Basal Cell Nevus Syndrome with Abnormal Karyotype — Report of a Case and Genetic Pedigree —

Tsuyoshi HATA and Masaru HOSODA

Department of Oral Surgery,
Kawasaki Medical School, Kurashiki 701-01, Japan

Accepted for publication on August 28, 1996

ABSTRACT. A 17-year-old girl was admitted to our hospital because of painful swelling in the right mandibular region. Her family history showed basal cell nevus syndrome (BCNS) with multiple jaw cysts in four family members. The patient had a rather broad-based nose, mild ocular hypertelorism, peculiar pits of the hands and ankyloglossia. Roentgenographic examination revealed two well-defined cystic radiolucencies with impacted third molars in both mandibular molar regions. No other osseous abnormalities were noted. Chromosome examination showed a small deletion in the long arm of the No. 9 chromosome (mos46,XX/46,XX,del(9)(q32)). A final diagnosis of BCNS with multiple odontogenic keratocysts was made and enucleations of the cysts were performed. By a review of literature, the significance of multiple odontogenic keratocysts is discussed.

Key words: basal cell nevus syndrome (BCNS) — keratocyst — abnormal karyotype

Basal cell nevus syndrome (BCNS), established by Gorlin and Goltz (1960),[1] is an autosomal dominant hereditary disorder characterized by multiple odontogenic keratocysts, various skin tumors, peculiar pits of the hands and feet, and skeletal anomalies of the ribs, spine, and skull. Of major interest to the oral and maxillofacial surgeon is the fact that multiple jaw cysts may be the chief complaint of patients, and they show a high tendency to recur after enucleation. Furthermore, various kind of tumors, including carcinoma associated with BCNS in the oral and maxillofacial region, have been reported.[2–5] After presentation of the findings in a rare case of BCNS with an abnormal karyotype and genetic pedigree, the significance of odontogenic keratocysts will be discussed in this report.

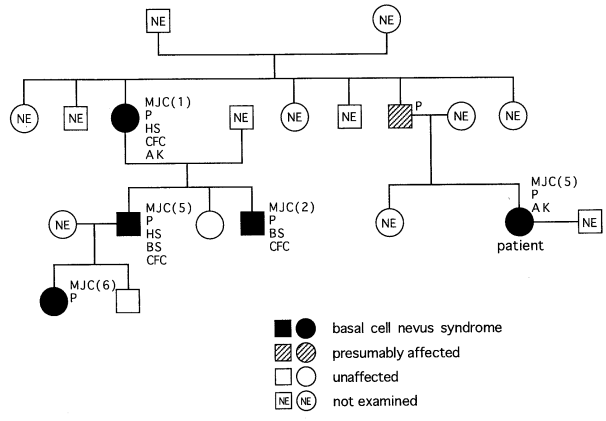
CASE REPORT

A 17-year-old girl was admitted to the Oral Surgery Clinic of Kawasaki Medical School Hospital on April 27, 1987, with a complaint of painful swelling in the mandibular right canine region. Her family history showed BCNS with multiple jaw cysts in four family members (Fig 1). The patient had diffuse swelling with tenderness in the right mental region and discharge of pus in the mandibular gingiva around the right canine. Her fever reached the 37°C level. Laboratory examination showed an increased number of leukocytes

畑　毅, 細田　超

(9200/μl) and an elevated CRP level (6.5mg/dl). Roentgenographic examination revealed an impacted mandibular right canine and two well-defined, unilocular cystic radiolucencies with impacted third molars in both mandibular molar regions (Fig 2). The mandibular right lateral incisor was extracted and curettage of soft tissue around the root was performed after antibiotic therapy. The bony cavity was packed with gentamicin-applied gauze. The clinical course was uneventful. Histologic examination of the soft tissue revealed granulation tissue.

