhood for undescended testis. He had significant family history as his mother had Diabetes and Hypertension & his father had Hypothyroidism.

On examination, he was morbidly obese (Pic. 1), drowsy, disoriented to time place and person. He had typical facies with flat nasal bridge, upturned nose, thin upper lip and smooth philtrum. (Pic.2)He was febrile, with a pulse of 114/min, regular, good volume; Blood pressure of 110/70mmHg and respiratory rate was 26/min. His accessary muscles of respiration were working indicating severe respiratory distress. Systemic examination revealed crepitations and rhonchi allover lung field bilaterally, abdomen was soft and distended, CNS examination showed gross hypotonia in all 4 limbs, normal deep tendon reflexes and flexor plantars; CVS:S1, S2 normal.

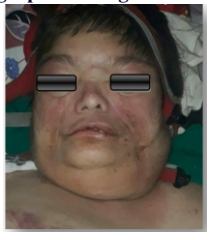
His investigations revealed-

- Hb-10, PCV-30, TLC-16000, Platelets-1.5 lacs.
- Urea-19, Creatinine-0.8, Na+-149, K+- 3.7.
- Bilirubin-0.7, Alkaline PO4-520, SGOT-24, SGPT-36.
- Peripheral smear was normal and CRP-31.16.
- T3- 83.28, T4- 8.1, TSH- 1.381.
- ECG- Within Normal Limit.
- Chest XRay PA view- bilateral patchy opacities allover lung fields s/o ARDS (Pic.3), which was proved on ABG report having PH-7.5, PCO2-52.2, PO2-54, HCO3-44.2, SO2-90% and PO2/FiO2=90%.
- His 2D echo was absolutely normal.
- His sputum culture showed Klebsiela Pneumonie which was resistant to Amikacin, Ceftazidime, Cefotaxime, Meropenem, Piperacillin-Tazobactum.
- His MS-PCR Report demonstrated an abnormal methylation pattern consistent with absence of the paternally derived copy of the PW/AS critical region.

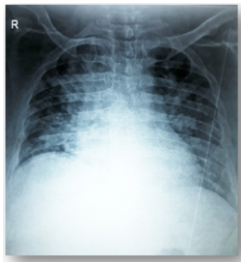
Based on all the above clinical features and investigations, a diagnosis of Prader Willi Syndrome (PWS) with bilateral pneumonia was made.



Pic. 1 Clinical photograph showing morbid obesity.



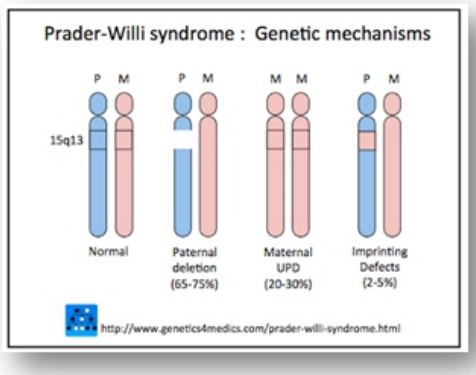
Pic. 2 Photograph showing characteristic dysmorphic facial features.



Pic.3 Chest X Ray showing bilateral patchy opacities

DISCUSSION:

Prader Willi syndrome is a hereditary disorder associated with genomic imprinting, was originally described by by Prader and associates in 19561. Several mechanisms of Prader Willi syndrome include (a) a paternally derived large deletion of 15q11-q13, accounting for 70% of all patients. (b) a maternal uniparental diasomy, accounting for approximately 20%-25%. (c) a defect in the genomic imprinting mechanism, about 2%-4%. And (d) other rare reasons, such as chromosome translocation and microdeletion, less than 1%2.



Patients of PWS usually develop Respiratory failure due to morbid obesity and secondary bacterial infections. Obesity in PWS is a consequence of hyperphagia which is due to a dysfunctional hypothalamic-pituitary axis, leading to voracious eating. Sleep disorders, like excessive sleeping and obstructive sleep apnoea (OSA), are another type of problem seen in PWS. PWS patients have poor muscle coordination and poor gag reflex. These characteristics together with obesity play a key role in respiratory failure[3].

Impaired respiratory function is frequently observed in patients with Prader-Willi syndrome. Cassidy *et al.* found that seven of eight affected individuals over the age of 30 yr had restrictive lung disease[1], and Laurance et al. reported that cor pulmonale was the most common cause of death among nine patients with this condition. A further complication seen in affected patients with reduced lung function is hypercapnia. Until recently, this was thought to be a secondary effect of respiratory muscle weakness or the result of Pickwickian syndrome brought about by increased abdominal and thoracic fat. However, investigators have now found that affected individuals have an impaired response to short periods of hypercapnia and a reduced ventilatory volume, indicating that the sensitivity of peripheral chemoreceptors to changes in blood oxygen and carbon dioxide is decreased. Thus, it seems that impaired respiratory function in Prader-Willi syndrome is not caused solely by obesity or muscle weakness.

Restriction of growth is also frequently observed as a sequel of PWS, approximately 90% of affected individuals are short in stature.

During early childhood, children with PWS fail to achieve normal levels of cognitive, motor and language development. Borderline mental retardation was observed in 28% of patients while 34% were mildy,27% moderately and 5% were severely mentally retarded as reported by Burman et al. There is also high incidence of stubbornness, verbal perserverance, skin picking and temper tantrums. Furthermore affected individuals have a tendency toward depression and a diminished ability to initiate and maintain social contacts[4].

A number of reports suggest that glucose tolerance is abnormal in individuals of PWS. In a study by Burman et al, involving 23 patients aged 15-41 year, 17% had diabetes mellitus, the majority of whom required insulin therapy4. A high incidence of type 2 diabetes mellitus in adults with PWS was also shown by Cassidy et al., who studied 22 individuals aged 30–55 yr over a period of 1–12 yr. Nine of the patients (41%) developed diabetes mellitus[1].

Muscular hypotonia is more characteristic of infancy. All of the cases described by Zellweger and Schneider (1968) learned to walk between the ages of 2 and 4. When the children become active enough to forage for food, the main clinical problem becomes obesity and its consequences.[5]

Our case had all the clinical features described in the literature and his MS-PCR studies were positive for PWS. Thus a diagnosis of Prader Willi Syndrome with bilateral pneumonia was made. He was started on higher antibiotics and continuous NIV support was given. But despite of all the overzealous efforts he could not improve and has continued living on home NIV support.

SUMMARY:

Prader Willi Syndrome is a rare genetic disorder. A high degree of suspicion is required in every case of congenital obesity. Our patient had morbid obesity, dysmorphic facial features, ambiguous genitalia, hypotonia, diabetes mellitus and hypothyroidism based on which he was diagnosed to have Prader Willi Syndrome.

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