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Ectodermal Dysplasia, Cleft Lip/Palate, and Severe Cutaneous and Osseous Syndactyly in a Mentally Retarded Girl: A New Multiple Malformation Syndrome

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A 13-year-old mentally retarded girl with severe cutaneous and osseous syndactyly of the hands and feet, cleft lip/palate, and ectodermal dysplasia is presented. We conclude that the pattern of malformations described represents a new multiple malformation syndrome. A comparison with Zlotogora-Ogür syndrome is presented. Am. J. Med. Genet. 70:211–215, 1997.

KEY WORDS: cleft lip/palate; ectodermal dysplasia; syndactyly; Zlotogora-Ogür syndrome

INTRODUCTION

Cleft lip and/or palate are found in more than 150 syndromes, but many patients with multiple malformations which include cleft lip and/or palate cannot at present be classified [Gorlin et al., 1990]. Almost simultaneously, Zlotogora et al. [1987] and Ogür and Yuksel [1988] described children with cleft lip and palate, malformed pinnae, pili torti, syndactyly, ectodermal dysplasia, renal anomalies, and mental retardation. After comparison of the clinical manifestations, it became clear that they described the same syndrome, currently named Zlotogora-Ogür syndrome [Zlotogora et al., 1987; Ogür and Yuksel, 1988]. Recently, Zlotogora [1994] reviewed the clinical manifestations based on 31 patients affected with the syndrome from age 4 months to 65 years.

Martinez et al. [1987] described a noninbred girl with cleft lip and palate, complete absence of deciduous teeth, hypodontia of permanent teeth, hair alterations, hypertelorism, midface hypoplasia, abnormal EEG, syndactyly, and other findings. The mother had minimal abnormal findings including small teeth and mildly coarse scalp hair. Autosomal or X-linked dominant inheritance was suggested, and similar conditions combining ectodermal dysplasia and cleft lip and palate were reviewed [Martinez et al., 1987]. Rodini and Richieri-Costa [1990] described 3 Brazilian brothers born to normal consanguineous parents, who had ectodermal dysplasia, cleft lip and palate, mental retardation, syndactyly of fingers 2–3, accessory nipples, and ear anomalies. They are now considered to have Zlotogora-Ogür syndrome. Bustos et al. [1991] described seven related families containing 20 affected persons with similar clinical findings but with normal psychomotor development. Recently, we examined a patient with clinical manifestations resembling those of Zlotogora-Ogür syndrome, as well as those of Martinez et al. [1987], but who has her own peculiarities.

CLINICAL REPORT

A 13-year-old girl from Bonaire (Dutch Antilles) was referred to our Department of Oral and Maxillofacial Surgery for closure of a bilateral cleft-palate defect. Little information was available on the parents or on family history. The parents are consanguineous. The mother is said to have had the same hair as the proposita before she became hairless. An aunt on the mother's side has a cleft, but information on the exact type of cleft is unavailable. The patient has an older sister and a younger brother who are said to be normal. Maternal abuse of alcohol and benzodiazepines was suggested.

Physical examination at age 13 showed a mentally retarded girl with very short but proportionate stature (length 1.09 m, <3rd centile). She had an OFC of 51.5 cm (<10th centile) and weighed 23.5 kg (Fig. 1). She showed dystrophic nails and thin, sparse hair. The eyebrows were rather voluminous and the eyelashes were unusually long. A hairshaft analysis showed thin, scarcely pigmented hair. Her skin was generally dry, with ichthyosiform changes on the head and the legs. A test for sweating was not performed.

Frontal bossing, high frontal hairline, slanted palpebral fissures, lagophthalmos, broad base of the nose, maxillary hypoplasia, and prominent and everted lower lip were present. On examination of the oral structures, macroglossia, severe oligodontia, short lin-

