Syndromes-Pathologies

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Bloom syndrome

Syndrome de Bloom

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I. INTRODUCTION

The cardinal skin lesions suggested by BLOOM in 1954 [1, 2] are telangiectatic erythematous lesions, appearing on the face in infancy, especially over the butterfly areas, but occasionally also over the dorsa of the hands and feet. These areas are sun-sensitive, made worse by exposure. The other cardinal feature is short stature, mostly pre-natal in onset but persisting into childhood and adulthood. Most individuals remain below 148 cms in height. The skin lesions sometimes become scarred, atrophic and depigmented and the eyelashes might fall out. The lateral incisors can be absent and mild retardation has been reported. Whereas most patients are Jewish in origin this is not exclusively the case, and a number of Japanese children have been reported [3, 4].

Males are infertile with azoospermia, although females can be fertile.

In this paper, we describing for the first time the unusual tarsal and metatarsal synostosis in a child with Bloom syndrome and discussing the other family subjects presentations.

II. CLINICAL REPORT

The patient is a 13-year-old female (II-5 in the family pedigree), was born in Tunis to a first related parents. She was born after a normal 38-weeks gestation and the mother and father's ages were 35 and 42 years respectively. Labor was normal, but smallness in size was notable (birth at home, and no measurements were recorded). She had four older, variably affected with orthopedic, ophthalmological and skin abnormalities.

The patient was referred to our department because of difficulty in walking secondary to congenital synostosis of the metatarsals of the left foot.

Developmental history: There was marked delay in acquiring the motor development, walking was achieved around the age of two years, albeit with difficulty, other aspects of developments were around the normal.

History of illnesses: The child's first two years of life were so bothersome to parents because of the frequent hospital admissions to the hospital secondary to frequent bouts of pulmonary infections.

Physical examination:

Growth: Severe shortness of stature of prenatal onset (height 131 cm) and microcephaly (OFC 44cm) (Figure 1).

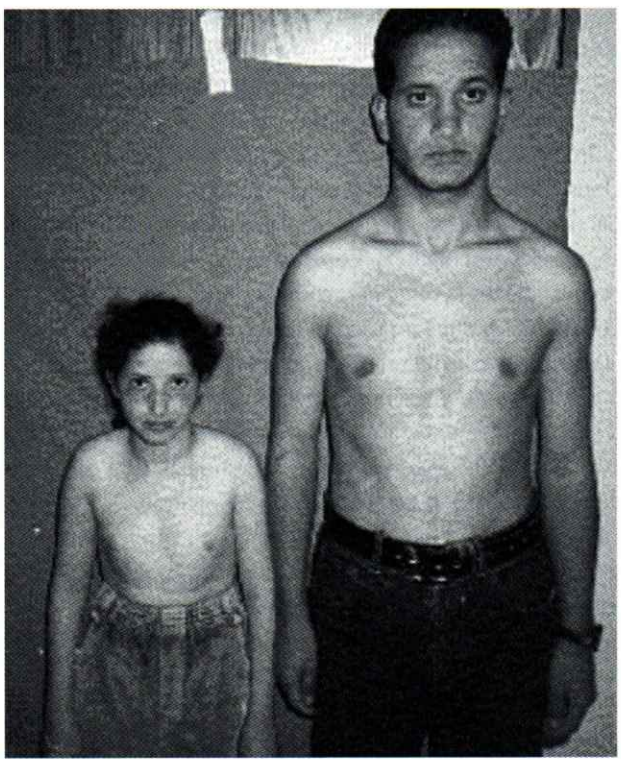

Figure 1: *To the left is the proband (II.5) with the full classic form of BLOOM syndrome, next her older male sib (II.4) despite his normal phenotype he had progressive diminution of vision, which ended up with blindness because of retinitis pigmentosa*

Craniofacial: Disproportionate microcephaly, the head is somehow dolicocephalic, there is prominent nose and ears with receding chin, apparent telangiectatic erythema of the face (Figure 1), which appeared in this child in infancy, the erythema get worse when exposed to sun-light, chronic cheilitis is a bothersome problem in this child. The skull X-ray showed partial craniosynostosis of the coronal sutures with signs of sclerosis of the base of the skull with increased convolutional cranial markings secondary to craniosynostosis (Figure 2).

