148 MARCH-APRIL 2000
JOURNAL OF DENTISTRY FOR CHILDREN

REPORT

Coffin-Lowry syndrome and premature tooth loss: A case report

Peter Day, BDS, MFDS, RCS (Eng)
Ben Cole, BDS, MSc, FDS (Edin)
Richard Welbury, BDS, MBBS, PhD, FDS RCS (Eng)

Coffin Lowry syndrome (CLS) was first described by Coffin 1966 and later by Lowry 1971.[1,2] In 1975, Temtamy recognized these signs and symptoms to be the same syndrome and named it the Coffin-Lowry syndrome (CLS). It is now recognized that CLS is an X-linked inherited disease with a mutation at Xp 22.1-22.2.[3-6] This results in a defective kinase Rsk- 2 protein, a growth factor regulator. The frequency has been reported as rare, although CLS may be under-reported, due to the difficulty of the diagnosis. Unlike other malformation syndromes, which are obvious at birth, diagnosis of CLS is often established late, after skeletal deformities have appeared.[7]

CLS is characterized by:

- Puffy, lax, tapering fingers which are virtually diagnostic of CLS.[8] (Figure 1)
- Mental retardation, with greater severity in males.[1,2,9,10]
- Coarse facial features, similar to those of acromegaly, which get more prominent with age and which are usually apparent by the second year of life.[8,11,12]
- Various other musculoskeletal, central nervous system, cardio vascular system and skin features including: delayed closure of fontanelles; pectus carinatum or pectus excavatum; thoracolumbar kyphosis or scoliosis; delayed ambulation and clumsy broad-based gait; delayed growth and development; generalized seizures; ventricular dilation; various cardiac anomalies and loose and easily stretched skin.[12]

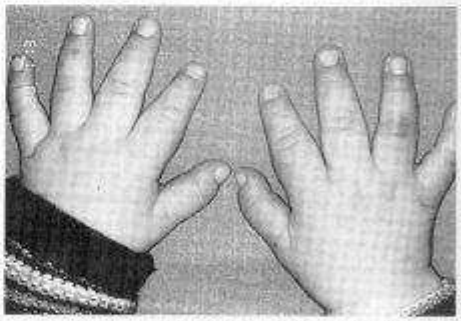

Figure 1. Patients hand and fingers, showing puffy lax tapering fingers.

Specific facial features include: frontal bossing; hypertelorism; antimongoloid slant of the eyes; prominent supraorbital ridges; ptosis of eyelids; large nose with broad base; hypoplastic midface, and prominent ears.[8,9,12] (Figure 2)

We are grateful to Dr. Heather Fletcher, Dr. Andrew Shaw and Mrs. Jan Howarth for their help in the management of this case.

Drs. Day, Cole, and Welbury are in the Department of Child Dental Health, Dental Hospital, Richardson Road, Newcastle upon Tyne, NE2 4AZ, UK.

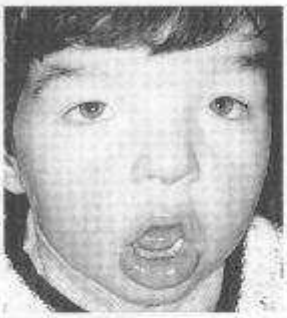

Figure 2. Patient frontal facial profile.

Figure 3. Macroscopic appearance of prematurely exfoliated upper right central primary incisor.

Oral manifestations include: thick and pouting lips; deep midline furrowed tongue; highly vaulted palate; mandibular prognathism and variable tooth anomalies including: microdontia especially of the anterior teeth, spacing between teeth, early loss of teeth and delayed eruption of teeth.[1-3,7,8,10,11,13-18]

CASE REPORT

A two-year-old boy was referred by his general dental practitioner to the Dental Hospital, because of premature exfoliation of his primary teeth. A consultant community pediatrician was investigating the patient at the time for an undiagnosed syndrome.

There was a history of recent loss of both mandibular primary central incisors (71,81) and the loss that morning of the maxillary right central primary incisor (51). There was no history of premature tooth loss in the family and no knowledge of any medical syndromes.

