LAURENCE-MOON-BIEDL SYNDROME*

BY

D. RAM AND J. N. ROHATGI

Department of Ophthalmology, Medical College, Patna, India

THE syndrome, consisting of obesity, hypogenitalism, polydactyly, mental retardation, and retinal changes of the retinitis pigmentosa type, is recognized as a clinical entity. It is, however, unusual to find all the manifestations of the syndrome in a single case. The case described here is interesting in that it presented as a complete syndrome.

Case Report

A boy aged 10 years was brought to the children's out-patient department of the Patna Medical College Hospital on account of his abnormal flabbiness and mental deficiency. In addition he had not been able to see very well for some time, particularly at night.

He was the third child of his parents, who were healthy and not consanguineous. The family, traced to four generations on the father's side and three on the mother's, was essentially normal with no history of consanguinity. Two children, a brother and sister, had died in infancy, and as far as could be ascertained showed no ocular or general manifestations of the syndrome. The patient's surviving sister was 12 years old and normal in all respects. His younger brother was aged 4 years, was quite intelligent, but had supernumerary fingers—seven on the right hand, and six toes on both feet. His ocular and general examinations revealed no other abnormality.

Examination.—The patient was obese, and of short stature (height 3 ft 4 in.), and weighed 8 stone. He was dull and listless, and had not started speaking until the age of 5 years.

There was a marked accumulation of fat in the abdominal wall, thighs, hips, and shoulders. Breast and abdomen were pendulous. The genitalia were under-developed with testis descended in scrotum. A supernumerary finger was attached to the little finger of each hand and the right little toe.

Ophthalmic Examination.—There was a fine horizontal nystagmus more marked in darkness. The visual acuity in both eyes was reduced to counting fingers at one metre only. The patient walked unaided in the day, but found great difficulty at night or in darkness and often had to be guided.

The extra-ocular muscles were normal and the pupils were normal in size and reactions. The ocular media were clear.

Fundus Oculi.—Both discs were pale and waxy-looking with a normal physiological cup. The retinal arteries showed marked attenuation, many appearing as mere threads. Pigment was irregularly distributed all over the fundus with no preference for the equatorial or macular areas. The pigment deposits were varied in size and shape and arranged

* Received for publication February 21, 1957.

in small patches, showing no similarity to the so-called "bone-corpuscle" arrangement typically seen in cases of retinitis pigmentosa. The central nervous system and hearing were normal.

Laboratory Investigations.—Routine blood examinations, including erythrocyte sedimentation rate and blood sugar within normal limits. Wassermann reaction negative.

Glucose tolerance test normal. No sugar in urine.

X rays showed no evidence of any abnormality or decalcification.

Electrocardiogram: sinus arrhythmia.

Discussion

Höring (1864, 1865) and Stör (1865) described cases of retinitis pigmentosa associated with polydactyly, but did not call attention to the possible existence of a new syndrome. Laurence and Moon (1866), considering four cases of retinitis pigmentosa associated with other unusual anomalies, including obesity, hypogenitalism, and mental deficiency, first described this new clinical entity. Their four cases all belonged to the same family of ten children, of whom two died in infancy, four were healthy, and the remaining four were afflicted with visual and general bodily disturbances.

Bardet (1920) further correlated these cases of adiposo-genitalism and retinitis pigmentosa with polydactyly, but did not mention mental deficiency and the familial incidence of the syndrome. These components were added by Biedl (1922), who described two cases in one family.

Burn (1950), in describing two families presenting this syndrome, reviewed the literature exhaustively and tried to ascertain how far deafness could be fitted into the syndrome. He found that of a total of 611 members of affected sibships (in 178 family groups), eighteen were deaf, giving an incidence of 2.94 per cent. (sixty times greater than the percentage of deaf in the general population). These figures strongly suggest that deaf-mutism does not occur merely by chance in the Laurence-Moon-Biedl syndrome but is in some way related to it.

Very many concomitant anomalies associated with this syndrome have since been described both by pediatricians and ophthalmologists. These include:

- (a) *Eye.*—Nystagmus, microphthalmos, myopia, strabismus, and posterior polar cataract.
- (b) *General.*—Congenital heart disease, bilateral genu valgum, bilateral hydro-nephrosis, hypospadias, hypothyroidism, diabetes insipidus, decreased carbohydrate tolerance, tetany, dwarfism, external ophthalmoplegia, and bilateral ptosis (Sussman, 1951).

The Laurence-Moon-Biedl syndrome is not very common. According to Radner (1940), only 200 cases had been reported up to that date. A review of the literature from 1940 to the present day has yielded about eighty more cases (Gantayan and Suryaprasadarao, 1952; Agarwal, 1953; Bergman and Eden, 1954; Wolff and Etzine, 1955). Thus, 280 cases have been reported, in only a fraction of these has the complete syndrome been described, and

of the 102 patients on whom data were tabulated by Warkany, Fraumenberger, and Mitchell (1937), only 24 exhibited the complete syndrome.

The onset of the condition occurs in early life and may be detected even before the child reaches school age. The family history is generally negative although some workers have reported alcoholism and mental instability in the family. Consanguinity has varied from 14 per cent. (first cousins) to 23 per cent. (first and second cousins).

The night blindness and the progressive limitation of the visual fields are well-known characteristic symptoms. Although the fundus typically shows a marked attenuation of the vessels, with pigmentary changes of the "bone-corporuscle" type, Cockayne, Krestin, and Sorsby (1935), Sorsby (1941), Ellis and Law (1941), and Taylor (1947) have reported that the range of fundus appearances extends to at least four types: typical retinitis pigmentosa; atypical retinitis pigmentosa with increased pigmentary disturbance in the central area of fundus rather than the periphery; macular dystrophy; atypical retinitis pigmentosa combined with macular dystrophy.

