REPORT ON TWO PAIRS OF BROTHERS SHOWING MARFAN'S SYNDROME*

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Two pairs of brothers were observed in the Out-Patient Department of the Hadassah University Hospital, Jerusalem, who showed Marfan's syndrome—arachnodactyly with subluxation of the lens.

Family history.—Both parents were healthy. The mother was of a pyknic type, 35 years of age, and had given birth to 5 living children. No miscarriage or abortion. The father was 38 years of age, had never been ill, was a rather asthenic type and resembled the two oldest sons who are to be discussed here. The grandparents had all good vision, and were either living or had died in old age. Two younger sisters and one younger brother, aged 5, 4, and 1 year respectively, had normal eyes and did not show any abnormalities.

The oldest brother, M.L., was 14½ years of age. His height was 129 cm. (the normal height for his age is 150 cm.). He was undeveloped, had a feeble musculature, meagre subcutaneous tissue, and showed hypogenitalism, right cryptorchism and very small left testicle with scanty pubic hair. The thyroid was not palpable.

Heart and blood vessels:—Heart margins normal, pure sounds. Frequent extra-systoles. Marked hypertrophied veins on the chest. B.P. 95/75.

Lungs: N.A.D. *Abdomen:* Liver and spleen not enlarged. C.N.S.: Brisk reflexes.

He had a typical bird face with receding forehead and chin, and high tower palate. The skin of the face was dry and wrinkled; facies senilis. The limbs as a whole and especially the fingers and toes were very long and slim. The radiographs of the limbs showed a particular gross design of the trabeculae in a form which is frequently encountered in persons with endocrine disturbances. (cretins). The spine and the skull were normal, but the sella turcica was very small and showed a bony bridge connecting the anterior and posterior clinoid processes.

The basal metabolism was increased by 18.5 per cent.

Eyes: Visual Acuity R.E. 6/24; with -5.0 D.Sph.: 6/12. L.E. 6/24; with -5.0 D.Sph. -1.0 D.Cyl. 180 deg.: 6/12. Field of vision: slight bitemporal restriction of about 20 deg. for white and 10 deg. for colours. Corneae normal, but near limbus, separated from it by normal cornea were small whitish spots involving all layers (incomplete embryotoxon).

Iris: Slightly irregular shape of pupils, iridodonesis. Reaction

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to light and convergence normal; slow and insufficient mydriasis with homatropine. The right eye showed at "7 o'clock" two small bridge-colobomata of the iris, situated one near the other. In its temporal lower part the iris showed a peculiar spongy structure, making the parenchyma partly float in the anterior chamber like seaweed. Both lenses were luxated, in the right eye more than in the left one. The right lens was displaced up and in by about one-third of its diameter. The lenses were clear and no zonular fibres were visible. The right fundus was normal, the left disc showed a marginal excavation. The tension was normal.

The younger brother of the two, M.L., was 12 years of age, 119 cm. high (normal height for his age 139 cm.), and was on the whole very like his brother. In order to avoid repetitions only the points of importance will be mentioned:

Poor general development. Both testicles have descended but are very small; no pubic hair. The thyroid was palpable. Bird face with facies senilis, and tower palate. Slight atrophy of the left facial skull. The limbs were too long in comparison with the height of the child. Arachnodactyly. The radiographs showed the same gross design of the trabeculae. Strikingly small sella turcica with bony bridge. A most important fact must be mentioned here: that the father of the children, otherwise normal, showed the same abnormality of the sella. Basal metabolism increased by 19 per cent.

Eyes: Visual Acuity R.E.: Fingers at two metres; L.E. Fingers at 1 metre. No correction possible. Field of vision: L.E. slight temporal constriction of 10-15 deg. Both corneae showed the same spots near the limbus and the pupils the same irregularity as in the older brother. The iris in both eyes showed atrophic spots in the lower outer parts. Subluxation of both lenses, in a greater degree than in the brother. The lenses are displaced up and in by about one-half of their diameter. Fundus and tension were normal.

External reasons unfortunately did not permit examination of these brothers and their family as extensively as it could be done in the first pair.

Family history.—The children came from a family in which almost all members suffered from more or less severe endocrine disturbances. The mother suffered from an endocrine obesity. The oldest sister (aged 28 years) showed general myasthenia, turned-in legs, funnel-shaped chest, and general hormonal disturbances. In addition she had high myopia. A sister, aged 16, years had also high myopia and suffered from a very severe congenital kypho-scoliosis, marked funnel-shaped chest, severe general insufficiency and a congenital vitium cordis. One sister, aged 12, years was myopic, the same applied to the father; he and two brothers lived abroad and were said to be healthy. Another

brother, aged 18 years, had high myopia. The youngest sister, aged 6 years, was said to be healthy and to have normal eyesight.

