Isolated and Syndromic Syngnathism

Management, Implications, and Genetics

Jillian K. Tomlinson, MBBS(Hons), Dip Anat, Nguyen Thanh Liem, MD, PhD,† Ravi Savarirayan, MBBS, FRACP, MD, ARCPA,‡ and John G. Meara, FRACS, MBA§*

Abstract: We present 2 contrasting cases of congenital interalveolar synechiae. The first occurred in the setting of Van der Woude syndrome and was associated with a cleft palate. In the second case, it was an isolated abnormality and there was no contributory family history or syndromic associations. We review the literature on interalveolar synechiae and discuss its management, implications, and genetics. Interalveolar synechiae is a condition with an excellent prognosis; its presence necessitates careful examination for associated abnormalities and syndromes.

Key Words: syngnathism, interalveolar synechiae, cleft palate, Van der Woude syndrome, popliteal pterygium syndrome, interferon regulatory factor 6, IRF6

(*Ann Plast Surg* 2006;57: 231–235)

CASE REPORTS

Case Report 1: Cleft Palate and Congenital Interalveolar Synechiae in an Infant With Van der Woude Syndrome (VWS)

A 38-week male infant was delivered via emergency cesarian section for fetal distress to a primigravida mother. The parents were unrelated but the mother and maternal relatives had phenotypes consistent with VWS (see pedigree, Fig. 1). Apgar scores at 1 and 5 minutes were 5 and 9, respectively. Birth weight was 3300 g (53rd centile), length 49 cm (50th centile), and head circumference 32 cm (<10th centile). Micrognathia and severely restricted mouth opening was noted on physical examination; the maximum intergum distance was 2 mm. Ultrasound scans at 20 and 36 weeks' gestation had demonstrated no abnormalities.

At 3 days of age the infant was transferred to us from a peripheral hospital for ongoing management. Nasogastric feeding was commenced and elective tracheostomy performed on the fifth day of life for marked desaturations while in the prone position.

Karyotyping, echocardiogram, head ultrasound, renal ultrasound and EEG were normal. Facial CT demonstrated a symmetrical but hypoplastic mandible, with obtuse mandibular angles and normal mandibular condyles (Fig. 2). There was a bony defect of the hard palate and a defect of the soft palate. MRI was unremarkable, demonstrating no evidence of masseteric or temporalis scarring or banding.

Examination under anesthesia (EUA) was performed at 1 month of age. There was no improvement in mandibular mobility with muscle relaxant, and no cause was found for the rigid obstruction to mouth opening. Over subsequent weeks intraoral adhesions between the maxilla and mandible became evident on examination (see Fig. 3) and at 14 weeks of age the infant underwent EUA and lysis of intraoral adhesions between the gingiva of the maxilla and mandible posteriorly (see Fig. 4). Mouth opening was 3 mm preoperatively and 6 mm following diathermy division of the soft tissue adhesions. The masseter muscles were tight bilaterally. The floor of mouth was abnormal, and the tongue was posteriorly displaced and protruding into the nasopharynx above the palate. Passive movements were commenced postoperatively, and at review 8 weeks later, the infant had a 30-mm interalveolar opening.

Tongue base advancement with a circummandibular Prolene suture was performed at 8 months of age (see Figs. 5 and 6) and in the following weeks oral intake increased to the extent that nasogastric feeding was able to be ceased. The patient underwent successful elective decannulation of his tracheostomy at 12 months of age. The circummandibular suture was removed and the tongue remained in an anatomically normal position. Mouth opening is now normal. The patient had an uncomplicated cleft palate repair at 18 months of age and has had no further difficulties with either feeding or airway.

Case Report 2: Isolated Unilateral Congenital Interalveolar Synechiae

A 6-day-old female was transferred from another hospital following a normal pregnancy and vaginal delivery. The parents were related, but there were no abnormalities noted in either parent or other relatives. Apgar scores were 8 and 9 at 1 and 5 minutes. Birth weight was 1900 g, length 47 cm, head

Received November 23, 2005, and accepted for publication January 30, 2006.

From the *Royal Children's Hospital Melbourne; †National Hospital of Pediatrics, Hanoi; ‡Murdoch Children's Research Institute and Department of Paediatrics, University of Melbourne; and the §Royal Children's Hospital Melbourne, Australia.

Reprints: Dr Jillian Tomlinson, 8 Maple Crescent, Camberwell 3124, Victoria, Australia. E-mail: jilliantomlinson@hotmail.com.

