Acta Derm Venereol (Stockh) 1995; 75: 479–481

Setleis' Bitemporal "Forceps Marks" Syndrome in a Japanese Family

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Setleis' syndrome is an uncommon inherited condition characterized by bilateral "scarlike" depressions on the temples and a wide spectrum of associated facial abnormalities. We report on a typically affected Japanese boy, whose mother and grandfather show a much milder expression of this disorder, suggesting an apparent autosomal dominant inheritance. ***Key words: focal facial dermal dysplasia; autosomal dominant inheritance.***

(Accepted May 5, 1995.)

Acta Derm Venereol (Stockh) 1995; 75: 479–481.

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In 1963, Setleis et al. (1) described 5 children in 3 apparently unrelated Puerto Rician families who had bitemporal "scarlike" depressions, associated with unusual dysmorphic facial features. The representative facial features of this disorder include: bitemporal "scarlike" lesions which resemble forceps marks, aged leonine appearance with puckered skin about the eyes, eyebrows that slant sharply upward laterally and a rubbery feel of the nose and chin. To date, there have been 18 cases of Setleis' bitemporal "forceps marks" syndrome (Setleis' syndrome, McKusick no. 227260) reported in English literature (1–8). The majority of the patients have been of Puerto Ricial descent, and autosomal recessive inheritance has been proposed in this disorder. Some authors (7, 8), however, have recently emphasized that Setleis' syndrome is assumed to be inherited in an autosomal dominant fashion. Di Lernia et al. (9) also reported a newborn boy who exhibited bilateral atrophic areas, as well as facial features similar to those described in patients with Setleis' syndrome, but proposed an autosomal dominant transmission with variable expressivity.

We describe here a Japanese family who show the facial features of Setleis' syndrome, but with an apparently autosomal dominant inheritance pattern.

Table I. *Craniofacial anomalies in Setleis' syndrome*

Craniofacial anomaly	Present cases		
	Case 1	Case 2[a)]	Case 3[b)]
Bitemporal 'forceps marks'	+	+	+
Eyebrows which slant upwards & laterally	+	–	+
Abnormalities of eyelashes	–	–	–
Aged, leonine appearance	+	–	+
'Rubbery' nose & chin	+	–	+
Flattened nasal bridge	+	–	+
Periorbital puffiness	+	–	+
Thick lips	+	–	+
Median ridge of the chin	–	–	–
Epicanthus	–	–	–
Low frontal hair line	+	–	+
Abnormalities of hair	–	–	–
Recurrent conjunctivities	–	–	–
Linear depressions on the forehead	–	–	–
Skin pits on both cheeks	–	–	–
Redundant facial skin	+	–	+
Abnormalities of the ears	–	–	+

[a)] Craniofacial anomalies were not observed except bitemporal small 'forceps marks'.

[b)] Craniofacial anomalies were manifest at birth but became less noticeable with age.

CASE REPORTS

Case 1 (IV: 1 in the pedigree, Fig. 5). In 1990, this Japanese boy was born at full-term, weighing 3,484 g, to a 28-year-old woman (Case 2) and a 30-year-old man. There was no inbreeding in the family with consanguineous marriages. He was the product of an uncomplicated pregnancy and spontaneous vaginal delivery without the use of forceps. At birth, smooth depressed areas were noted on both temples. On examination at 4 years of age in the Kurume University Hospital, the following unusual craniofacial manifestations (Table I) were present: "scarlike" areas of thin shiny skin over each temple (left; 37 × 21 mm, right; 34 × 18 mm), eyebrows slanting upwards and laterally, aged leonine appearance, periorbital puffiness, "rubbery" nose and chin on palpation, flattened nasal bridge, thick lips, low frontal hair line and redundant skin and soft tissue. These significant facial features are illustrated in Fig. 1. Extracranial manifestations including growth and development had been normal. Ultrasound examinations of the kidney and ureter was normal. Results of routine laboratory studies were all within normal limits. Chromosome studies on peripheral blood revealed a normal male karyotype. The patient expressed the HLA-phenotypes A24, A26, B52, B62, and CW3.