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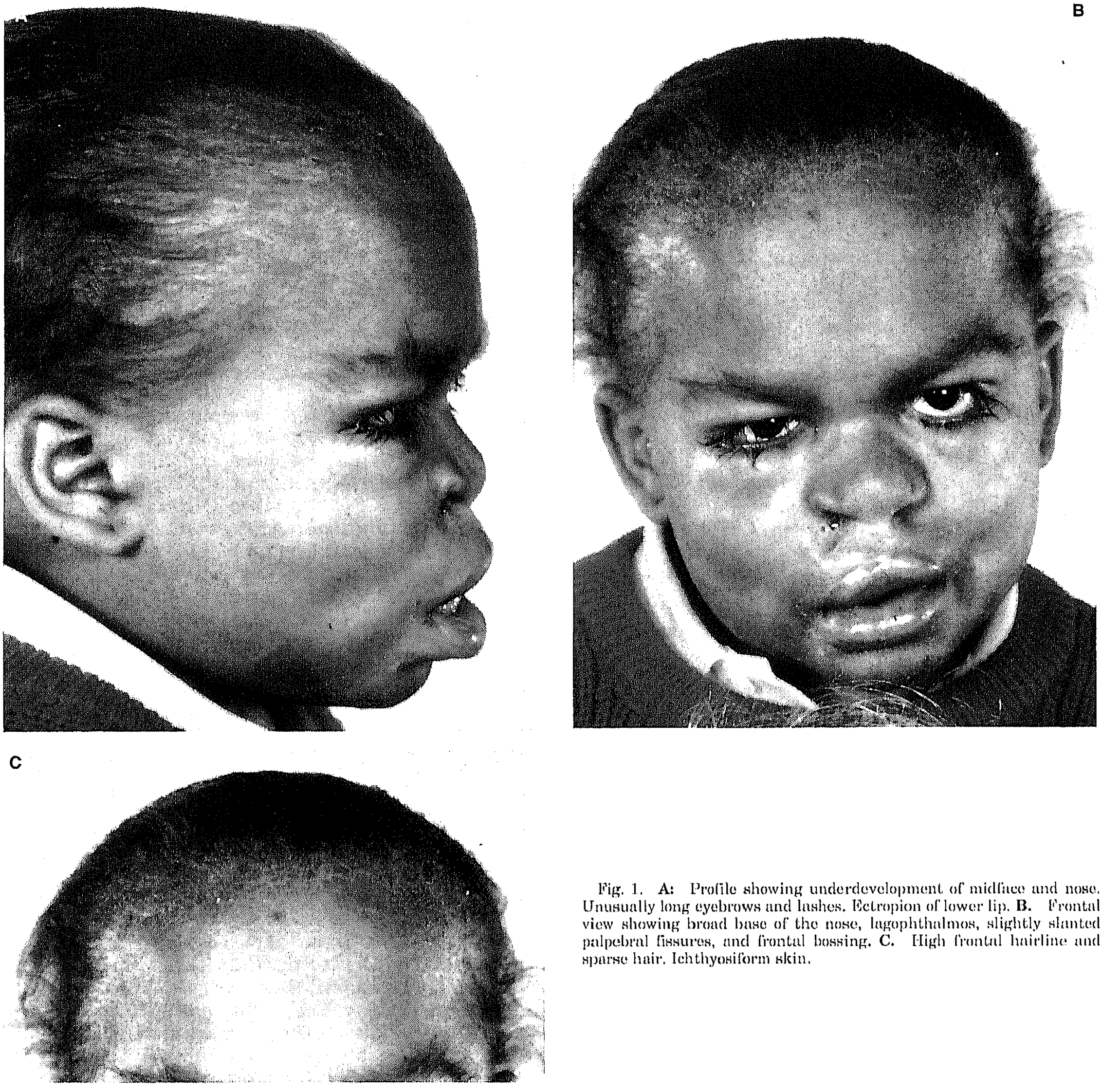
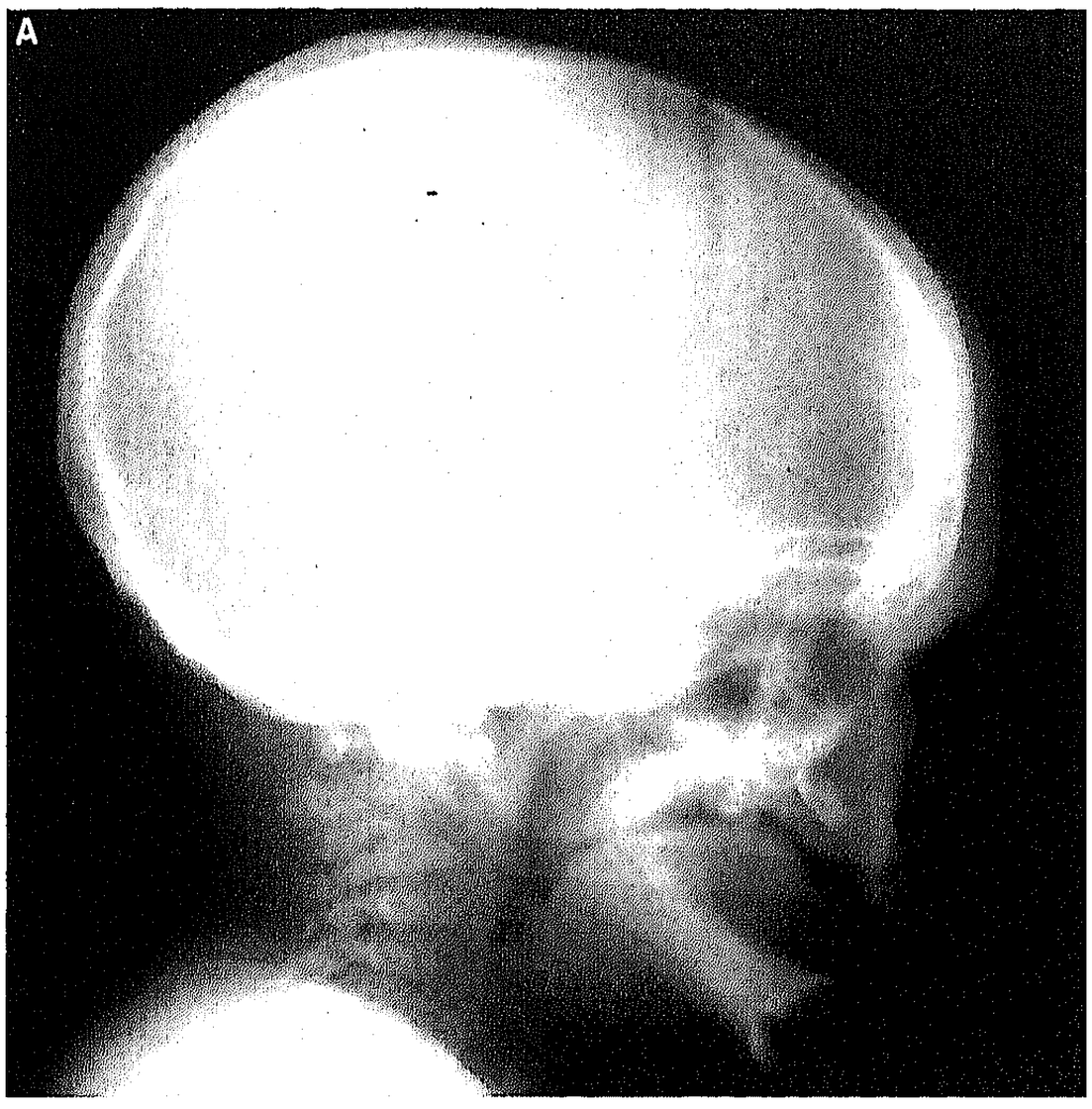