ISSN: 0148-7043/06/5702-0231

DOI: 10.1097/01.sap.0000215265.68252.f0

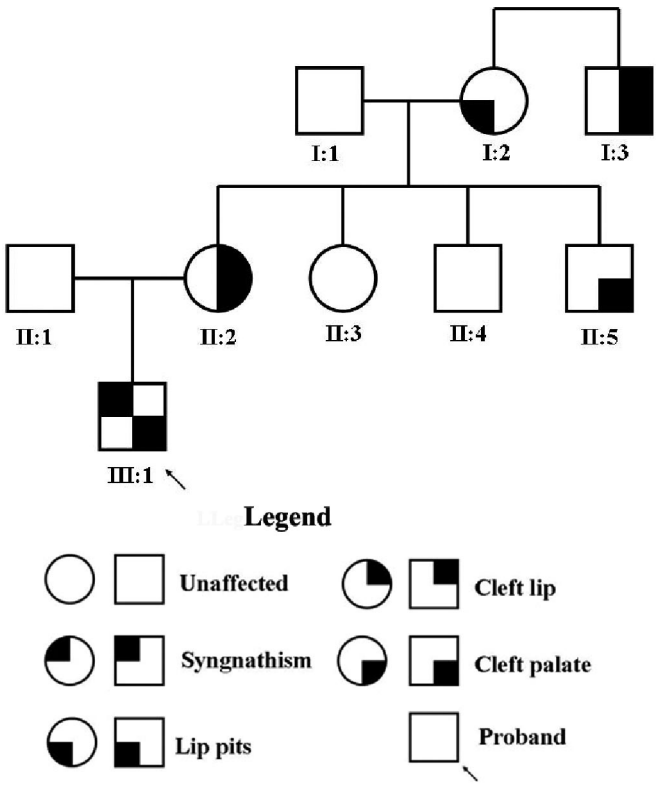

FIGURE 1. Case 1 pedigree.

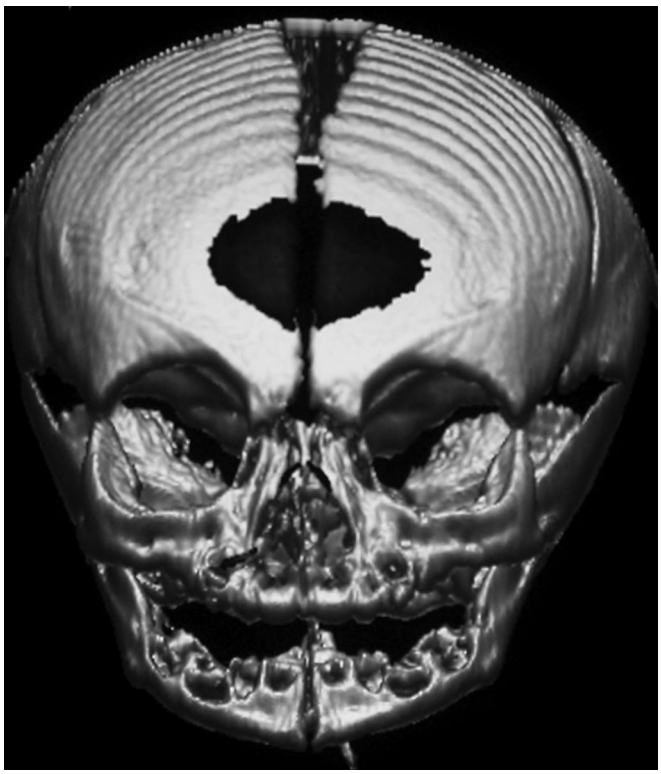

FIGURE 2. 3D CT image, case 1.

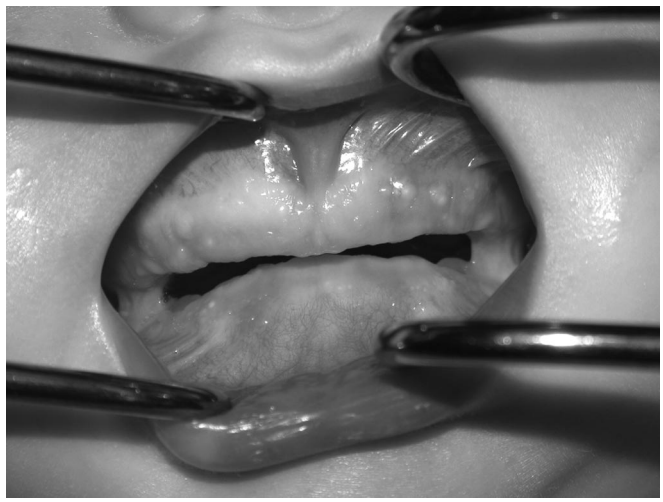

FIGURE 3. Preoperative image, bilateral interalveolar adhesions, case 1.