Further investigation demonstrated a rather broad-based nose, mild ocular hypertelorism, peculiar pits of the hands and ankyloglossia. No other osseous



MJC: muliple jaw cysts (number); P: pits; HS: hyposcoliosis; BS: bridging of sella
CFC: calcification of falx cerebri; AK: abnormal karyotype

Fig 1. Genetic pedigree and clinical findings

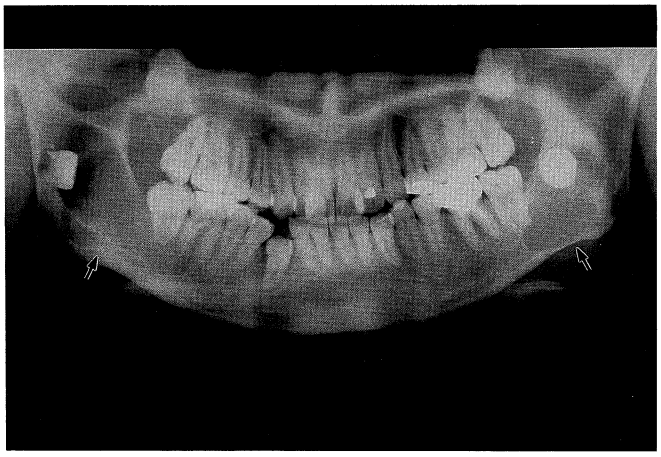


Fig 2. A panoramic radiograph revealed an impacted mandibular right canine and two well-defined, unilocular cystic radiolucencies with the impacted third molar in both mandibular molar regions (arrows)

abnormalities were noted on roentgenograhic examination of the head and chest. Chromosome examination using peripheral blood lymphocytes showed a small deletion in the long arm of the No. 9 chromosome (mos46,XX/46,XX, del(9)(q32)) (Fig 3). After consideration of the above data, a diagnosis of BCNS with multiple jaw cysts was made by Gailani's criteria.[6]

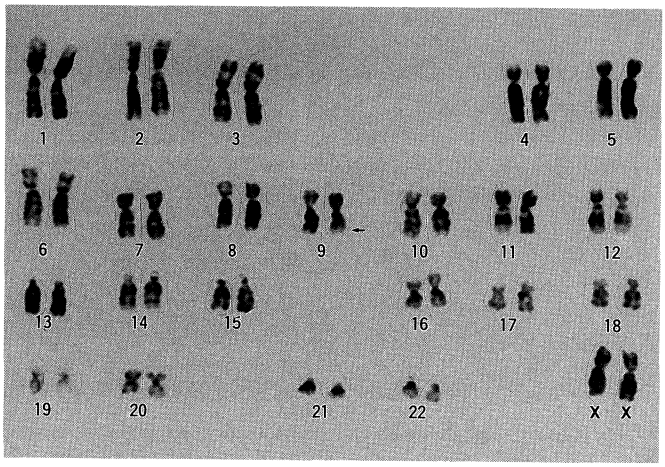


Fig 3. The karyotype of this patient showed a small deletion (arrow) in the long arm of the No. 9 chromosome (mos46,XX/46,XX,del(9)(q32))

The patient was scheduled for a second admission for removal of cysts and impacted teeth on July 23, 1987. Enucleations of the cysts of the mandible, extractions of the impacted third molars and neighboring molars and ankylotomy of the lingual frenum were performed under general anesthesia. Both impacted third molars and the left inferior alveolar nerve were located within the cyst cavities. The left inferior alveolar nerve was resected with the cysts to prevent recurrence of cysts. The cysts contained yellow, creamy contents and had thin cyst walls. The postoperative course of these lesions was favorable without any recurrence.

Histologically, the cysts, which contained keratin in the lumen, had a thin epithelial lining of parakeratinizing stratified squamous epithelium with columnar basal cells (Fig 4a). Pseudocarcinomatous hyperplasia was present in a small area of the cyst wall but no cellular atypia was identified (Fig 4b). Many satellite cysts (daughter cysts), resembling the structure of the main cyst, were observed in the capsule of the main cysts (Fig 4c). Part of the main cyst wall contained epithelial remnants or epithelial islands resembling the residues of the dental lamina (Fig 4d). The crowns of the impacted third molars were in a pseudodentigerous relationship[7] to the cyst cavity, in that the cyst lining was attached to the layer of fibrous tissue separating the crown from the adjacent cyst cavity. The diagnosis of the enucleated cysts was odontogenic keratocyst.