Fig. 1. **A:** Profile showing underdevelopment of midface and nose. Unusually long eyebrows and lashes. Ectropion of lower lip. **B.** Frontal view showing broad base of the nose, lagophthalmos, slightly slanted palpebral fissures, and frontal bossing. **C.** High frontal hairline and sparse hair. Ichthyosiform skin.

gual frenum, and surgically treated bilateral cleft lip and palate, without stabilization of the premaxilla, were noted (Fig. 2).

There was severe cutaneous syndactyly of the right hand (digits 2–5) in combination with synonychosis (digits 2–4). Radiographically, partial osseous syndactyly (digits 2–4) and broad metacarpals (digits 3–5) were seen (Fig. 3). The left hand had a similar cutaneous syndactyly, with associated partial osseous syndactyly (digits 3 and 4) and broad metacarpals (Fig. 4). Both feet showed severe cutaneous syndactyly. Hypoplastic toes and absent distal phalanges were also noted (Fig. 5). Function of the extremities was surprisingly good. Bone age was within normal limits.

The patient appeared to have mild impairment of hearing, but lack of cooperation precluded reliable audiometric testing. An electroencephalogram to detect epileptic activity was not performed due to poor cooperation of the patient. She has a small umbilical hernia. High-resolution (GTG-banded) chromosome analysis (850 band level) with special attention to chromosome 7 was normal.