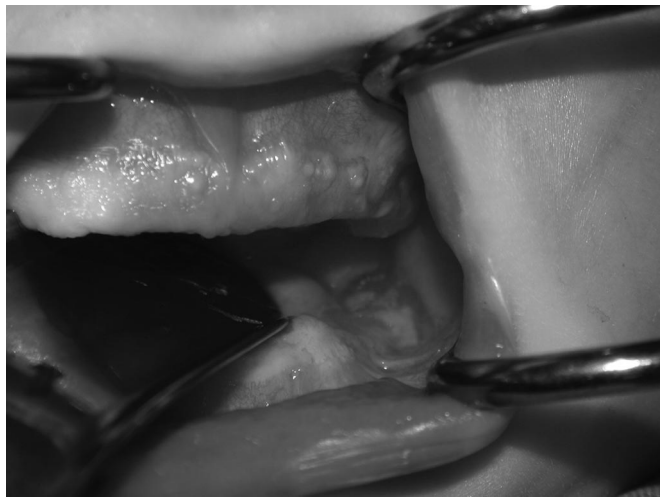

FIGURE 4. Postoperative, left interalveolar region, case 1.

circumference 30 cm. Mouth opening was severely restricted, with a maximum intergum distance of 5 mm. There were no other anomalies noted.

The child had no airway difficulties preoperatively and was fed orally. The child was referred to the NHP in Hanoi, where on examination an interalveolar synechiae was identified. The patient was taken to the operating room and lysis of this adhesion was performed at 6 weeks of age under intravenous anesthesia. Adhesions in the premolar/molar region were divided with diathermy without complication (see Figs. 7 and 8).

Postoperatively the child had no airway or feeding difficulties. Jaw movement is now normal.

DISCUSSION

Syngnathia

Syngnathia occurs when an ectopic membrane forms a fibrous or bony adhesion between the maxillary and mandib-

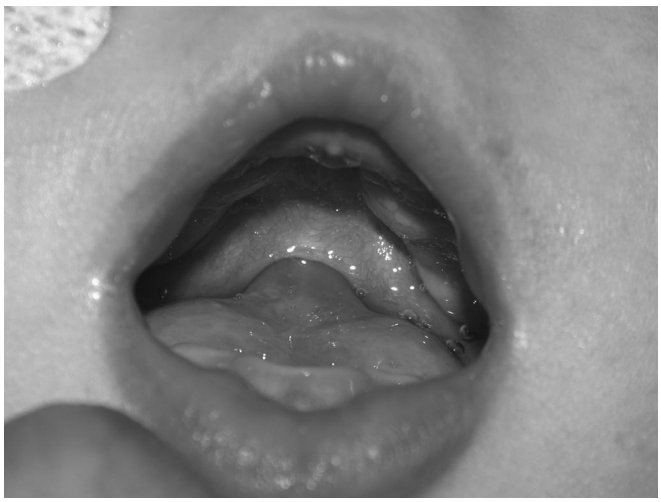

FIGURE 5. Preoperative image, tongue base advancement, case 1.

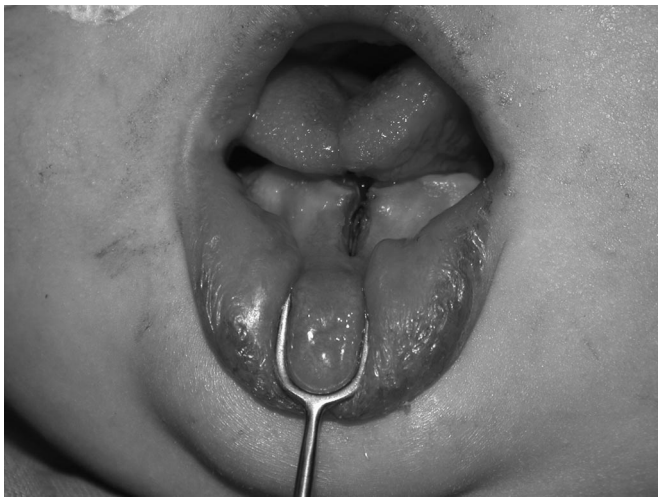

FIGURE 6. Postoperative image, tongue base advancement, case 1.

