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Case Report

Chronic benign neutropenia diagnosed due to severe stomatitis: a case report

Yumiko Otsuka, Junko Matsuyama, Fumiko Iwano*, Mieko Tomizawa and Tadashi Noda

Division of Pediatric Dentistry, Niigata University Graduate School of Medical and Dental Sciences
2-5274 Gakkocho-dori, Niigata 951-8514, JAPAN
* Iwano Dental Clinic
2932 Ohno, Kurosaki machi, Niigata 950-1111, JAPAN

Abstract Chronic benign neutropenia is seen in children and is usually detected when repeated occurrence of infectious diseases such as acute otitis media, gastroenteritis, tonsillitis and skin infection, are observed. It is rarely diagnosed as a result of detection of oral lesions. A case of chronic benign neutropenia diagnosed during evaluation of severe stomatitis in a 20-month-old Japanese girl is described in this paper. In order to establish a treatment plan, we examined a dental plaque sample by PCR method, but found no specific causal bacteria. When pediatric dentists encounter repeated gingivitis or stomatitis, the possibility of hematologic disease should be considered.

Key words
Chronic benign neutropenia,
Gingivitis,
Oral bacteria,
Polymerase chain reaction,
Stomatitis

Introduction

Neutropenia is a condition in which circulating neutrophils in peripheral blood decrease in number to less than 1,000/μl in infants or 1,500/μl in children more than 1 year of age. If the neutrophil count is less than 500/μl, neutropenia affects the general condition of the patient and leaves the patient vulnerable to severe general infections. Neutropenia is classified into several types, with chronic benign neutropenia starting in infancy but usually characterized by a self-limiting course of 10–18 months[1]. Neutropenia is usually discovered fortuitously during infections as acute otitis media, gastroenteritis, tonsillitis and skin infection[2]. Although oral ulceration, chronic gingivitis and chronic periodontitis have been reported in relation to different types of neutropenia[1], to the best of our knowledge there has been no case report of neutropenia diagnosed based on oral lesions.

We experienced a case in which we suspected hematologic disease due to severe stomatitis and referred the patient to a pediatric clinic where she was ultimately diagnosed as chronic benign neutropenia. Follow-up of her oral condition has been continued.

The clinical course and treatment of this case are described and moreover the role of pediatric dentist is emphasized in this report.

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Case report

A 20-month-old Japanese girl was referred to the Pediatric Dental Clinic at Niigata University for evaluation of gingival ulceration. Her mother had found a white gingival lesion at the lower primary incisor 2 days earlier. Intraoral examination revealed that all of primary teeth were present and that second primary molars were erupting. The marginal gingivae of all of the primary teeth were edematous and erythematous. A shallow ulcer was found on the labial gingiva of the lower right primary central incisor. The surface was covered with white pseudomembranous slough with an erythematous swelling border (Fig. 1a). The mandibular right primary central incisor was caries-free and exhibited slight mobility. A periapical radiograph revealed no abnormal findings

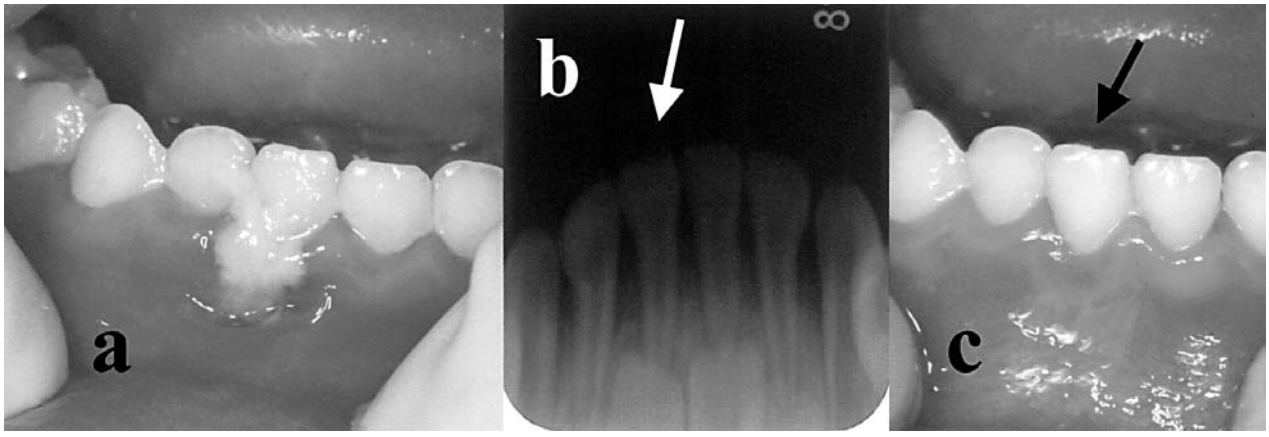

Fig. 1a Shallow ulcer covered with white pseudomembranous slough (1Y8M).
1b Periapical radiograph revealed no abnormalities (1Y8M).
1c The ulcer had disappeared (1Y9M).