Both our patients happened to be the same age as the other brothers described previously.

The older one, I.T., aged 14 years, was 172 cm. high (normal height 150 cm.). He was well developed, although of slack carriage and of an asthenic type. The palate was high and pointed, and he showed a marked arachnodactyly. The limbs, and particularly the hands and feet, were disproportionally long. Habitual subluxation of the humerus and the fingers. No other abnormalities were detected except a slight mitral stenosis. The X-ray examination showed the same changes as in the first pair: gross design of the trabeculae and small sella turcica.

Eyes: Visual Acuity R.E. Fingers at 1 metre, L.E. fingers at 1 metre. Subluxation of both lenses; the lower margin of the lens was visible in the centre of each pupil. The vision could therefore be corrected in two ways: both eyes saw with -5.0 D.Sph. -3.0 D. Cyl. 90 deg. 6/24, and with +8.0 D.Sph. +3.0 D.Cyl. 90 deg. even 6/12. This correction, however, comprehending the aphakic part of the pupil, was not tolerated. With the slit-lamp both eyes showed numerous zonular fibres. There was a marked iridodonesis present, iris and fundus were otherwise normal. The field of vision and the ocular tension were also normal.

The younger brother, M.T., was 11 years old and strongly resembled his brother. His height was 150 cm. (normal height for his age 139 cm.), he had slim limbs and very large, slim hands and feet. Apart from the arachnodactyly, a high, pointed palate and subluxation of the finger joints were present. No other abnormalities were detected. The X-rays of this boy showed again the gross design of the trabeculae and a very small sella turcica.

Eyes: Visual acuity R.E. 6/36, L.E. 6/18. No correction was possible. Subluxation of both lenses, in the right eye the lens was displaced up and in by about one-third of its diameter, in the left eye the lower margin of the lens was only visible in strong mydriasis. Very slight iridodonesis. No change of iris or fundus. Field of vision and tension were normal.

Marfan's syndrome is attributed by many authors to an endocrine disturbance in the development with a hypophysary basis. Francois assumes that there exists a hypersecretion of the growth hormone. Hambresin and Van der Maele speak of an affection of the cells of the anterior horn of the spinal cord caused by a surplus of the growth hormone. Schilling describes a case showing striae of the skin in spite of leanness and points out that in cases of Cushing's disease, caused by a disturbance of the hypophysis, this symptom can also be present. Jeandelize and Drouet rightly point out that the hormonal theory of Marfan's

syndrome is founded only on speculation and that there are no biological tests suitable to prove the theory. Ida Mann remarks that the hormonal disturbances in Marfan's syndrome are probably only co-ordinated symptoms of a genotypic affection, producing general and ocular troubles which affect not only the mesoderm but the endocrine glands and the ectoderm as well.

The four cases presented here seem to corroborate this view. The first two cases show marked troubles of the hormonal apparatus, mainly of the sexual glands, and the whole picture is that of a severe endocrine disturbance. The other pair of patients come from a family in which troubles of the hormonal functions, affecting mainly the development of the skeleton, are marked and numerous. The most important points detected in these four cases are the finding of a pathological structure of the bones—seen for the first time in cases of Marfan's syndrome but known to occur in endocrine troubles—and chiefly the finding of a very small sella turcica (together with the fact that the father of one of the pairs, merely outwardly regarded as the carrier of the gen, showed the same small sella). These facts speak unmistakably for the hypophysis taking part in the syndrome. One must admit that the smallness of the hypophysis does not say anything about its abnormal function; but as long as there is no biological test for the function of the hypophysis one must take the findings described here as the first proof of an affection of the hypophysis in Marfan's syndrome.

Another important point is that one pair of brothers was abnormally small, the other pair abnormally tall. This means that the hypophysary trouble is of a very general character—the two pairs apparently represent two liminal cases of the disturbance, once in the sense of an inhibition, the other time in the sense of a stimulation of the growth, leading both, however, to the sharply defined complex of Marfan's syndrome.

REFERENCES

- FRANCOIS, T.—*Bull. de la Soc. Franc. d'Ophtal.*, p. 157, 1935.
 HAMBRESIN ET VAN DE MAELE.—*Bull. de la Soc. Belge d'Ophtal.*, No. 69, Vol. LXX, 1934.
 SCHILLING, V.—*Medizinische Welt*, 1936, quoted in *Zentralb. f. d. ges. Augenheilk.*, 1936, Vol. XXXVI, p. 581.
 JEANDELIZE ET DROUET.—*L'oeil et l'hypophyse*, Concilium, Cairo, Vol. II, 1937.
 MANN, IDA.—Quoted by Morard, G., *Arch. d'Ophtal.*, Vol. LII, p. 344, 1935.