Polydactyly is a hereditary mesoblastic fault or maldevelopment, but the remaining components are ectoblastic in origin and possibly of an abiotrophic nature. The seat of the neuro-ectodermal disturbance is thought to be in the forebrain (prosencephalon) from which develops the optic vesicle to form the nervous and pigmentary layers of the retina.

Bauer (1927) thought polydactyly was dominant and pointed out that it sometimes skipped a generation and was independent of the retinal and cerebral changes which were recessive. Sorsby, Avery, and Cockayne (1939), however, disagreed with this view and put forward two main theories to explain the syndrome:

- (1) That one gene produced all the signs and the incompleteness of the syndrome was due to the action of modifying genes, secondary mechanical effects, endocrine disturbances, etc. (Franceschetti, 1930; Franceschetti and Streiff, 1936; Stroesco, 1936; van Bogaert, 1938).
- (2) That the syndrome was determined by two or more genes (Bauer, 1927; Rieger and Trauner, 1929; Savin, 1935; Cockayne and others, 1935; Sorsby and others, 1939).

Reiger and Trauner (1929) thought that the mesoblastic and epiblastic parts of the syndrome were recessive and due to mutations of two genes in the same chromosome, one causing the abnormalities of the ectoderm and the other of the mesoderm. According to Sorsby and others (1939), this combination of ectodermal and mesodermal defects makes it more likely that two recessive genes in the same chromosome determine the syndrome, or that it is dependent on some chromosomal error such as dislocation or translocation. Macklin (1936) suggested that there were two genes, one dominant and autosomal and the other recessive and sex-linked. She thought that two recessive genes in an autosome could not account for the high ratio of affected to normal children or for the great excess of the males.

Summary

A classical case satisfying the five cardinal diagnostic criteria of the Laurence-Moon-Biedl syndrome, as suggested by Warkany and others (1937), is described. An additional interesting fact is that the younger brother of the case was otherwise normal except for polydactyly.

REFERENCES

- AGARWAL, L. P. (1953). *J. Indian med. Ass.*, **22**, 467.
 BARDET, G. (1920). Thèse de Paris, No. 470.
 BAUER, J. (1927). "Innere Sekretion", p. 314. Springer, Berlin (cited by Sorsby and others, 1939).
 BERGMAN, B., and EDEN, A. N. (1954). *J. Pediat.*, **45**, 603.
 BIEDL (1922). *Dtsch. med. Wschr.*, **48**, 1630 (cited by Duke-Elder, 1940).
 BURN, R. A. (1950). *Brit. J. Ophthal.*, **34**, 65.
 COCKAYNE, E. A., KRESTIN, D., and SORSBY, A. (1935). *Quart. J. Med.*, **28**, 93 (n.s. 4).
 DUKE-ELDER, S. (1940). "Text-book of Ophthalmology", vol. 3, pp. 2765-2783. Kimpton, London.
 ELLIS, R. W. B., and LAW, F. W. (1941). *Arch. Dis. Childh.*, **16**, 105.
 FRANCESCHETTI, A. (1930). In "Kurzes Handbuch der Ophthalmologie", ed. F. Schieck and A. Brückner, vol. 1, p. 793. Springer, Berlin (cited by Sorsby and others, 1939).
 ——— and STREIFF, E. B. (1936). *Klin. Mbl. Augenheilk.*, **97**, 688 (cited by Sorsby and others, 1939).
 GANTAYAN, S. N., and SURYAPRASADARAO, H. (1952). *J. Indian med. Ass.*, **21**, 367.
 HÖRING (1864). *Klin. Mbl. Augenheilk.*, **2**, 233 (cited by Duke-Elder, 1940).
 ——— (1865). *Ibid.*, **3**, 236 (cited by Duke-Elder, 1940).
 LAURENCE, J. Z., and MOON, R. C. (1866). *Ophthal. Rev.*, **2**, 32.
 MACKLIN, M. T. (1936). *J. Hered.*, **27**, 97.
 RADNER, S. (1940). *Acta med. scand.*, **105**, 141.
 RIEGER, H., and TRAUNER, R. (1929). *Z. Augenheilk.*, **68**, 235 (cited by Sorsby and others, 1939).
 SAVIN, L. H. (1935). *Brit. J. Ophthal.*, **19**, 597.
 SORSBY, A. (1941). *Ibid.*, **25**, 524.
 ———, AVERY, H., and COCKAYNE, E. A. (1939). *Quart. J. Med.*, **32**, 51 (n.s. 8).
 STÖR (1865). *Klin. Mbl. Augenheilk.*, **3**, 23 (cited by Duke-Elder, 1940).
 STROESCO, G. (1936). *Presse méd.*, **44**, 1747 (cited by Sorsby and others, 1939).
 SUSSMAN, I. (1951). *Arch. Ophtal. (Paris)*, n.s. **11**, 661 (cited by Thygeson, 1952).
 TAYLOR, D. (1947). *Brit. J. Ophthal.*, **31**, 211.
 THYGESON, P. (1952). *Amer. J. Ophthal.*, **35**, 750.
 VAN BOGAERT, L. (1938). *Z. menschl. Vererb.-u. Konstit.-Lehre*, **21**, 314 (cited by Sorsby and others, 1939).
 WARKANY, J., FRAUENBERGER, G. S., and MITCHELL, A. G. (1937). *Amer. J. Dis. Child.*, **53**, 455.
 WOLFF, J. E., and ETZINE, S. (1955). *S. Afr. med. J.*, **29**, 280.