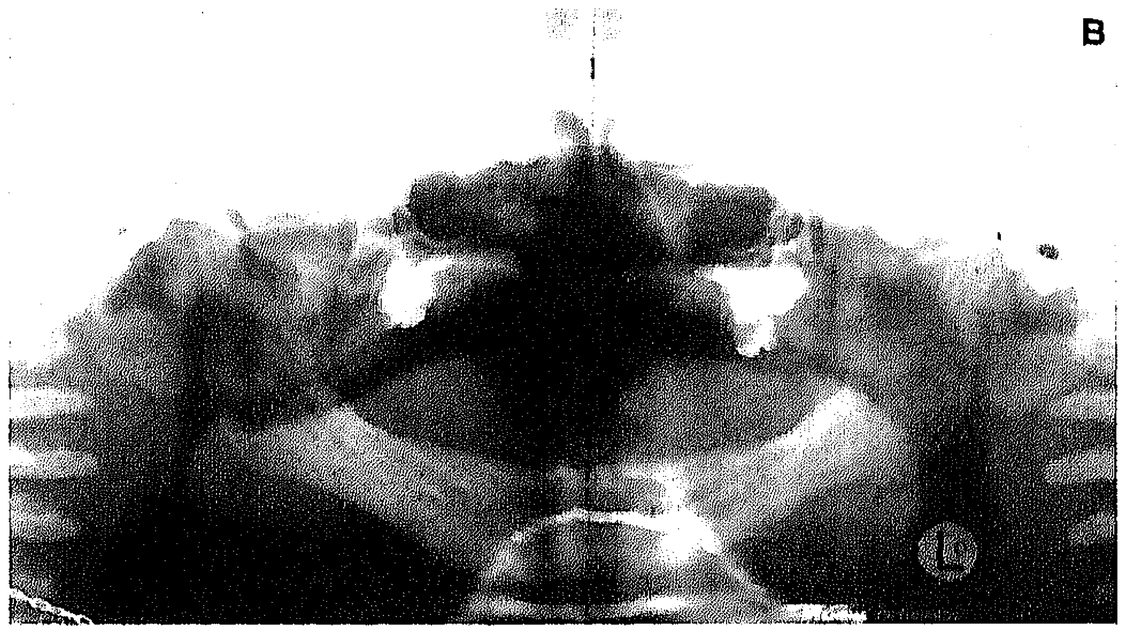
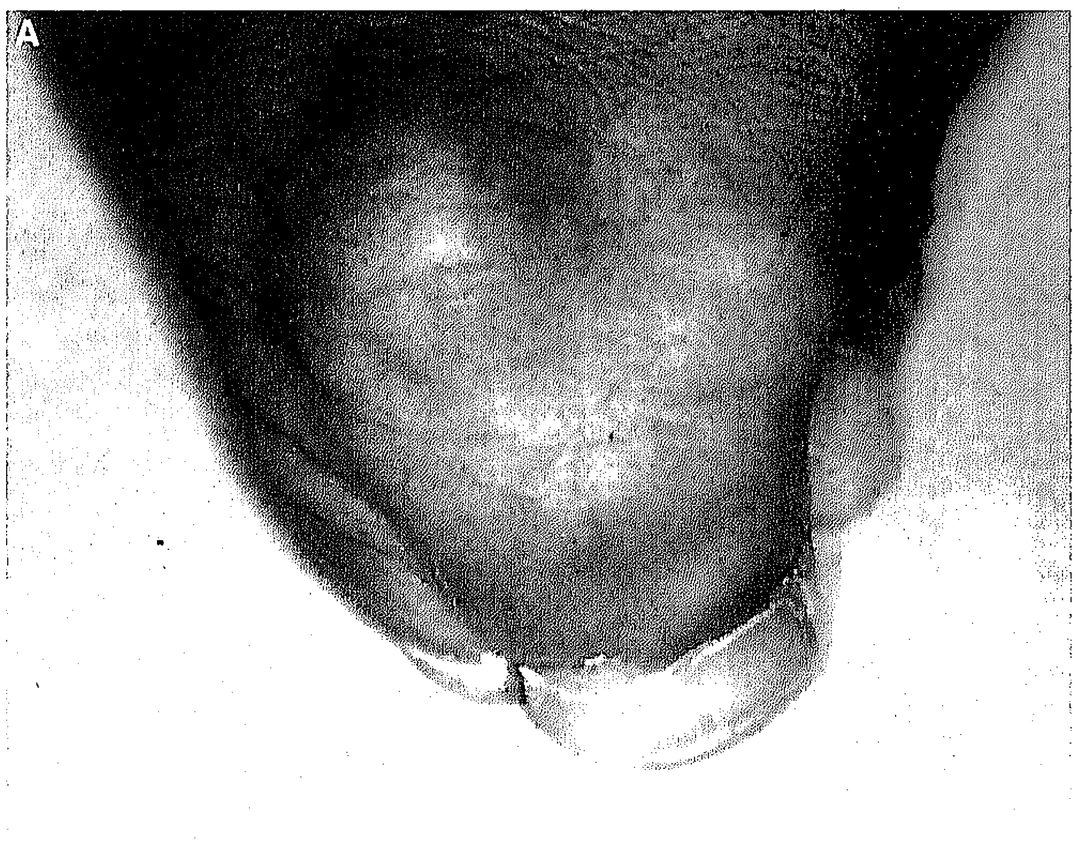