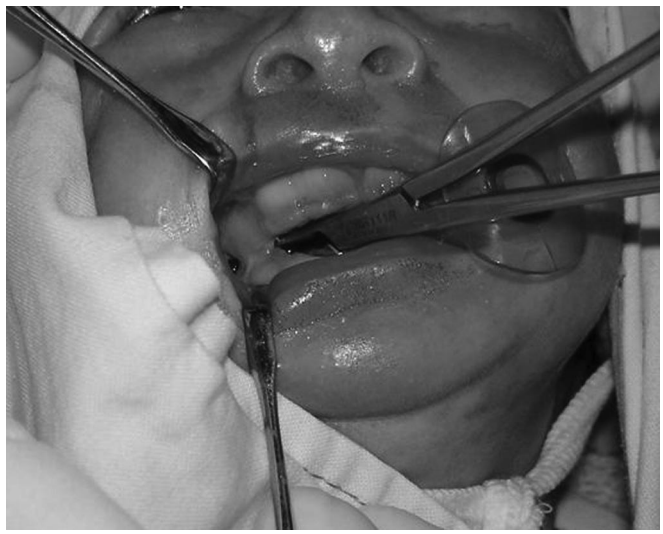

FIGURE 7. Preoperative image, case 2.

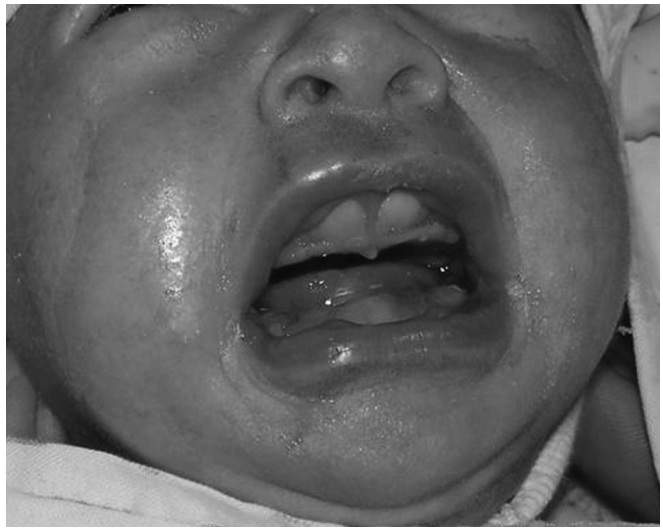

FIGURE 8. Postoperative image, case 2.

ular alveolar processes. Soft tissue adhesions are commoner than bony adhesions, but division is associated with excellent outcomes as the temporomandibular joints and muscles of mastication are generally normal.

Associated Syndromes

Interalveolar adhesions are associated with congenital syndromes, including VWS, popliteal pterygium syndrome (PPS), orofacial digital syndromes, and cleft palate lateral synechiae syndrome (CPLSS). VWS is characterized by lower lip pits, cleft palate, cleft lip, and hypodontia. Inheritance is autosomal dominant, with very high penetrance and variable expressivity. VWS is one of the most frequent causes of syndromic clefting, accounting for 2% of all cleft lip and palate cases.[1] There is also a predisposition toward ectopic oral mucosal adhesions.[2] PPS is a related disorder characterized by popliteal and intercrural pterygium, cleft palate and/or cleft lip, genital and hand anomalies, including syndactyly. VWS and PPS are allelic and have phenotypic overlap as both syndromes are due to genetic mutations affecting interferon regulatory factor 6.[3] Interalveolar synechia occur in 33% to 43% of patients with PPS.[4–7]

Orofacial digital syndromes involve cleft lip and cleft palate, multilobulated tongue, multiple buccal frenulae, and digital and neural anomalies.[8] In CPLSS, oral synechiae originate in the margins of a palatal cleft and attach to the mandibular alveolar ridge or the floor of the mouth.[9] This has been described as being distinct from the syndrome of cleft palate and congenital lateral alveolar synechia syndrome. However, this separation is likely artificial, with the different phenotypes resulting from the variable penetrance and expressivity in VWS and related conditions rather than a predisposition towards synechiae occurring between specific areas of oral mucosa.