Six months after enucleation of the mandibular cysts, a bony defect and swelling developed in the maxillary left third molar region. Needle aspiration cytology from this region disclosed many exfoliative keratinizing squamous epithelia with inflammatory cells. This finding was suggestive of odontogenic

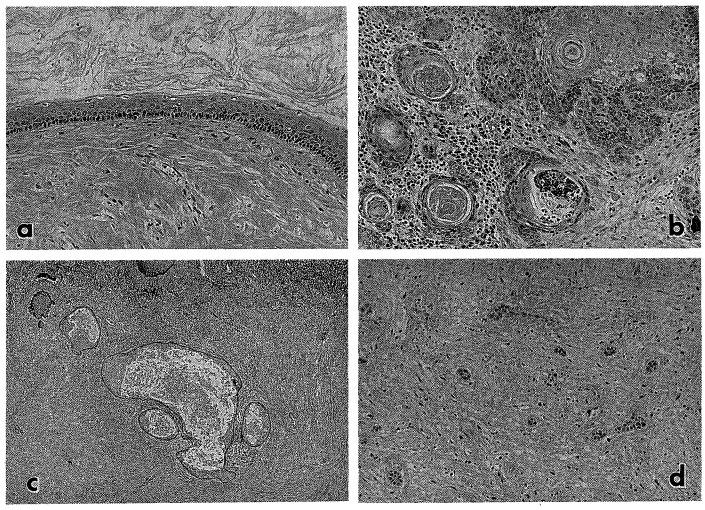


Fig 4. Photomicrograph of the manbibular odontogenic keratocysts (Hematoxylin and eosin staining)
a : a thin epithelial lining of parakeratinizing stratified squamous epithelium with columnar basal cells (original magnification ×33)
b : pseudocarcinomatous hyperplasia without cellular atypia (original magnification ×33)
c : many satellite cysts observed in the capsule of the main cysts (original magnification ×7)
d : epithelial remnants resembling residues of the dental lamina in the main cyst walls (original magnification ×33)

keratocyst according to Kramer's report.[8)]

Ten months after enucleation of the mandibular cysts, a discharge of yellow pus from the maxillary gingiva around the right third molar region was examined by cytology. Cytological findings similar to those seen in the maxillary left third molar region were observed. A panoramic radiograph and tomograms of the maxilla showed three well-defined, cystic radiolucencies in the mandibular right lateral incisor and both maxillary third molar regions (Fig 5). On August 4, 1988, enucleations of the two maxillary cysts and extractions of the impacted maxillary third molars were performed under general anesthesia. Enucleation of the remaining cyst in the mandibular right lateral incisor region was performed under local anesthesia on February 27, 1990. The postoperative course of these cysts was uncomplicated. The diagnosis for these enucleated cysts was odontogenic keratocyst.

Three years after enucleation of the maxillary cysts, painful swelling developed in the maxillary right second molar region. A panoramic radiograph showed recurrence of cysts in both maxillary molar regions. On August 8, 1991, enucleation and packing open of two maxillary cysts and extractions of both maxillary second molars were performed under general anesthesia. The prognosis was favorable without recurrence. The diagnosis for enucleated cysts was odontogenic keratocyst. Nine years after the first enucleations of mandibular cysts, there was no evidence of recurrence or development of any new cysts.