Fig. 2 Severely erythematous, edematous and painful gingivitis and several ulcers are seen on her buccal gingivae, buccal mucosa around molars (1Y10M).

Table 1 Blood data at the age of 1 year and 10 months

Complete blood count	
White Blood Cells	$2540/\mu l$
Red Blood Cells	$457\times10^4/\mu l$
Hemoglobin	10.8 g/dl
Hematocrit	32.6%
MCV	71.3 fl
MCH	23.6 pg
MCHC	33.1%
Platelets	$38.5\times10^4/\mu l$
Differential leukocyte count	
Neutrophils	16.9%
Eosinophils	2.8%
Basophils	0.4%
Monocytes	22.0%
Lymphocytes	57.9%

(Fig. 1b). Although exact cause of the ulcer was unknown, we diagnosed the lesion as a traumatic ulcer clinically and prescribed antibiotics for 3 days. The ulcer gradually improved and disappeared after 1 month (Fig. 1c). The mandibular right primary central incisor still continued to exhibit slight mobility.

Two months later, at the age of 22 months, she was brought to our clinic with a slight swelling on her right cheek due to a bruise. Intraoral examination revealed that all of her gingivae were severely erythematous, edematous and painful. We found several ulcers on her gingivae and buccal mucosae around the primary molars (Fig. 2). We suspected that these oral findings were symptoms of hematological disease and immediately referred her to the Pediatric Clinic of Niigata University Medical Hospital.

A pediatrician performed a blood cell test and bone marrow examination. Her white blood cell count had decreased to 2,540/μl, and her neutrophil count

Fig. 3 Slight redness and bleeding after brushing were localized just around first primary molars (2Y3M).

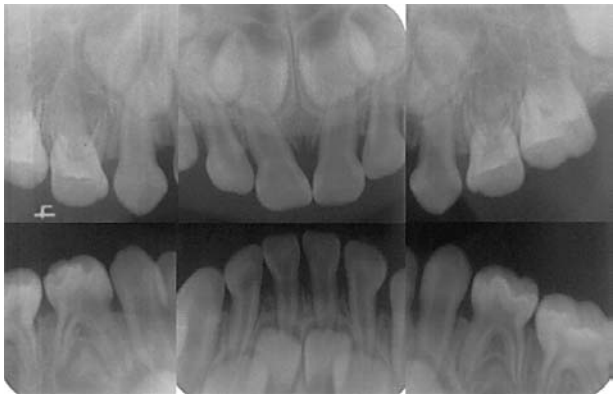

Fig. 4 Slight loss of marginal bone in the lower anterior regions and around the first primary molars (2Y3M)

Table 2 Oral bacteria detected by PCR analysis

Pathogen	Lower left first molar	Lower right first molar
Actinobacillus actinomycetemcomitans	−	−
Bacteroides forsythus	+	+
Campylobacter rectus	+	+
Capnocytophaga gingivalis	+	+
Capnocytophaga ochracea	−	−
Capnocytophaga sputigena	+	+
Eikenella corrodens	+	+
Fusobacterium nucleatum	−	−
Prevotella intermedia	−	−
Prevotella gingivalis	−	−
Treponema denticola	−	−

was 429/μl (Table 1). Bone marrow examination demonstrated myeloid hyperplasia but no malignancy. Based on these findings, she was diagnosed as having chronic benign neutropenia. Since her general condition was not severe, she has been under observation without any medication by her pediatrician and a blood test was carried out once a month.

A treatment plan was devised to improve her oral condition, including instruction to her mother to brush softly so as not to injure the gingivae and to rinse with 1% povidone-iodine solution after brushing. We saw her in our clinic once or twice a month and cleaned her teeth mechanically, swabbing her gingivae with 25% iodine solution. Her erythematous and edematous gingivae gradually improved, and the slight redness and bleeding after brushing were localized just around the first primary molars (Fig. 3).

