The Stickler syndrome presenting as a dominantly inherited cleft palate and blindness*

JUDITH G. HALL and HENRY HERROD

From the University of Washington Medical School, Division of Medical Genetics, and Children's Orthopedic Hospital and Medical Center, Seattle, Washington, USA

Summary. The Stickler syndrome is a newly recognized, but probably relatively frequent inherited generalized connective tissue disorder involving skeleton, eye, and oro-facial structures. A family with three affected generations is discussed. Severe myopia leading to blindness, cleft palate, or submucous cleft, Pierre Robin anomaly, premature degenerative arthritis, or a family history of any of these indicates further evaluation.

The Stickler syndrome is a newly recognized, but probably relatively frequent inherited connective tissue disorder involving skeleton, eye, and oro-facial structures. We have recently seen a family which presented with dominantly inherited cleft palate and blindness.

Case report

A 4-year-old Caucasian girl was referred because of recurrent otitis media, severe myopia (−17.5 diopters) relative hypotonia, and anaemia. She had a cleft palate which had been repaired at 1 year of age and mild mid-facial hypoplasia. She did not have arthritis, hyper-extensibility of joints or, arachnodactyly. Her family history was remarkable (Fig. 1) in that she had an older brother (V.1) who died unexpectedly at 3½ months of age and had had the Pierre Robin anomaly (micrognathia, cleft palate, and glossoptosis) treated with tracheostomy. Her 6-year-old sister (V.2) had cleft palate with a normal sized jaw, flattening of the right face which had decreased with age, mild mid-facial hypoplasia, severe myopia (−20.0 and −23.0 diopters), and strabismus (Fig. 2). She had no arthritis, but radiographs showed the changes seen in Fig. 3.

The 34-year-old mother (IV.3) had also had Pierre Robin anomaly, facial asymmetry (with a flattened left face), myopia with cataract and retinal detachment in the right eye, and degenerative uveitis, retinal detachment and glaucoma in the left eye, post-operative ptosis of the left eyelid, and mild arthritis of her arms and fingers during the last few years (Fig. 2).

The 31-year-old uncle (IV.4) had bilateral cataracts diagnosed at ½ years of age. Removal of the left cataract led to retinal detachment, glaucoma, and enucleation. The right eye had retinal degeneration in addition to the cataract and eventually developed glaucoma and was enucleated. He also had facial asymmetry and post-operative ptosis. He has a submucous cleft of the posterior quarter of his palate and was late in learning to

Received 12 July 1974.
* This study was supported in part by the National Institute of Health Grant No. 5 P01 GM 15253-07 and Grant No. 5501 RR 0565505 and the National Foundation—March of Dimes Grant CA-90.
Reprint requests to Judith G. Hall MD, Division of Medical Genetics, Children's Orthopedic Hospital, 4800 Sand Point Way, N.E., Seattle, Washington 98105, USA.

Fig. 1. Pedigree.
was an adult. She has myopia in her hips, hand, and eye. No family members of the Stickler syndrome were characterized by overtubulation of long bones, mild flattening and irregularity of epiphyses, mild irregularity and flattening of vertebrae, hypoplasia of the midfacial bones and steep base of the skull (Fig. 3). Schreiner et al (1973) pointed out that as in the present family, the radiological changes were often the most helpful clue to a specific diagnosis of the Stickler syndrome in otherwise asymptomatic individuals in an affected family.

The typical body habitus described by Stickler et al (1965) is slender with disproportionately long arms and legs, but definitely affected individuals have been short and stocky (Schreiner et al, 1973; Herrmann et al, 1975). Some patients have had prominent joints (which may be noted at birth [Stickler et al, 1965]), decreased musculature, hypotonia, scoliosis, increased lumbar lordosis, and hyperextensibility of joints (Herrmann et al, 1975). Among the members of the present family, none had arachnodactyly, hyperextensible joints, nor incapacitating degenerative arthritis. Nevertheless,
The Stickler syndrome presenting as a dominantly inherited cleft palate and blindness

Micrognathia so severe as to be called Pierre Robin anomaly has been reported frequently (Knobloch and Layer, 1972; Opitz et al, 1972; Herrmann et al, 1975). The disproportion of facial structures appears to improve with age with growth of the midface and mandible such that asymmetry is less apparent by adulthood (Knobloch and Layer, 1972).