Fig. 2. **A.** Profile showing retrodisplaced, vertically underdeveloped, small maxilla. Mandible is of normal size. **B.** Orthopantomogram shows near edentulism and defect in the area of premaxilla.



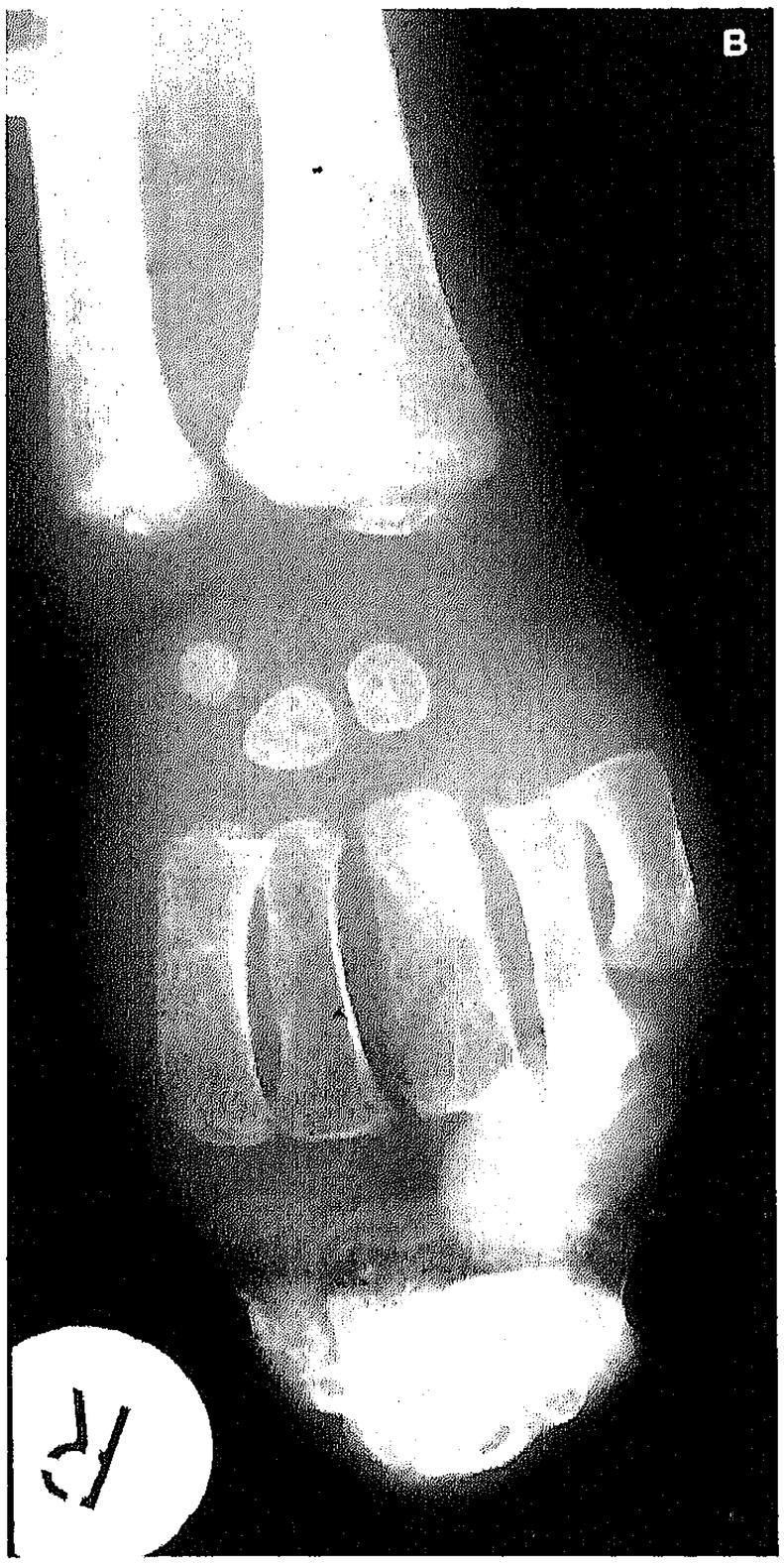


Fig. 3. Right hand. **A.** Cutaneous syndactyly of digits 2–5 with synonychosis of digits 2–4. **B.** Radiograph showing synostosis of phalanges 2–4 and broad metacarpals, especially 3 and 5.