A biopsy specimen was taken from a lesion on the right temple under general anesthesia with sevoflurane. Histopathologic examination of the "scarlike" lesion showed a thinned epidermis and dermis, and lack of adnexal structures. Skeletal muscle bundles were located at the superficial level in the atrophic dermis (Fig. 2).

Case 2 (III:2 in the pedigree, Fig. 5). This 28-year-old woman, the

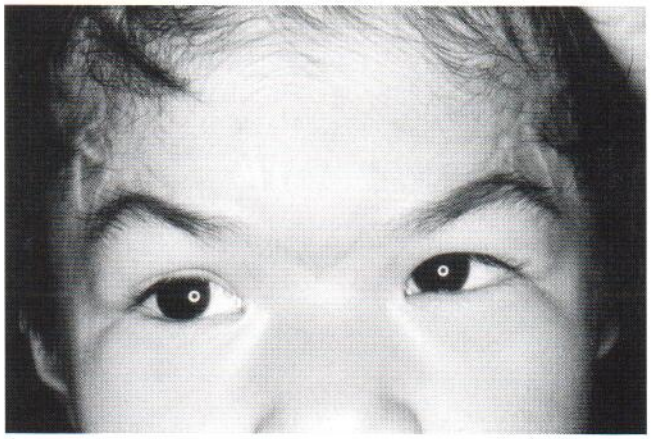

Fig. 1. Full front view of case 1. Note bitemporal "scarlike" lesions, eyebrows which slant upwards and laterally and flattened nasal bridge.

 ISSN 0001-5555

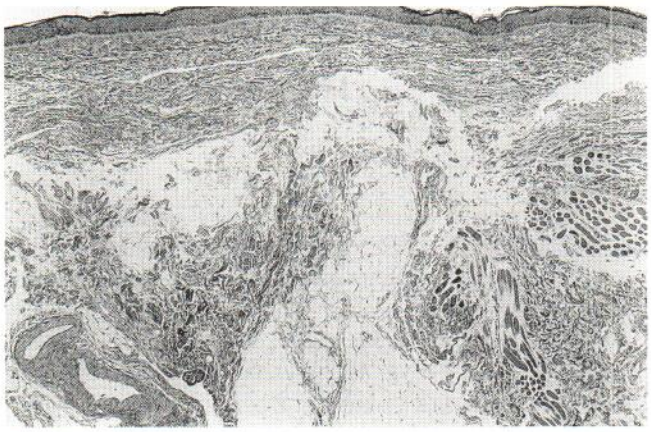

Fig. 2. Photomicrograph of biopsy specimen from one of the "scarlike" lesions in case 1, showing atrophic epidermis and thinned dermis devoid of adnexal structures (hematoxylin-eosin stain ×25).

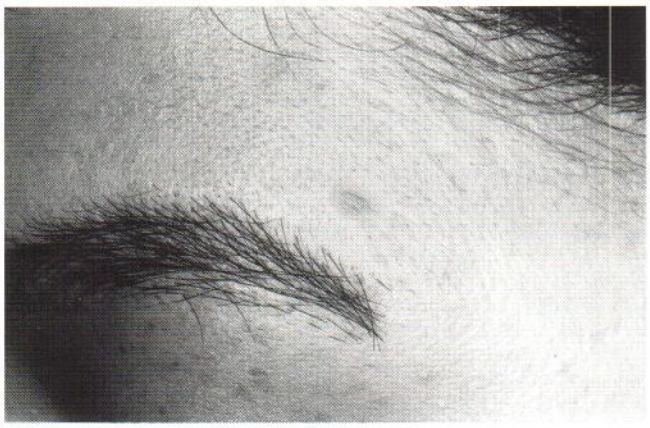

Fig. 3. Left front-lateral view of case 2 (mother of case 1). Note the small "scarlike" lesion.

mother of case 1, had similar, but less obvious, depressed lesions on both temples (5×4 mm each) (Fig. 3). The bitemporal depressions were first noted at birth, but had become less noticeable with age. No other cranial and extracranial disorders were observed. There were no abnormalities in the laboratory data. The patient expressed the HLA-phenotypes A2, A24, B35, B52 and CW3. Histopathologic findings were identical with those of case 1.