Etiology

Interalveolar synechiae have been postulated to result from persistence of the buccopharyngeal membrane,[10] a genetic predisposition towards anomalous fusion of adjacent epithelial surfaces, or local ischemia of the amniotic bands causing pressure on the first branchial arch.[11] It has been suggested that cleft palate predisposes to the formation of synechiae by permitting closer-than-usual contact between mucosal surfaces,[12] but this does not explain the cases where synechiae occur in the absence of cleft palate. A tendency towards anomalous fusion of adjacent epithelial surfaces is supported by the occurrence of interoral and eyelid adhesion in VWS and PPS. The discovery of specific genetic mutations in IRF6 in VWS and PPS has gone some way to providing a genetic explanation, although the variable penetrance and expressivity seen in VWS strongly point towards the existence of other unknown stochastic factors or modifying genes that influence gene expression and function.

The Genetic Implications of VWS

When occurring in isolation, cleft lip and cleft palate are thought to be developmentally and genetically distinct,[13,14] despite the existence of syndromes that involve both types of cleft. VWS is the best example of a single gene disorder that encompasses the clefting phenotypes of both cleft lip and palate. Identification of the IRF6 gene as the cause of VWS and PPS is thus of considerable value in understanding the complex puzzle of cleft lip and palate.

Genetic Counseling

VWS has an incidence of 1:75,000 to 100,000,[15] and approximately 30%–50% of cases are de novo mutations.[16] Genetic counseling involves discussing the likelihood of inheriting the gene (50%), its penetrance (up to 100% in carefully assessed pedigrees) and its variable expression. While relative risks of transmitting any single feature have been calculated by some authors based on pedigree analysis, the accuracy of such predictions is unknown.

Management of Interalveolar Adhesions

Airway management is of great concern when managing a neonate with interalveolar synechiae and limited mouth opening. In most reported cases a surgical airway is not required. Timing of division of synechiae has ranged from day 1 after birth[17] to 8 months.[18] Stretching and spontaneous breakdown of synechiae can occur[11] and in mild or uncomplicated cases patients may be managed expectantly in the initial months of life. However, extensive synechiae are unlikely to resolve with conservative management and if adequate oral feeding is not possible synechiae should be divided as soon as practicable.

Small synechiae may be divided in the nursery without anesthesia.[11,19,20] More commonly, an operative procedure is undertaken, with the airway managed either by elective tracheostomy or nasotracheal intubation. Bony fusion and TMJ ankylosis should be ruled out preoperatively with plain x-ray, CT, or MRI. Lysis of the adhesion may be performed either sharply or with diathermy.

Nasogastric feeding may be required prior to division of the adhesions if oral intake is inadequate. Immediately after surgery, it may not be possible for the infant to feed normally because of associated abnormalities and/or trismus of the muscles of mastication due to prolonged immobility. These may require additional surgical management or may improve with nonoperative management.

Active and passive physiotherapy is commenced after operative intervention to maximize the likelihood of achieving normal mouth opening. Reports indicate that even after release at 8 months of age,[18] the temporomandibular joint ankylosis that results from immobilization may resolve completely.

Case Discussion

This paper presents 2 contrasting cases of interalveolar synechiae. The first patient has a family history of VWS and an associated cleft palate, while the second patient has no relevant family history or associated abnormalities. There are 40 case reports in the literature similar to case 1.[2,4,8–13,17–19,21–42] These patients have associated features that support a diagnosis of VWS; some cases have bony adhesions. It is unclear whether a distinction should be made between cases of interalveolar synechiae and those where the synechiae run from a cleft palate to the floor of the mouth; 10 such of these cases have been reported.[38,43,45,46] We suspect that these ectopic membranes have a similar etiology and, importantly, that the different locations reflect a variable phenotype rather than a predisposition toward synechia formation between specific areas of oral mucosa. This is further supported by 2 reports[17,20] where cleft palate coexists with a medial band running from the incisive foramen to the anterior floor of the mouth. There are 6 other reported cases of isolated interalveolar synechiae that are similar to our second case report.[12,35,47–50]

CONCLUSION

Congenital interalveolar synechiae frequently have syndromic associations, although isolated instances do occur. The Van der Woude phenotype is common among patients with interalveolar synechiae; recent identification of the IRF6 gene as the cause of VWS and PPS is of interest in explaining both the etiology of interalveolar synechiae and the complex puzzle of cleft lip and palate. Fibrous interalveolar synechiae are associated with excellent outcomes as the muscles of mastication and temporomandibular joints are almost invariably normal. Every patient with interalveolar synechiae warrants careful examination for signs of an associated syndrome.