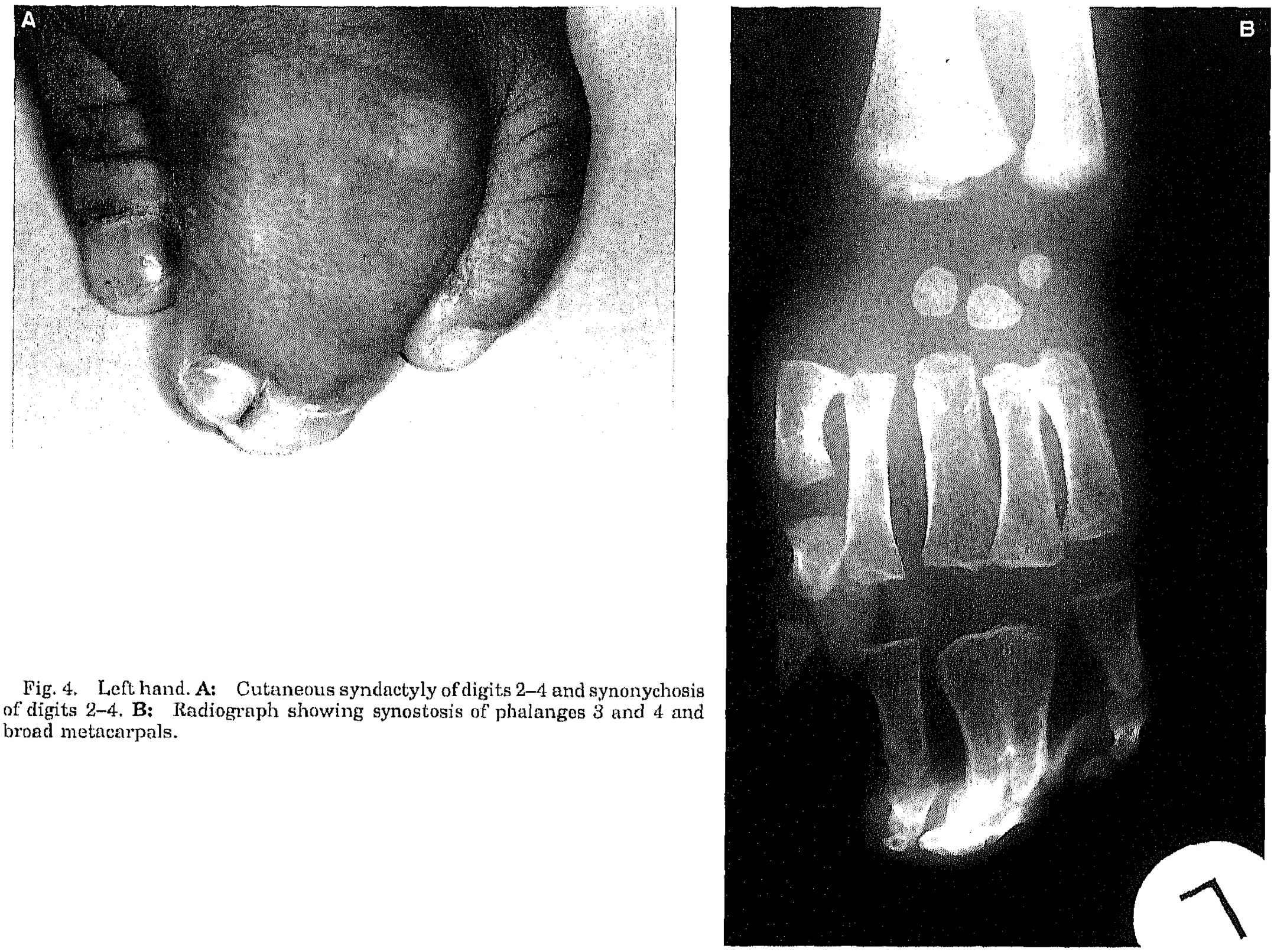


Fig. 4. Left hand. **A:** Cutaneous syndactyly of digits 2–4 and synonychosis of digits 2–4. **B:** Radiograph showing synostosis of phalanges 3 and 4 and broad metacarpals.