Case 3 (II: 3 in the pedigree, Fig. 5). This 59-year-old man, the father of case 2, had depressed areas on both temples (left; 10×5 mm, right; 10×7 mm), eyebrows slanting upwards and laterally, flattened nasal bridge, low frontal hair line, malformation of the ear and redundant skin and soft tissue (Fig. 4a, b). These craniofacial characteristics had been manifest at birth but they had become less noticeable with age. No extracranial disorders except hyperpigmentation were observed. There were no abnormalities in the laboratory data. Studies of HLA-phenotypes and histopathology were not carried out.

DISCUSSION

On the basis of the distinctive bitemporal depressions and the other facial features, a diagnosis of Setleis' syndrome was made in these three cases. Fig. 5 shows the family tree of the patients, suggesting autosomal dominant inheritance. There was no history of consanguinity in the family.

The focal facial dermal dysplasias (FFDD) are a genetically heterogeneous group of disorders characterized by congenital bilateral "scarlike" facial lesions, with or without associated anomalies. Kowalski & Fenske (10) classified FFDD into three distinct varieties. According to their classification, Setleis' syndrome is the preferred designation for type III FFDD. It is characterized by bitemporal "scarlike" depressions, associated with unusual dysmorphic facial features, as shown in Table I. The majority of the reported patients have been of Puerto Ricial descent, and have inherited the disease as an autosomal recessive trait (10). On the other hand, patients with type I FFDD (Brauer's syndrome, McKusick no. 136500) who show evidence of autosomal dominant transmission typically exhibit "scarlike" facial lesions, without other significant facial anomalies (11–13). Type II (autosomal recessive FFDD) also exhibits typical bilateral facial lesions, but the patients are otherwise physically and developmentally normal, without other facial anomalies (10, 12). The one patient described by Magid et al. (14) may be sporadic and does not actually exhibit any mode of transmission (10).

Recently, Di Lernia et al. (9) reported an affected mother and child under the title "FFDD", both of whom exhibited features of Setleis' syndrome. The authors proposed them as an autosomal dominant transmission with variable expressivity. Ward & Moss (8) also proposed evidence for the genetic homogeneity of Setleis' syndrome and FFDD. They pointed out the evidence by

