CLINICAL AND CYTOGENETICAL STUDY OF A PATIENT WITH SYNDROME OF NONNE—MILROV—MEIGE COMBINED WITH SYNDROME OF LAURENCE—MOON—BARDET—BIEDL

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The Syndrome of Nonne—Milrov—Meige (SNMM), reported first in 1881 and later again in 1892 and 1928, is a hereditary disease with an innate insufficiency of the walls and valves of lymph vessels (3, 4, 7, 8, 9). It is manifested clinically with a swelling of one or both lower extremities; the oedema is most expressed under the knee. The histological preparation is very typical: enlarged and filled with lymph fluid subdermal lymph spaces (9). The Syndrome of Laurence—Moon—Bardet—Biedl (SLMBB) is also a hereditary-innate disorder including hypogonadism, obesitas, pigment degeneration of retina, mental abnormalities even oligophrenia, polydactilia often combined with other malformations, nanism, neurologic symptoms, etc. (4, 5, 6).

We could not find any reported combination between SNMM and SLMBB in the available literature. Something more: until now SLMBB has no precise investigation concerning its type of heredity: autosomal, recessival or X-determined (4, 14), as well as its cytogenetic preparations. Some authors report patients with normal cariotype (11, 12), others — autosomal and genosomal aberations in a total or in a mosaic type (5, 6, 13). No data of cytogenetic investigations of SNMM can be found too. There exist some reports (4, 10) about the dominant-recessival relations between a pathological and normal allel with a total penetration and various expression of the pathological one.

Therefore, we presume our present study as a very interesting and actual investigation concerning the rare combination.

The patient herself:

D. K. D., female, age 50.

Inquiry data (unsatisfactory): first walking steps — at the age of 6 years; late beginning of speech; no school at all; bad vision; swelling of lower extremities.

Examination: obesitas IIIrd degree; undersized; dry skin; short neck; bilateral exophthalmus; hard of hearing; low voice; oligophrenia; hard of contacting; stiff (firm) oedema of the lower extremities (under the knee) with pale-rose colour of skin dotted by lighter spots; 6 toes on the right foot; rest organs and systems — no pathological disorders.

Laboratory data: sedimentation test — 15/24 mm; Hb — 12 g %; Leuco— 4900; cell counting — normal; urine — normal; Weltmann — 6; Timol test — 15 FU; SGOT — 4 IU; SGPT — 2 IU; total protein — 8,6 g % with normal protein fractions; glucose loading — definite diabetic blood-sugar tendency; cholesterin — 296 mg %; electrolites — normal; 17-KS and 17-OS — normal values.

X-rays investigation: cor et pulmo — normal; the IVth finger metacarpal bones are hypoplastic; the toe falanges show a deviation; pelvis bones, lower extremities and joints — normal; the first several ribs are asymetrical.

Ophthalmological examination: excessive degenerative binocular myopathia, bilateral complex catharacta.

Gynecological examination: bilateral thickening of the uterus tubes.

Histological study of the ankle skin: Biopsy No. 1679/31st March, 1975 — enlarged and overfilled subdermal lymph spaces; no signs of inflamation; decreased number of sweat glands; vessel infiltration of derma.

Cytogenetic investigation: analysis of 50 metaphasic plates of cultivated lymphocytes is done. 4% of the cells show hypodiploidia which corresponds to the age features of our patient and does not effect definite chromosomal groups. No structural chromosomal aberations are registered in the studied metaphases. Cariotype 46XX is established from the 11 plates subjected to typing.

Discussion

The firmness of the swellings of lower extremities, their characteristic skin-appearance, biopsy results, innate signs of all symptoms allow the conclusion that the Syndrome is SNMM. From the other hand the obesitas, oligophrenia, polydactylia (6 toes), nanism, hypogonadism, all being also innate symptoms, make it possible to diagnose the SLMBB. Excessive myopathia and complex catharacta hinder the thorough investigation of the eye and for that reason the pigmentous retinitis is not proved nor denied.

The genealogous study is based only on the patient's explanations, therefore, the hereditary type of both syndromes can not be determined; the same refers to their eventual closeness of transmission.

The data of cytogenetical study allow us to suggest that the combination of SNMM and SLMBB in our patient is not a result of chromosomal aberation.

The reported case is very interesting due to the exclusively rare combination of two rare hereditary syndromes.

Certain authors refer those syndromes to the diencephalic ones. Thus, our patient's diabetes requires greater attention. It is quite probably that diencephalic disorders provide a prevailing pathogenic role in the origin of the syndromes and diabetes mellitus. To support this view comes the excess weight of our patient.

REFERENCES

1. Попов, Л. Дерматология и венерология. С., 1963, 452. — 2. Попов, Л. Синдроми и рядко диагностицирани болести. С., Мед. и физк., 1967, 297—298. — 3. Попов, Л. Синтетична дерматология, 1960, 37. — 4. Стивенсон, А., Б. Давидсон. Медикогенетическое консультирование. М., Мир, 1972. — 5. Цонева-Манева, М. Т., Е. Бозаджиева, Б. Петров. Цитогенетични проучвания при семейна форма на синдрома ЛМББ, ВМИ, Варна. — *Год. труд.*, 1965, **IV**, 3, 226—235. — 6. Bowen, P. et al. The Laurence-Moon syndrome association with hypogonadism and sex chromosome aneuploidi. — *Arch. Int. Med.*, **4**, 1965, 116/4, 598—604. — 7. Coltou, A., T. Popescu, D. Roxin. *Derm. Vener.*, Bucuresti, **5**, 1971, 16, 447—454. — 8. Darier, J., A. Civatte, A. Tzanek. *Precis de Dermatologie,* Paris, 1947, 517. — 9. Duperrat, B. *Precis de Dermatologie,* Paris, 1959, 376. — 10. Esterley, J. R. Congenital hereditaly lymphoedema. — *J. Med. Genet.*, **2**, 1965, 2/2, 93—98.—

11. Jafusco, F. Syndrome di Laurence—Moon—Bardet—Biedl. — *Pediatria,* Napoli, 3, 1970, 78/3, 443—465. — 12. Loviseto, P. et al. Le syndrome di Laurence—Moon—Bardet—Biedl, *Minerva Med.,* 57, 1966, 61—62, 2650—2660. — 13. Ortiz, M. O. and F. B. Herreros. Estudios citigeneticios on diversos transtornos constitutionales y procesos hematologicos humanos. — *Rev. Clin. Esp.,* 5, 1963, 90/5, 295—307. — 14. Scarpelli, P. F. and G. Vailati. *Rass. Neurol. Veg.,* 2, 1964, 18/2, 144—166.

КЛИНИЧЕСКИЕ И ЦИТОГЕНЕТИЧЕСКИЕ ИССЛЕДОВАНИЯ БОЛЬНОЙ С СИНДРОМОМ NONNE—MILROV—MEIGE В КОМБИНАЦИИ С СИНДРОМОМ LAURENCE—MOON—BARDET—BIEDL

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РЕЗЮМЕ

Проведен анализ исключительно редкой комбинации синдромов Nonne—Milrov—Meige и Laurence—Moon—Bardet—Biedl. В работе обобщаются результаты клинических, лабораторных, рентгенологических, офтальмологических, гинекологических, цитогенетических, гистологических и психологических исследований больной.