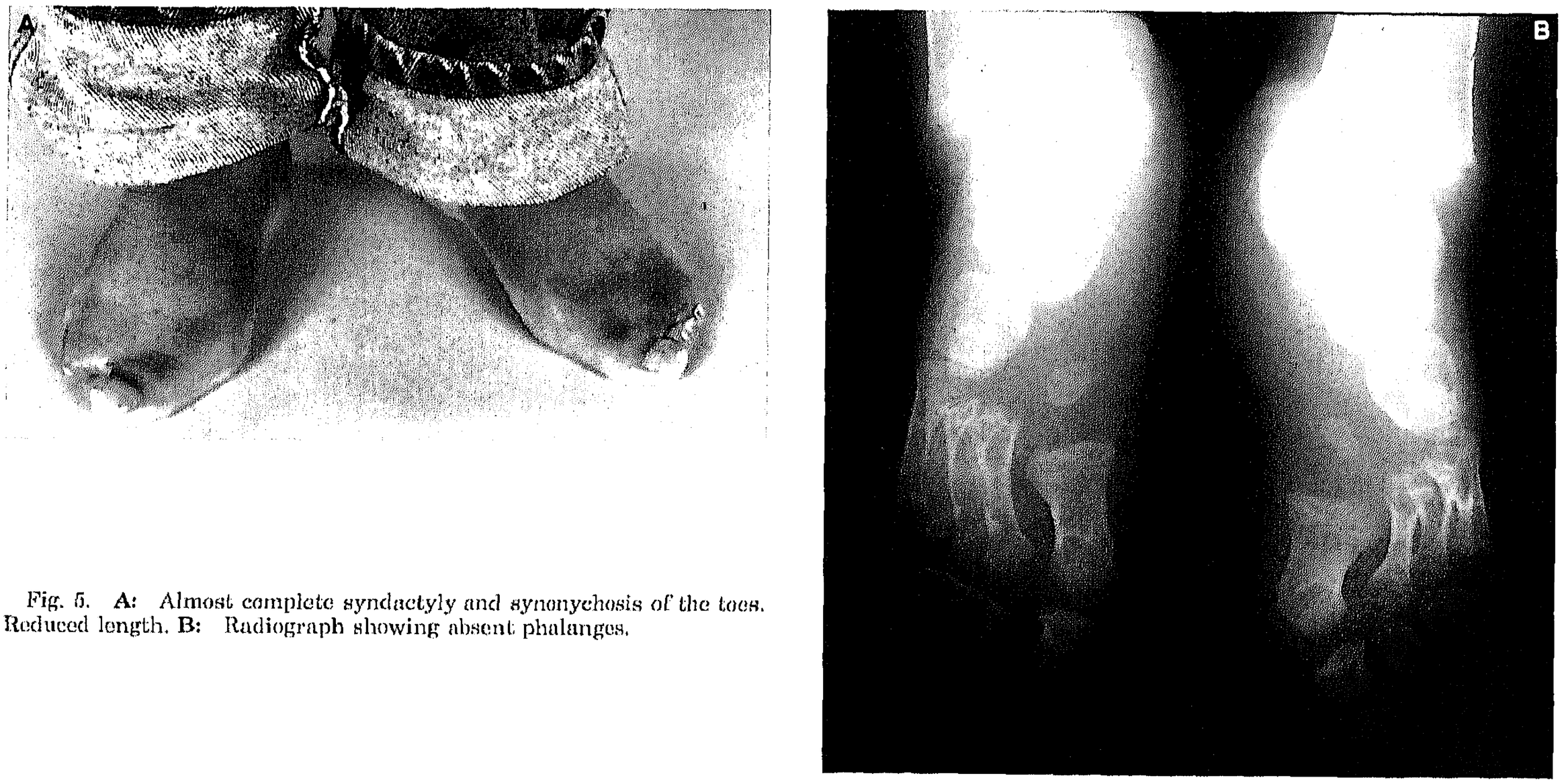


Fig. 5. **A:** Almost complete syndactyly and synonychosis of the toes. Reduced length. **B:** Radiograph showing absent phalanges.

TABLE I. Differential Diagnosis of the Cases Described*

Facial signs	Zlotogora-Ogür	Martinez et al.	E.E.C.	Out-patient
Cleft lip	+	+	+	+
Cleft palate	+	+	+	+
Microcephaly	–	+	–	–
Frontal bossing	+	+	+	+
Hypertelorism	–	+	–	–
Prominent eyes	–	+	–	–
Lagophthalmos	–	+	–	+
Slanted palpebral fissure	–	–	–	+
Hypoplastic lacrimal puncta	–	–	+	–
Nasal anomalies	–	+	+	+
Micromaxillism	+	+	–	+
Abnormal ears	+	+	+	–
Oligodontia	+	+	+	+
Macroglossia	?	?	?	+
Short lingual frenum	?	?	?	+
Hair changes				
Sparse hair	+	–	+	+
Pili torti	+	+	?	–
Long eyelashes	–	+	–	+
Skin				
Dry skin	+	–	+	+
Abnormal nipples	+	–	+	–
Limbs				
Syndactyly	+	+	+	+
Ectrodactyly	–	–	+	+
Broad metacarpals	–	–	–	+
Deafness	+	–	+	+
Mental retardation	+	–	+	+
Inheritance	AR	?	AD	?

*+, present; –, absent; ?, unknown; AD, autosomal dominant; AR, autosomal recessive.

Under general anesthesia, the premaxilla was stabilized with autogenous mandibular bone, and closure of the oronasal defect was performed in combination with a lengthening of the frenum [Freihofer et al., 1991].

DISCUSSION

It is very difficult to classify the patient described into a distinct syndrome. The main signs, i.e., ectodermal dysplasia, cleft lip and palate, cutaneous syndactyly, mental retardation, and hearing impairment resemble Zlotogora-Ogür syndrome to some degree. But other signs, such as maxillary hypoplasia and lagophthalmus, differ. The latter clinical signs are more consistent with the syndrome described by Martinez et al. [1987]. Malformed protruding ears, nipple anomaly, lumbar lordosis, hypoplastic lacrimal puncta, and pili torti were not seen in our patient, and therefore we rule out Zlotogora-Ogür syndrome.

Retarded mental status is sufficient to differentiate the present case from the syndrome in Martinez et al. [1987]. The severity of syndactyly, similar to that in Apert syndrome, is very different from that in Zlotogora-Ogür and Martinez syndromes. To our knowledge, osseous syndactyly, broad metacarpals, and absence of phalanges have not been described in the above-named syndromes.

On the other hand, severity of mental retardation, growth retardation, severe syndactyly, and the absence of tear duct anomalies differentiate our patient from E.E.C. syndrome. Midface hypoplasia, which is not present in E.E.C. and Zlotogora-Ogür syndromes, cannot be used as a reliable discriminating feature. All the patients have cleft lip and palate. It may be that the observed jaw anomalies are a consequence of different primary surgical managements of the cleft, further enhanced by the degree of oligodontia. The everted lower lip as described by Martinez et al. [1987] is probably also secondary to the maxillary hypoplasia as seen in cleft patients. The same applies to the nasal anomalies. In addition, speech disability and reduced hearing may be attributable to the cleft palate.

Based on the clinical manifestations, differential diagnosis can be reduced to the three above-named syndromes (Table I). One can argue that the case presented is a severe form of Zlotogora-Ogür or Martinez syndrome. However, we are more inclined to believe that this is a new multiple malformation syndrome.

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