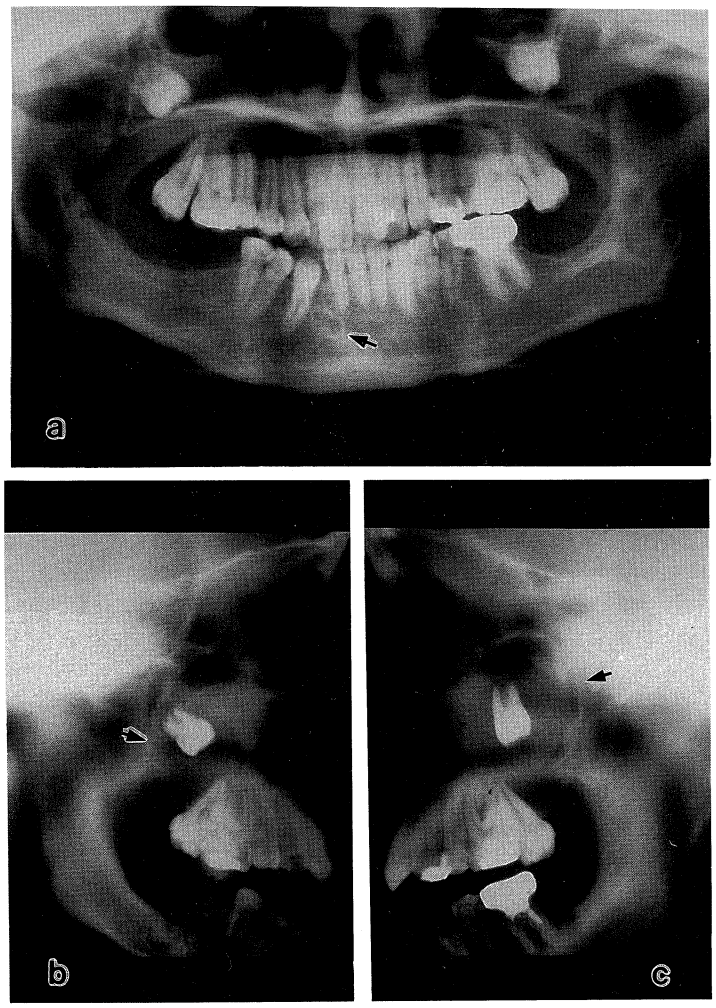


Fig 5. A panoramic radiograph(a) and tomograms of the maxilla(b : right, c : left) showed three well-defined, cystic radiolucencies in the mandibular right lateral incisor and both maxillary third molar regions (arrows)

DISCUSSION

Patients with BCNS suffer from multiple odontogenic keratocysts, which appears to be a constant feature[9-11] of BCNS, and have a high propensity for both recurrence and development of new cysts. The following three factors[12] seem the most tenable as mechanisms of recurrence or development of new cysts : (1) remnants of dental lamina epithelium within the jaws which are not associated with the original odontogenic keratocysts (development of new cysts), (2) incomplete removal of the original cyst lining (recurrence), (3)

residues of the dental lamina and satellite cysts remaining in the tissues following incomplete removal of the capsule (recurrence). In our patient, two cysts treated with enucleation and primary closure recurred in the maxillary molar regions. On a pathological finding of recurred cysts, daughter cysts were found to be present in connective tissue. The factor involved with the recurrence of odontogenic keratocysts in our patient is probably related to factor3, but it was difficult to distinguish recurrences from the development of new lesions. Despite the various treatments to prevent recurrences of cysts, which include marsupialization, enucleation and packing open, enucleation and primary closure, there have been no significant differences in recurrence.[13] To the best of our knowledge, the most important factor in reducing the risk of recurrence may be to enucleate totally in one piece.[12]

However, in patients with BCNS, as great a danger as recurrence is the development of new cysts.[14] Odontogenic epithelial residues in BCNS have a greater growth potential and give rise to satellite cysts (small cysts).[15] Some of these may develop new cysts in the future. Patients with BCNS probably have some genetic abnormalities which are involved in keratocyst formation. In one report[16] an abnormal long arm of one of the No. 1 chromosomes was described in one patient with BCNS, but no constant abnormality in chromosome number or structure has been identified. A recent report[6] proposed that BCNS is caused by mutation in a tumor suppressor gene on the No. 9 chromosome (chromosome 9q), which appears to function in different tissue types during the postnatal period as reflected by various abnormalities. Chromosome examination in our patient showed a small deletion in the long arm of the No. 9 chromosome. This small deletion may play a role in various abnormalities including new keratocyst formation in this patient, but no constant deletion in the No. 9 chromosome was identified in her family.