REFERENCES

1. Schutte BC, Sander A, Malik M, et al. Refinement of the van der Woude gene location and construction of a 3. 5-Mb YAC contig and STS map spanning the critical region in 1q32-q41. *Genomics*. 1996;36:507–514.
2. Denion E, Capon N, Martinot V, et al. Neonatal permanent jaw constriction because of oral synechiae and Pierre Robin sequence in a child with van der Woude syndrome. *Cleft Palate Craniofac J*. 2002;39:115–119.
3. Kondo S, Schutte BC, Richardson RJ, et al. Mutations in IRF6 cause Van der Woude and popliteal pterygium syndromes. *Nat Genet*. 2002; 32:285–289.
4. Valnicek SM, Clarke HM. Syngnathia: a report of two cases. *Cleft Palate Craniofacial J*. 1993;6:582–585.

5. Hunter A. The popliteal pterygium syndrome: report of a new family and review of the literature. *Am J Med Genet*. 1990;36:196–208.
6. Deskin RW, Sawyer DG. Popliteal pterygium syndrome. *Int J Pediatr Otorhinolaryngol*. 1988;15:17–22.
7. Froster-Iskenius UG. Popliteal pterygium syndrome. *J Med Genet*. 1990;27:320–326.
8. Addus H, Pruansky S. Postnatal craniofacial development in children with the oro-facial-digital syndrome. *Arch Oral Biol*. 1964;9:193.
9. Dinardo NM, Christian JM, Bennet JA, et al. Cleft palate lateral synechiae syndrome: review of the literature and case report. *Oral Surg Oral Med Oral Pathol*. 1989;68:565–566.
10. Gartlan MG, Davies J, Smith RJ. Congenital oral synechiae. *Ann Otol Rhinol Laryngol*. 1993;102:186–197.
11. Dalal M, Davison PM. Cleft palate congenital alveolar synechiae syndrome: case reports and review. *Br J Plast Surg*. 2002;55:256–257.
12. Goodacre TE, Wallace AF. Congenital alveolar fusion. *Br J Plast Surg.* 1990;43:203–209.
13. Fish J. Congenital intermaxillary fibrous bands. *J Dent*. 1973;1:117–119.
14. Ghassibe M, Revencu N, Bayet B, et al. Six families with van der Woude and/or popliteal pterygium syndrome: all with a mutation in the IRF6 gene. *J Med Genet*. 2004;41:e15.
15. Cervenka J, Gorlin RJ, Anderson VE. The syndrome of pits of the lower lip and cleft lip and/or palate: genetic considerations. *Am J Hum Genet*. 1967;19:416–432.
16. Souissi A, El Euch D, Mokni M, et al. Congenital lower lip pits: a case report. *Dermatol Online J*. 2004;10:10.
17. Murphy SM, Rea S, McGovern E, et al. Cleft palate and congenital synechiae syndrome: a case report. *Cleft Palate Craniofac J*. 2004;41:206–207.
18. Sahin U, Ozdil K, Uscetin I, et al. Cleft palate and congenital alveolar synechiae syndrome. *Plast Reconstr Surg*. 2005;115:1212–1213.
19. Puvabanditsin S, Garrow E, Sitburana O, et al. Syngnathia and Van der Woude syndrome: a case report and literature review. *Cleft Palate Craniofac J*. 2003;40:104–106.
20. Ogino A, Onish K, Maruyama Y. Congenital oral synechia associated with cleft palate: cleft palate medial synechia syndrome? *Eur J Plastic Surg*. 2005;27:7338–7340.
21. Verdi GD, O'Neal B. Cleft palate and congenital alveolar synechiae syndrome. *Plast Reconstr Surg*. 1984;74:684–686.
22. Mathis VH. Ubereinen fallvon erriahrungsschwierigkeit. *Dtsch Zahn Z*. 1962;17:1167–1171.
23. Haramis HT, Apesos J. Cleft palate and congenital lateral alveolar synechia syndrome: case presentation and literature review. *Ann Plast Surg*. 1995;34:424–430.
24. Pillai KG, Kamath VV, Kumar GS, et al. Persistent buccopharyngeal membrane with cleft palate: a case report. *Oral Surg Oral Med Oral Pathol*. 1990;69:164–166.