On examination there were delayed development and dysmorphic features including hypertelorism, antimongoloid slant, an open anterior fontanelle, hypertrichosis and short hands. The lips were thick and prominent (Figures 1,2 were taken at approximately eighteen months after his initial presentation). Intraorally the soft tissues were normal and the following teeth were present: DCB/ABCD (54, 53, 52, 61, 62, 63, 64, 72, 73, 74, 82, 83, 84) DCB /BCD

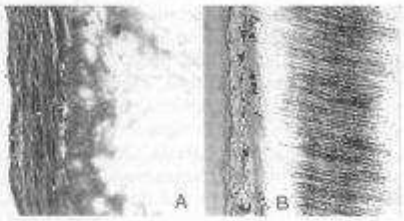

Figure 4A. Decalcified ground section showing periodontal ligament fibers arranged parallel to the root surface. Sharpey's fibers are not prominent (X650).

Figure 4B. Ground section showing thin layer of a cellular cementum (x75).

Figure 5. Patient's oral appearance at age of three years six months.

The most notable abnormality was the marked gingival inflammation, recession and mobility associated with the maxillary left primary central incisor (61). The remaining anterior teeth were slightly conical and microdont. The erupted first primary molars were of normal morphology.

Lateral oblique radiographs showed normal root morphology of primary molars and an appropriate number of developing permanent teeth for his age.

Histological examination of the recently exfoliated (51) revealed the following:

- ☐ Macroscopically: Cervical caries with no evidence of any residual periodontal membrane (Figure 3).
- ☐ Microscopically: thin acellular or sparsely cellular cementum covered by fibrous tissue. There was little evidence of fiber insertion into cementum and irregular secondary dentin was present on the pulpal aspect of the cementum (Figure 4A and 4B).
- ☐ Radiographically: normal opacity of enamel and dentin with an enlarged pulp chamber and cervical caries.

The cemental and pulpal changes were consistent with a histological diagnosis of hypophosphatasia. Because the tooth was originally received dry, the possibility of a fixation artefact, however, cannot be excluded.

Blood tests at first showed a raised alkaline phosphatase and normal calcium, phosphate, parathyroid hormone and renal function. Three months later, however, the alkaline phosphatase was within normal range. There were no other signs to support a clinical diagnosis of hypophosphatasia. Over the next nine months a diagnosis of CLS was made on the basis of the morphological features and developmental delay.

DENTAL TREATMENT

Over the last year and a half, further teeth have exfoliated prematurely (52,62,72,82) (Figure 5). At the last visit all four primary canines showed loss of attachment with exposure of root surfaces. The maxillary primary first molars (54, 64) were extracted due to caries. The newly erupted second primary molars (55,65,75,85) are microdont.

Oral hygiene instruction, dietary advice and topical application of fluoride continues on a regular basis. The periodontal health of the primary canines (53,63,73,83) continues to deteriorate despite once daily application of chlorhexidene 0.2 percent gel.

DISCUSSION

Although the oral manifestations of CLS have been well described previously, the first report to go into detail was that of Hartsfield 1993.[16] He reported the premature exfoliation of (51,61,71,72,81,82) in a patient, age four years and ten months, with CLS. These teeth had all erupted, but the mother could not remember at what age they were lost. Although hypodontia had been described in numerous cases, he postulated that in some cases it may be due to early loss rather than failure of eruption.[1,3,7,8,10,13-15] Certainly there are reported cases of premature loss of permanent teeth and primary teeth.[10,16,19,20]

In the report of a thirty-four-year-old male with CLS, only a few teeth remained. Radiographs showed shortened roots and considerable loss of bone around each remaining tooth, suggesting loss of periodontal attachment.[19]

In the report of the early loss of primary teeth in CLS, no further explanation other than poor oral hygiene was given.[16] Our case report suggests that early tooth loss was due to hypoplastic cementum with insertion of only a few periodontal membrane fibers. This could have been the cause of early loss in other reports. Verification would only be possible by histological examination of exfoliated teeth in the other reports. Whether joint laxity and collagen defects noted in numerous cases is involved in this pathological failure of periodontal membrane insertion is unknown.[3,5,13,15,20]

If our findings are confirmed in further CLS cases, then CLS could be added to the list of differential diagnoses where primary teeth are lost prematurely. The histological appearance of such teeth is similar to that described in hypophosphatasia.

