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Prader-Labhart-Willi Syndrome: A Report on 22 cases

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The present study reports the clinical aspects of a series of 22 patients with Prader-Labhart-Willi syndrome. Apart from the classical features of obesity, hypotonia, short-stature, hypogonadism and mental retardation, a wide range of other features were observed, the commonest being fish-shaped mouth, almond-shaped eyes and acromicria, which may be important for differential diagnosis.

Key words -
Prader-Willi syndrome

Prader, Labhart and Willi described in 1956 a syndrome of obesity, short-stature, cryptorchism and mental retardation, with muscular hypotonia in early infancy [1]. Dunn [2] reviewed the literature and reported 9 new cases. Many of these patients have a typical appearance due to their obesity, which mainly affects the trunk and the proximal part of the limbs, with small hands and feet, and a triangular mouth with downturned corners (shark-mouth).

The disorder proceeds through 2 phases in its clinical course [3]. The earliest feature is diminished foetal movements towards the end of pregnancy. Ten to 40 % of the patients present by the breech. The mean birth weight is less than average. However, with the onset of the second phase after a few months or years, the patient develops constant, painful hunger, and seeks food constantly, resulting in marked obesity. It often leads to life-threatening cardio-respiratory difficulties and hypercapnia, and occasionally, even a stomach perforation due to over-eating [3].

Intelligence may range from borderline or mild to profound mental retardation, with IQ ranging from 20-90 [3]. Speech is delayed more than motor development. These children are often goodnatured and cheerful, but lack drive and initiative, and are unable to control emotions [3], [4].

Life expectancy is decreased and few patients survive beyond the age of 40 years. Death occurs due to respiratory insufficiency of complications or diabetes mellitus which develops as the age progresses. Prader-Willi syndrome (PWS), as this disorder is now commonly known, manifests a variety of other features, the number and frequency of which were studied in a large series of patients by the authors.

Material and Methods

The present study comprises a part of the findings of a wider study of 22 patients with PWS who presented at the mental retardation clinic at the National Institute of Mental Health & Neuro Sciences, Bangalore . The diagnosis was based on the typical history and the classically described features of PWS (obesity, short-stature, hypogenitalism, mental retardation and hypotonia) (Figure 1). All the patients underwent a detailed physical examination and investigation as part of their evaluation. An analysis of these forms the basis of this study. The genetic aspects shall be covered in a separate paper.

Fig. 1. Obesity & hypotonia

Results

Twelve of the patients were male and 10 female. Their age ranged from 1 year to 30 years (mean 8.95 years). Apart from the classical features of PWS (hypogenitalism and hypotonia were not found to be universal), a wide range of less common and or less noticeable features were found to occur with a varying frequency. These are presented in the Table 1.

Table 1 - Clinical features of Prader-Labhart-Willi syndrome - (N=22)

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Figures in parentheses indicate percentages

The most common physical features observed were fish-shaped mouth, almond-shaped eyes, acromicria, malformed ears, retarded speech, higharched palate, microdontia and enamel hypoplasia, strabismus, genu valgum, and narrow hands and feet - all present in over 50 % of the cases - in decreasing order of frequency. The least common were coloboma and narrow fingers, which none of the patients had (but are frequently present in Cohen syndrome, which constitutes an important differential daignosis). Other rare features - in increasing order of frequency - were mottled retinal pigmentation, open mouth, prominent central incisors, myopia/ microphthalmia, cubitus valgus, slanting eyes, short upper lip with long philtrum, hyperextensible joints, high nasal bridge, simian crease and narrow external ear canal.

Feeding difficulties in infancy (13 patients), diabetes mellitus or an abnormal glucose tolerance curve (12 patients), and retarded bone age (9 patients) were frequent. Low gonadotropin levels were present in 5 patients, and a deletion on the long arm of chromosome 15, in 4 instances.

Discussion

A survey of the clinical findings in a fairly large sample of patients assumes a special importance from the point of view of the differential diagnosis of PWS from other 15q deletions with non-classical PWS phenotypes [5], and Cohen syndrome, which shares many characteristics such as obesity, mental retardation, short-stature, hypogenitalism and hypotonia, with PWS. The differentiation in this case rests more on the other associated symptoms and signs. This also applies to those cases of 15q deletions who show a non-PWS phenotype with a variable degree of overlap with PWS [5]. It may also be of interest to correlate these phenotypic variations with the size and nature of the deletion [5].

Despite the male:female ratio of about 2:1 in most published studies, PWS is generally thought to be evenly distributed between the sexes [3], a finding consistent with the present study, where the ratio is 1.2:1. Obesity in PWS is a result of gross over-eating, coupled with a dysfunctional insulin which increases the lipogenesis, and also leads to the abnormal glucose tolerance curves. The treatment of obesity remains extremely difficult, but some results have been claimed with nutritional behaviour modification, and a modified protein-sparing diet. Gastric bypass or gastroplasty may have to be resorted to occasionally [3]. Appetite reducing drugs may be effective only for a short period.

Gonadotropin levels are usually low in PWS, a finding seen in 5 of the patients in the present series. They may be rarely elevated [3]. Reproductive potential is severely impaired, with diminished or absent spermatogenesis in males and primary amenorrhoea or anovulatory cycles in females. Pre-pubertal growth spurt may not occur, and secondary sex characters are poorly formed. In exceptional cases, prolonged treatment with Clomiphene may lead to normal spermatogenesis [3].

1.Prader A, Labhart A & Willi H, Ein Syndrom von Adipositas, Kleinwuchs, Kryptorchismus and Oligophrenie nach myatonieartigem Zustand in Neugeborenealter
Schweiz Med Wochenschr Page: 86: 1260, 1956
2.Dunn H G, The Prader- Labhart-Willi syndrome : review of the literature and report of 9 cases
Acta Paediatrica Scandinavica Page: (Suppl), 186: 1-38, 1968
3.Zellweger H, Prader-Willi syndrome
In : Vinken P J & Bruyn G W (Eds) : Handbook of Clinical Neurology, Amsterdam, North Holland Publ Page: Vol.43, pp. 463-464, 1982
4.Smith D W., Recognizable patterns of human malformation : Genetic, embryologic and clinical aspects
In : Schaffer A J (Ed.) Major Problems in Clinical Paediatrics, Philadelphia, W B Saunders Co Page: 2nd edn., Vol. 7, 1976
5.Schwartz S, Max S R, Panny S R & Cohen M M, Deletions of proximal 15q and nonclassical Prader-Willi syndrome phenotypes
American Journal of Medical Genetics Page: 20 255-263, 1985