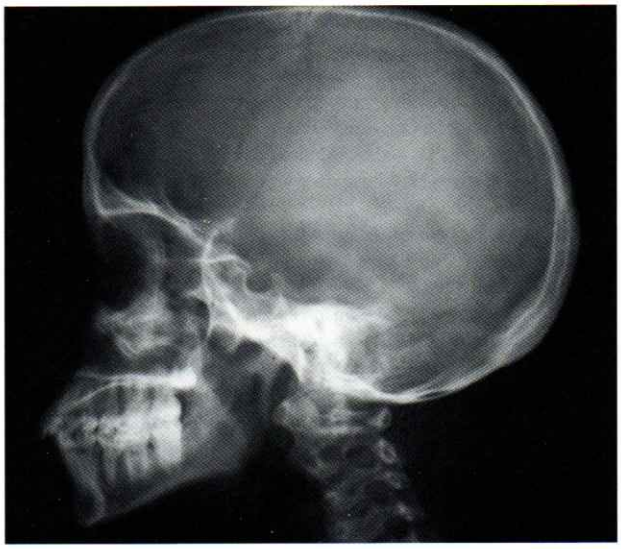

Figure 2: *X-ray skull of the proband: partial sclerosis of the coronal sutures with trace of sclerosis, and thickening of the cranial vault*

Skin: The erythema do involve the dorsum of the hands and foot, café-au-lait spots are seen on the trunk and legs. Musculoskeletal: Generalized ligamentous hyperlaxity is the paramount clinical picture; the hands are small with rudimentary thenar and hypothenar muscles; the fingers are somehow fusiform.
Spinal column: Thoraco-lumbar scoliosis, with platyspondyly of the thoracic and the lumbar vertebrae.
Limbs: Bilateral metatarsal synostosis of the 2nd, 3rd and the 4th metatarsals (Figure 3), furthermore synostosis of the talocalcaneal bones with upward incurvation of the calcaneus.

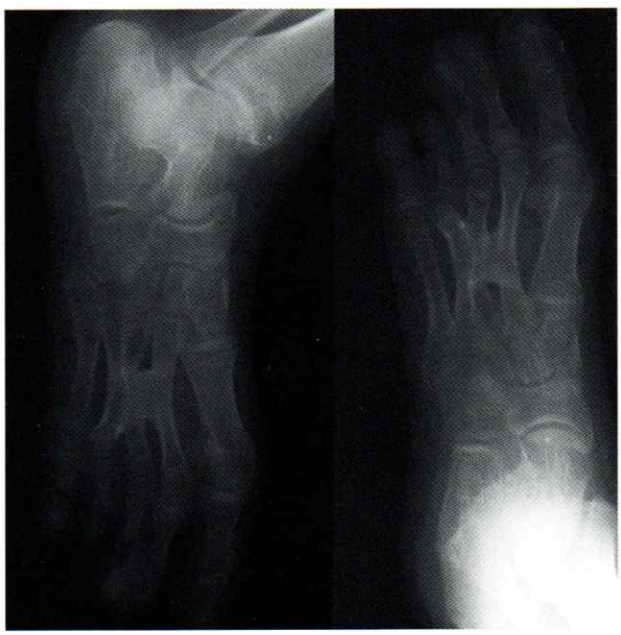

Figure 3: *AP radiograph of the foot showed synostosis of the 2nd, 3rd and 4th metatarsals*

Cytogenetics: Chromosomal breakage and sister chromatid exchange were evident in two subjects, the patient and her older male (II.4 and II.5): there was high rate of 100 sister chromatid exchange per cell in the patient, and 60 sister chromatid exchange in male sib, this despite the normal phenotype of the male sib.
Ultrasonography of abdomen and pelvis: Nothing of significance was detected.
Examination of the family (Pedigree ; Figure 4):

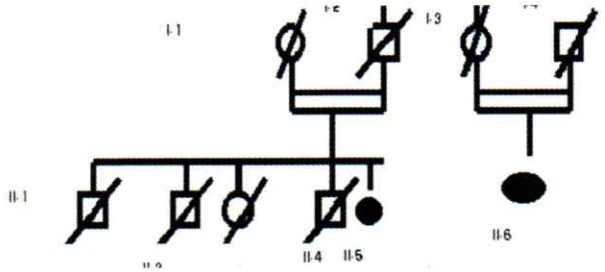

Figure 4: *Family pedigree: The blackened dots are subjects with the full clinical criteria of BLOOM syndrome, whereas the circles and squares with intercepted lines are partially affected*

Subject II.4: Morphologically, the patient is normal with no signs of the disorder, but he developed gradual diminution of his visual acuity and finally blindness was developed secondary to retinitis pigmentosa (Figure 5).