REFERENCES

1. Coffin, G.S.; Siris, E.; Wegienka, L.C.: Mental retardation with osteocartilaginous anomalies. Am J Dis Child, 112:205-213, September 1966.
2. Lowry, B.; Miller, J.R.; Fraser, F.C: A new dominant gene mental retardation syndrome: Associated with small stature, tapering fingers, characteristic faces and possible hydrocephalus. Am J Dis Child, 121:491- 500, June 1971.
3. Temtamy, S.A.; Miller, J.D.; Hussels-Maumenee, I.: The Coffin-Lowry syndrome: An inherited faciodigital mental retardation syndrome. J Pediatr, 86:724- 731, May 1975.
4. Hanauer, A.; Alembik, Y.; Gilgenkrantz, S. *et al*: Probable localization of the Coffin-Lowry locus in Xp22.2- p22.1 by multipoint linkage analysis. Am J Med Genet, 30:523-530, May-June 1988.
5. Partington, M.W.; Mulley, J.C.; Sutherland, G.R. *et al*: A family with the Coffin-Lowry syndrome revisited: localization of CLS to Xp21-pter. Am J Med Genet, 30: 509-521, May-June 1988.
6. Biancalana, V.; Braird, M.L.; David, A. *et al*: Confirmation and refinement of the genetic localization of Coffin-Lowry Syndrome locus in Xp22.1- p22.2. Am J Hum Genet, 50: 981-987, May 1992.
7. Gilgenkrantz, S.; Mujica, P.; Gruet, P. *et al*: Coffin-Lowry Syndrome: a multicenter study. Clin Genet, 34:230-245, October 1988.
8. Hunter, A.G.W.; Partington, M.W.; Evans, J.A.: The Coffin-Lowry syndrome: experience from four centres. Clin Genet, 21:321-335, May 1982.
9. Collacott, R.A.; Warrington, J.S.; Young, I.D.: Coffin-Lowry syndrome and schizophrenia: a family report. J Ment Def Res, 31:199-207, June 1987.
10. Procopis, P.G. and Turner, B.: Mental retardation, abnormal fingers and skeletal anomalies, Coffin's syndrome. Am J Dis Child, 124:258-261, August 1972.
11. Young, I.D.: The Coffin-Lowry syndrome. J Med Genet, 25:344-348, May 1988.
12. Gorlin, R.J.; Cohen Jr, M.M.; Levin, L.S.: *Syndromes of the Head and Neck*. Oxford: University Press, 1990, 3rd Edition, pp 827-829.
13. Haspeslagh, M.; Fryns, J.P.; Beusen, L. *et al*: The Coffin-Lowry syndrome: A study of 2 new index patients and their families. Eur J Pediatr, 143:82- 86, December 1984.
14. Plomp, A.S.; De Die-Smulders, C.E.M.; Meinecke, P. *et al*: Coffin-:Lowry Syndrome: Clinical aspects at different ages and symptoms in female carriers. Genetic Counseling, 6:259-268, 1995.
15. Kousseff, B.G.: Coffin-Lowry syndrome in an Afro-American family. Am J Med Genet, 11:373-375, March 1982.
16. Hartsfield, Jr, J.K.; Hall, B.D.; Grix, A.W. *et al*: Pleiotropy in Coffin-Lowry Syndrome: Sensorineural hearing deficit and premature tooth loss as early manifestations. Am J of Med Genet, 45:552-557, March 1993.
17. MacDermot, K.D.; Buckley, B.; Van Someren, V. *et al*: Osteopenia, abnormal dentition, hydrops fetalis and communicating hydrocephalus. Clin Genet, 48: 217-220, October 1995.
18. Fryns, J.P.: Letter to the Editor: Osteopenia, abnormal dentition, hydrops fetalis and communicating hydrocephalus: unusual early clinical signs in Coffin-Lowry syndrome. Clin Genet, 50:112, August 1996.
19. Sylvester, P.E.; Rundle, A.T.; Richards, B.W.: The syndrome of Coffin, Siris and Wegienka: Report of a case. J Ment Defic Res, 20:35-54, March 1976.
20. Padley, S.; Hodgson, S.V.; Sherwood, T.: The radiology of Coffin-Lowry syndrome. Br J Radiol, 63:72-75, January 1990.