25. Shaw WC, Simpson JP. Oral adhesions associated with cleft lip and palate and lip fistulae. *Cleft Palate J*. 1980;17:127–131.
26. Neuman Z, Shulman J. Congenital sinuses of the lower lip. *Oral Surg Oral Med Oral Pathol*. 1961;14:1415–1420.
27. Sternberg N, Sagher U, Golan J, et al. Congenital fusion of the gums with bilateral fusion of the temporomandibular joints. *Plast Reconstr Surg*. 1983;72:385–387.
28. Traaholt LM. Cleft lip and palate associated with alveolar synechiae and filiform palpebral synechia. *Plast Reconstr Surg*. 1990;86:337–339.
29. Snijman PC, Prinsloo JG. Congenital fusion of the gums. *Am J Dis Child*. 1966;112:593–595.
30. Itoh M, Takato T, Park S, et al. Congenital alveolar adhesions. *Ann Plast Surg*. 1992;29:89–91.
31. Deleted in proof.
32. Shah RM. Palatomandibular and maxillo-mandibular fusion, partial aglossia and cleft palate in a human embryo. *Teratology*. 1977;15:261.
33. Randall P. Cleft palate and congenital alveolar synechia syndrome. *Plast Reconstr Surg*. 1984;74:686.
34. Hoggins GS. Aglossia congenital with bony fusion of the jaws. *Br J Oral Surg*. 1969;7:63–32.
35. Narasimharao KL, Mitra S, Mitra SK. Congenital fusion of gums with ankylosis of temporomandibular joints. *Indian Pediatr*. 1984;21:656–657.
36. Seraj MA, Yousif M, Channa AB. Anaesthetic management of congenital fusion of the jaws in a neonate. *Anaesthesia*. 1984;39:695–698.
37. Salleh NM. Congenital partial fusion of the mandible and maxilla: report of a case. *Oral Surg Oral Med Oral Pathol*. 1965;20:74–76.
38. Gassner I. Familial occurrence of syngnathia congenita syndrome. *Clin Genet*. 1979;15:241–244.
39. Davis WB. Congenital deformities of the face. *Surg Gynecol Obstet*. 1935;61:201–209.
40. Seres-Santamaria A, Arimany JL, Muniz F. Two sibs with cleft palate, ankyloblepharon, alveolar synechiae, and ectodermal defects: a new recessive syndrome? *J Med Genet*. 1993;30:793–795.
41. Simpson JR, Maves MD. Congenital syngnathia or fusion of the gums and jaws. *Otol Head Neck Surg*. 1985;93:96–99.
42. Burket LW. Congenital bony temporomandibular ankylosis and facial hemiatrophy: review of the literature and report of a case. *JAMA*. 1936;106:1719–1722.
43. Preus M, Fraser FC, Fuhrmann W. Cleft palate-lateral synechia syndrome without the lateral synechia (CP+/−LS syndrome). *Teratology*. 1974;9:135.
44. Hay RJ, Wells RS. The syndrome of ankyloblepharon, ectodermal defects and cleft lip and palate: an autosomal dominant condition. *Br J Dermatol*. 1976;94:277–289.
45. Furhmann W, Koch F, Schweckendiek W. Autosomal dominant Vererbung von Gaumenspalte und Synechien zwischen Gaumen und Mundboden oder Zunge. *Humangenetik*. 1972;14:196–203.
46. Barendes J. Angeborene Synechie zwischen der Mund-Boden Schleimhaut und den Oberkieferfort-sazen am Rande einer Gaumensplate. *Z Hals Nasen Ohrenheilkd.* 1960-1961;9:180.
47. Tanrikulu R, Erol B, Gorgun B, et al. Congenital alveolar synechiae: a case report. *Br Dent J*. 2005;198:81–82.
48. Haydar SG, Tercan A, Uckan S, et al. Congenital gum synechiae as an isolated anomaly: a case report. *J Clin Pediatr Dent*. 2003;28:81–83.
49. Szelely F. Atresia oris. *Budapesti Orvosi Ujsag*. 1941;39:15–16.
50. Miskinyar SAC. Congenital mandibulo-maxillary fusion. *Plast Reconstr Surg*. 1979;63:120–121.