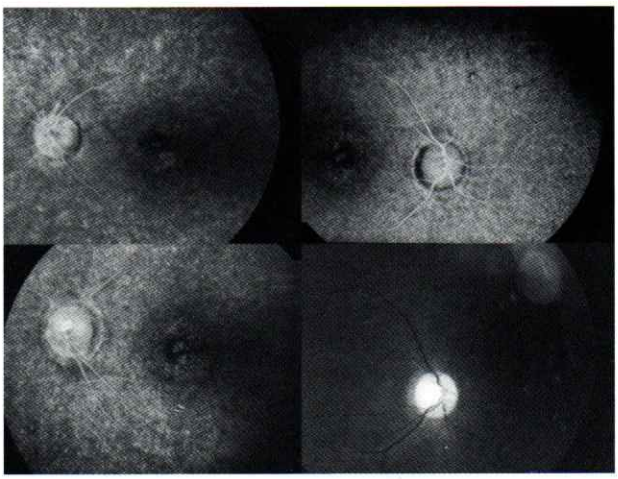

Figure 5: *Fundal examination of older male sib, revealed retinitis pigmentosa (note the bone spicule type and salt and pepper changes)*

Subjects II.1 & II.2 & II.3: All are of very short stature, with sunken eyes, prominent zygomas, and the first two are with axillary acanthosis negricans, whereas II.3 is with kyphosis.
Parents (I.1 & I.2) both are with short stature, strikingly both are with butterfly erythema of the face, get worse when exposed to sunlight.
Subjects (I.3 & I.4) similarly both are with short stature; subject I.3 with severe myopia; their female offspring (II.6) is with severe growth deficiency, very slight erythematous skin markings over the nose, but her facial features are somehow similar to her female cousin (the proband II.5).
The orthopedic presentation and the management of the patient
The girl (II.5) was initially referred because of obscure swelling of the right sole and the forefoot associated with intermittent pain on weight-bearing. Clinical examination

and radiographic documentation showed unusual tarsal and metatarsal synostosis. Surgical intervention was therefore performed by applying osteotomy which has proved successful in establishing pain free and somehow a normal weight-bearing outcome.

III. DISCUSSION

BLOOM syndrome, described by BLOOM in 1954 [1, 2], consists of intrauterine growth retardation, sunlight sensitivity leading to telangiectatic erythema, a tendency to chromosomal breakage with a high frequency of sister chromatid exchanges and immunodeficiency. GERAMAN [4] first recognized chromosomal breakage and emphasized the predilection for neoplasia.

Frequent sister chromatid exchanges are the rule and this has been used for prenatal diagnosis [5]. Malignancy, especially lymphomas or leukemia, might develop [6]. The average age of manifestation of leukemia is 22 years and of solid tumors 35 years [7]. BERGER et al., [8] reported a case that developed a WILMS' tumour at the age of 4 years. These authors found 3 other cases in the literature, full description of the syndrome but no description of any associated skeletal or ophthalmological abnormalities.

WEBSTER et al., [9] reported a girl with some features of BLOOM syndrome who died at 19 years from pneumonia, immunodeficiency and a lymphoma-like illness. Point mutations were demonstrated in both DNA ligase I alleles. Although there are clinical similarities, DNA ligase I mutations have not been demonstrated in BLOOM syndrome, similarly no data concerning any skeletal abnormalities.

SAHN et al., [10] reported a confusing case where there was telangiectasia of the conjunctiva. There were also erythematous scaly, lichenoid plaques on the dorsum of the hand. Sister chromatid exchange was increased, but so was chromosome breakage when cells were exposed to diepoxybutane.

WOODAGE et al., [11] reported a case with features of both PRADER-WILLI and BLOOM syndromes. The patient was found to have maternal uniparental disomy for chromosome 15. WOODS [12] and AUERBACH and VERLANDER [13] provide good reviews of DNA repair defects.

The striking clinical and radiological features encountered in this family were striking. The noteworthy skeletal deformity encountered in the proband and the ophthalmological disorder in the elder sib showed that the clinical spectrum in patients with BLOOM syndrome is diverse.

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