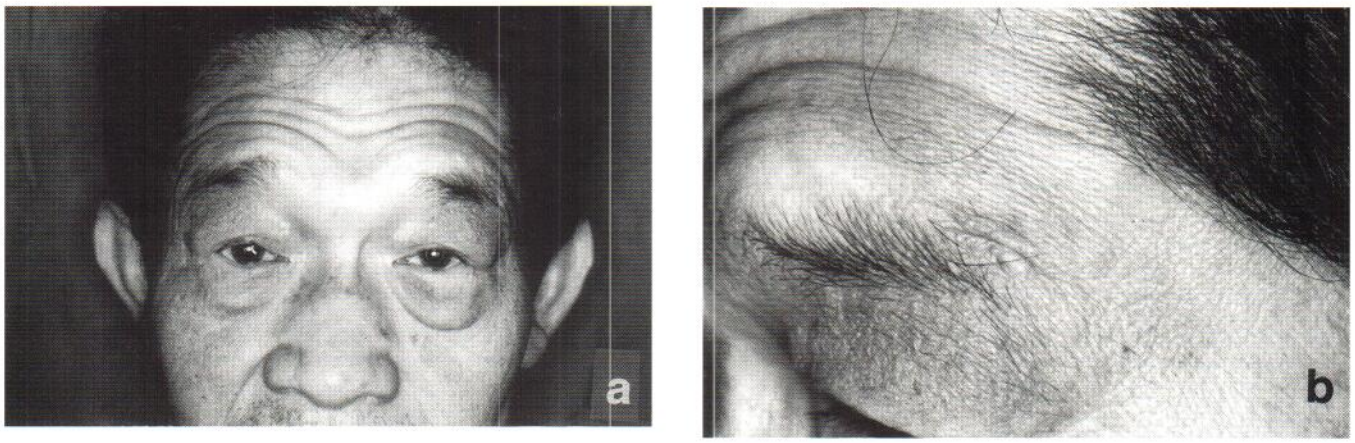

Fig. 4. Case 3 (grandfather of case 1), showing *a*) full front view and *b*) left front-lateral view. Note the "scarlike" lesions, slanting eyebrows and flattened nasal bridge.

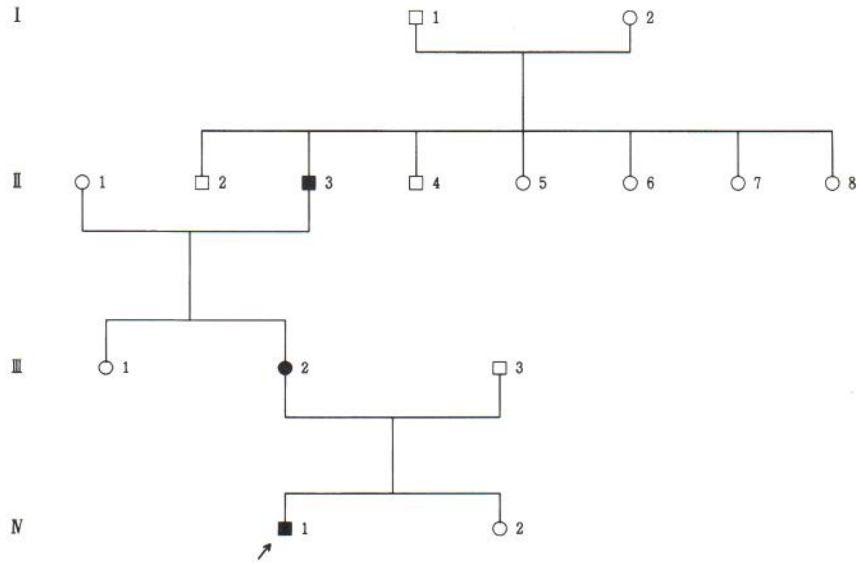

Fig. 5. Family tree of the patients. The proband is indicated with an *arrow*.

three observations: 1) both syndromes are characterized by identical "scarlike" depressions on the temples; 2) facial features said to be characteristic of Setleis' syndrome have previously been observed in FFDD; and 3) the reported differences in inheritance between the two syndromes may be apparent rather than real, because the temporal lesions may become less noticable with age in FFDD, and, in adults, may be missed without careful examination. As mentioned by Kowalski & Fenske (10), this may only be borne out by investigation of additional cases. They also insisted that type III FFDD (Setleis' syndrome) should be divided into the respective subtypes, if heterogeneity proved to be the case.

The precise mechanism, including craniofacial abnormalities, in Setleis' syndrome is unknown. Reporting on a Japanese boy, Matsumoto et al. (5) proposed that Setleis' syndrome may result from an insufficient migration of neural crest cells into the frontonasal process and the first branchial arch.

In summary, we have reported Setleis' syndrome in a typically affected Japanese boy, whose mother and grandfather show a much milder expression of this disorder, suggesting an apparent autosomal dominant inheritance. This is the third report in the English literature from Japan (5,15). Although we could not clarify the hereditary background between the present patients and the case of Matsumoto et al. (5), it is possible that variable penetrance might have occurred in their ancestors, since the families live in close vicinity to each other.

ACKNOWLEDGEMENTS

We thank Dr. Eiji Kato, Children's Clinic, for his clinical assistance and Dr. Shigeru Karukaya, Department of Pediatrics, Kurume University School of Medicine, for performing chromosome analysis.

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