The palate in patients with the Stickler syndrome may be normal or highly arched, have a submucous cleft or a complete cleft of the hard palate. A bifid uvula may be the only finding. Between one-third and one-quarter of the reported cases of the Stickler syndrome have clefting of the palate but in some families, such as the one reported here, the number of family members with palatal involvement is much greater (Knobloch and Layer, 1972). Cleft lip has not been seen. Many patients present as Pierre Robin anomaly and consequently require complex management during the newborn period. As with all patients who have cleft palates, Stickler patients with cleft palates are prone to recurrent otitis and secondary conductive hearing loss. In addition, neurosensory hearing loss in patients with the Stickler syndrome has been described (Stickler and Pugh, 1967). The combination of ophthalmological and palate problems seen in the Stickler syndrome underlines the necessity for careful eye examination and ophthalmological follow up of any

x-ray films demonstrate definite involvement of the skeleton. Perhaps because of significant eye involvement, the members of this family had less strenuous physical activity and thereby saved their joints some of the usual wear and tear. Avoidance of strenuous activity involving the joints is probably indicated in this condition.

The variety and progressive nature of the eye anomalies seen in patients with the Stickler syndrome is well demonstrated by the present family. All of these patients have severe myopia. Herrmann et al (1975) estimate two-thirds of patients have myopia. Cataracts, non-traumatic retinal detachment leading to blindness, retinal degeneration, glaucoma, ptosis, and esotropia have all been reported and were seen in this family. Lesions can be unilateral or bilateral. Potentially, careful ophthalmologic observation, avoidance of trauma, patient education, and aggressive therapy could prevent some of the retinal detachments and complications of glaucoma (Spranger, 1968; Knobloch and Layer, 1972; Hirose et al, 1973).

The oro-facial features of the Stickler syndrome were not elaborated by Stickler et al (1965; 1967), but appear to be a nearly constant feature. Midfacial hypoplasia, round facies, and facial asymmetry have been noted (Knobloch and Layer, 1972; Schreiner et al, 1973; Herrmann et al, 1975).
patient with cleft palate and particularly with Pierre Robin anomaly (Opitz et al, 1972; Schreiner et al, 1973).

Of the families reported with the Stickler syndrome, all have had a dominant pattern of inheritance. Male to male transmission has occurred and autosomal dominant inheritance can be assumed. In the present family, a new mutation probably occurred in III.14.

Genetic heterogeneity may exist among those families presently described as having the Stickler syndrome, that is, more than one distinct genetic lesion may give rise to a similar clinical picture. However, within a given family, marked variability of expression of the gene occurs both with regard to severity of involvement and organ systems involved. Recognition of affected families is important in order to try to prevent blindness and arthritis, and so that families can learn about the natural history and genetic nature of the condition.

The authors are grateful to Dr Roger Johnson, Dr Robert H. Johns, Dr Samuel H. Tarica, Jr, Dr J. I. Moreland, Dr Richard L. Voorhees, and Dr Gilbert Eade for making available additional historical information on the family; to Dr Eliose Giblett of the Seattle King County Blood Bank for performing blood grouping and serum protein studies; to Dr Frederick Hecht for help during a field study; to Dr David Smith, Dr Michael Cohen, Dr John Opitz and Dr Arno Motulsky for helpful suggestions and criticism, and to Miss Robin McIlvaine for assistance in the preparation of the manuscript.

REFERENCES

The Stickler syndrome presenting as a dominantly inherited cleft palate and blindness.

J G Hall and H Herrod

*J Med Genet* 1975 12: 397-400
doi: 10.1136/jmg.12.4.397

Updated information and services can be found at:
http://jmg.bmj.com/content/12/4/397

*These include:*

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

---

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/