Another question is when development of new cysts start and stop. Odontogenic keratocysts have arisen in an age range of from 1 to 83 years old,[14] often appearing initially during the first decade of life.[9] The time interval at which new cysts have been identified after diagnosis of the first cysts has varied, but in one case it was 23 years old.[17] In our patient's family, the first odontogenic keratocysts developed in family members in an age range of from 6 to 61 years old. Accordingly, the term multiple when applied to cysts in BCNS refers to the life-time history of the patient and does not necessarily imply that more than one cyst is present at any time.[17] Until human gene therapy of BCNS is successful, if possible, close follow-up, including accurate preoperative diagnosis of new cyst formation with panoramic radiographs and exfoliative cytology[8] at the earliest possible stage, will be required throughout life. Furthermore, if multiple odontogenic keratocysts arise in different regions during the first decade or the early second decade, it will be necessary to monitor jaw growth and to assess the need for prosthetic and orthodontic treatment.[14]

REFERENCES

1) Gorlin RJ, Goltz RW : Multiple nevoid basal-cell epithelioma, jaw cysts and bifid rib : A syndrome. N Engl J Med **262** : 908-912, 1960
2) Davidson F : Multiple naevoid basal cell carcinomata and associated congenital abnormalities. Br J Dermatol **74** : 439-444, 1962

3) Repass JS, Grau WH : The basal cell nevus syndrome : report of two cases. J Oral Surg **32** : 227-232, 1974
4) Kamiya Y, Narita H, Yamamoto T, Kameyama Y, Maeda H, Nakane S : Familial odontogenic keratocysts : report of 3 cases and review of japanese dental literature. Int J Oral Surg **14** : 73-80, 1985
5) Hasegawa K, Amagasa T, Shioda S, Kayano T : Basal cell nevus syndrome with squamous cell carcinoma of the maxilla : report of a case. J Oral Maxillofac Surg **47** : 629-633, 1989
6) Gailani MR, Bale SJ, Leffell DJ, Digiovanna JJ, Peck GL, Poliak S, Drum MA, Pastakia B, Mcbride OW, Kase R, Greene M, Mulvihill JJ, Bale AE : Developmental defects in gorlin syndrome related to a putative tumor suppressor gene on chromosome 9. Cell **69** : 111-117, 1992
7) Browne RM : The odontogenic keratocyst Histological features and their correlation with clinical behaviour. Brit Dent J **131** : 249-259, 1971
8) Kramer IR, Toller PA : The use of exfoliative cytology and protein estimations in preoperative diagnosis of odontogenic keratocysts. Int J Oral Surg **2** : 143-151, 1973
9) Gorlin RJ, Vickers RA, Williamson JJ : The multiple basal-cell nevi syndrome An analysis of a syndrome consisting of multiple nevoid basal-cell carcinoma, jaw cysts, skeletal anomalies, medulloblastoma, and hyporesponsiveness to parathormone. Cancer **18** : 89-104, 1965
10) Sakamoto K, Ibuki K, Matsuya T, Shirasuna K, Nishio J, Watatani K, Morimoto T, Miyazaki T : Basal cell nevus syndrome : report of five cases with a review of the literatures in Japan. Jpn J Oral Maxillofac Surg **31** : 1198-1208, 1985 (in Japanese with English summary)
11) Hata T, Hosoda M, Fukuda M, Segami N, Kowaka S, Hanafusa H, Hayashi Y, Fujimura K, Hirokawa M : Clinicopathologic studies on the odontogenic keratocyst. Jpn J Oral Maxillofac Surg **34** : 470-484, 1988 (in Japanese with English summary)
12) Brannon RB : The odontogenic keratocyst A clinicopathologic study of 312 cases. Part. II Histologic features. Oral Surg **43** : 233-255, 1977
13) Browne RM : The odontogenic keratocyst : Clinical aspects. Br Dent J **128** : 225 - 231, 1970
14) Rippin JW : Odontogenic keratocyst in an infant. Br Dent J **172** : 282-283, 1992
15) Woolgar JA, Rippin JW, Browne RM : A comparative histological study of odontogenic keratocysts in basal cell naevus syndrome and control patients. J Oral Pathol **16** : 75-80, 1987
16) Yunis JJ, Gorlin RJ : Chromosomal study in patients with cysts of jaw, multiple nevoid basal cell carcinomata and bifid rib syndrome. Chromosoma **14** : 146-153, 1963
17) Woolgar JA, Rippin JW, Browne RM : The odontogenic keratocyst and its occurrence in the nevoid basal cell carcinoma syndrome. Oral Surg Oral Med Oral Pathol **64** : 727-730, 1987