Radiographic examination at the age of 2 years and 3 months revealed a loss of marginal bone in the lower anterior regions and around the upper and lower first primary molars (Fig. 4). Probing depth were 3 mm in the primary molar regions and 2 mm in other regions.

To examine her oral microflora, dental plaque samples were collected from the first primary molars by using sterile explorers. After sampling, DNA was extracted from each sample, and the 16S rRNA genes of each bacteria were amplified by a polymerase chain reaction (PCR) method as described previously[3–5]. *Bacteroides forsythus, Campylobacter rectus*, *Capnocytophaga gingivalis*, *Capnocytophaga sputigena* and *Eikenella corrodens* were detected, but *Actinobacillus actinomycetemcomitans*, *Capnocytophaga ochracea*, *Prevotella intermedia*, *Porphyromonas gingivalis* and *Treponema denticola* were not detected (Table 2).

At the age of 2 years and 4 months, she had

a high fever due to tonsillitis and her gingival inflammation became severe. At that time, white blood cell counts were 1,700–1,800, and C-reactive protein (CRP) was over 7 (normal: nearly 0), she was prescribed antibiotics. While the white blood cell count remained under 2,000/μl for a few weeks, gingivitis alternately flared and reduced. After her blood cell count had recovered to over 2,000/μl, her gingivitis receded.

Since 2 years and 6 months of age, her gingival condition has been controlled well and the probing depth was 3 mm just around the right second primary molars, where slight gingivitis remained.

Discussion

Neutropenia is a condition in which number of neutrophils in the peripheral blood is decreased and is classified into several types[1]. There have been many case reports of severe neutropenia, such as cyclic and congenital neutropenia (Kostmann's syndrome), related to oral ulceration or gingivitis[6–19]. However, no case diagnosed as a result of detection of oral infectious lesions was found in our search of the literature. Thus, our case shows that dentists should consider hematologic disease when patients exhibited repeated severe stomatitis. Our patient had been suffered from severe otitis media for 1 month at the age of 13 months, chronic benign neutropenia had not been diagnosed yet at that time.

Possible involvement of specific oral microflora was considered when devising the treatment plan. We therefore examined her dental plaque using the PCR method. This method is very sensitive, and easy to obtain samples for it. It is said that early-onset periodontitis is related to *A. actinomycetemcomitans*, *P. gingivalis*, *Pr. intermedia*, *B. forsythus*, *Campylobacter*, *E. corrodens* and *Capnocytophaga*[20]. In the present case, of these bacteria only *B. forsythus* was found. Chen *et al.*[21] reported that *B. forsythus* was not detected in subgingival plaque in children aged 4 years and younger. Okada *et al.* (2001) reported that the prevalence of *B. forsythus* was higher in children in older age groups[22]. Ashimoto *et al.* (1996)[5] reported that the prevalence of *B. forsythus* in subjects with pediatric gingivitis subjects aged 2 to 11 years was 8%. *C. rectus* was found in the present patient. Okada *et al.* (2001) reported that *C. rectus* was detected in plaque samples from patients with chronic neutropenia[23], however, it was found in 100% of plaque samples from children aged 2 to 12 years[22]. *C. ochracea* was not detected in the present patients, but has *C. ochracea* has been reported to be present in all children with healthy gingiva[24]. In our case, we could not determine which specific bacterial species caused her gingivitis, and we therefore made a treatment plan to ensure maintenance of good oral hygiene.

Regarding management of neutropenia, early preventive care is important and Chlorhexidine 0.2% gel and mouthwash are reportedly useful[25]. When the present patient visited our clinic, we performed professional dental cleaning and instructed her mother in appropriate oral hygiene methods. We found that visiting to our clinic once or twice a month are sufficient for professional dental cleaning, swabbing with 25% iodine solution, and augmented by rinsing with 1% povidone-iodine solution at home.

When the patient had high fever due to tonsillitis, her gingival inflammation became severe. This might have been caused by the deteriorated in her general condition and also by the impossibility of sufficient brushing due to gingivitis. Her general condition has improved, and her chronic benign neutropenia was expected to recover spontaneously[1].

Gingivitis in children is not a rare disease in the pediatric clinic, and it is usually caused by poor oral hygiene. However, when repeated gingivitis is noted despite of professional oral hygiene, dentists should consider the possibility that a hematologic disease might underlie the gingival symptoms.

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