

Cyclic neutropenia: case report of two siblings

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Abstract

This case report describes the oral manifestations of cyclic neutropenia observed in two siblings. Of particular importance were the repeated weekly blood studies required to correctly diagnose the problem. A single set of blood studies would probably fail to identify the condition.

Neutropenia, or agranulocytosis, is a condition characterized by a marked decrease or lack of circulating neutrophils in the peripheral blood.¹ In addition to a consistent neutropenia, this condition is associated with normal to decreased leukocyte counts and usually with lymphocytosis, monocytosis, and variable eosinophilia. The symptoms, differential diagnoses and other characteristics of the disease have been reviewed by Cutting and Lang,^{2,3} and by Kalkwarf and Gutz.⁴ A rare variant of the disease, usually called cyclic neutropenia, is characterized by the cyclic disappearance of the neutrophils from the circulation at approximately three-week intervals.⁵

Oral manifestations of cyclic neutropenia typically include a severe gingivitis with ulceration corresponding to the period of the neutropenia, and is due to bacterial invasion in the absence of a defense mechanism. When the neutrophil count returns to normal, the gingival tissue assumes a nearly normal clinical appearance. Radiographic examination reveals a mild to severe loss of alveolar bone as a result of repeated cyclic gingivitis leading to periodontitis.⁶ In children with repeated episodes of infection, there is a considerable loss of supporting bone around the teeth. Cohen and Morris have outlined the periodontal manifestations of cyclic neutropenia.¹

The purpose of this case report is to describe the clinical and radiographic appearance of two children with cyclic neutropenia. This report will emphasize the need for repeated weekly blood studies to accurately diagnose the condition.

Case Report

A.Y., a well-developed, well-nourished six-year-old black male was referred for evaluation after his mother had noticed blood on his pillow and subsequently discovered "bleeding and ulcerated gums." The past medical history was unremarkable except for a history of frequent colds. These colds, approximately one every 4-5 weeks, had increased in frequency in the year since the child started school. The mother further reported that small circular white "spots" would often appear on the lower face (perioral area) when the child was sick. The mother was concerned about constant "bad breath" which seemed to be worse during certain times of the month.

Extraoral Findings

An extraoral exam was unremarkable except for a rash on both forearms and on the back concentrated adjacent to the spinal cord. The patient was afebrile and exhibited no regional lymphadenopathy.

Intraoral Findings

An intraoral examination revealed that the patient was in the early mixed dentition stage of dental development. The attached gingiva surrounding all of the primary teeth exhibited severe gingivitis with ulceration (Figure 1). This gingivitis extended to the mesial of the first permanent molars. The ulcerations were more evident in the interdental papillae. There was obvious loss of attachment surrounding the primary teeth and probing of these teeth elicited hemorrhage and revealed pocket depths ranging from 4-10 mm. The gingival tissue surrounding the permanent central incisors and the distal aspect of the first permanent molars appeared normal in color and configuration. Pocket depths of 4-5 mm were noted lingually on the maxillary permanent central incisors and mesially on the maxillary and mandibular first permanent molars. All of the primary teeth were mobile with the first primary molars noticeably more mobile. Decay was evident distally on the mandibular right first primary molar.



Figure 1. Intraoral view of patient A.Y. showing gingival inflammation and ulcerated interdental papillae.

Radiographic Findings

A radiographic examination revealed extensive horizontal bone loss around all of the primary teeth, the most severe area being the first primary molars (Figure 2). Bone loss was also apparent mesial to the first permanent molars. Although difficult to determine, it appeared that the erupting maxillary and mandibular permanent central incisors did not have adequate alveolar bone development. The intraoral and radiographic findings prompted gingival tissue biopsy, referral for medical evaluation, and laboratory studies to explore possible systemic etiologies of the problem.

Biopsy Evaluation

Two wedge biopsies were taken of the gingival tissues: one between the maxillary right primary canine and first primary molar, and a second between the maxillary left first and second primary molars. Sections prepared from the submitted specimens revealed a portion of gingiva composed of fibrous connective tissue containing a moderate infiltrate of lymphocytes and plasma cells. A few eosinophils were noted beneath the nonkeratinized epithelial surface. One area of ulceration was noted. The diagnosis of the right and left maxillary gingiva were consistent with chronic gingivitis and revealed no evidence of histiocytosis X or neoplastic disease.

Laboratory Value Findings

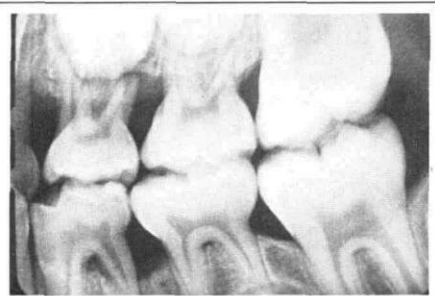
The patient was referred to his pediatrician for a medical evaluation which was to include a physical examination. An SMA-12 and a series of four successive CBCs over a four-week period were specifically requested. The results of the medical examination were unremarkable except that a heart murmur was detected. This was later determined to be a small ventricular septal defect which necessitated proper antibiotic coverage for all dental procedures. The etiology of the rash could not be determined. The SMA-12 values were reported by the pediatrician to be within normal limits for a six-year-old child.

The first CBC laboratory values (Table 1) were also reported as normal. The CBCs were not repeated weekly due to failure of follow-up by the parents. However, four CBCs were accomplished in a twelve-week period (Table 1). The last CBC revealed that the WBC count (4300 WBC/mm³) and neutrophil count (19%) were both significantly below normal values. On the same day that the last CBC was taken, tests to determine the levels of protein immunoglobulins IgG/A/M/E were also performed. The IgA levels (55 mg dl) were found to be depressed — a frequent feature of cyclic neutropenia. The elevated IgE levels (109 H IU/ml) were felt to be coincidental.

Upon examination of A.Y., the mother was admonished to bring the four-year-old sibling (K.Y.) for a dental examination. Intraoral and radiographic examinations were unremarkable except that the maxillary left primary lateral incisor was slightly mobile and probing revealed a pocket depth of 5 mm lingually. There was 2.5 mm of interproximal space between the maxillary left central and lateral primary incisors. By contrast, there was no space between the maxillary right central and lateral primary incisors (Figure 3). The maxillary primate space was the same for both sides. There was no evidence of gingivitis or gingival ulceration (Figure 4). The only significant radiographic finding was horizontal bone loss around the maxillary left primary lateral incisor (Figure 5.)



Figure 2. Bitewing radiographs of patient A.Y. Note generalized alveolar bone loss. The primary first molar areas were most severely involved.



	Date	HCT	WBC	STABS	SEGS	LYMPH	MONO	EOSIN	BASO
Table 1. CBC Laboratory Report (A.Y.)	3/26/79	34	9700	4	31	56	5	4	0
	4/17/79	33	8100	1	51	42	0	6	0
	5/3/79	32	9450	1	46	44	0	6	3
	6/11/79	37	4300	0	19	73	2	6	0



Figure 3. Intraoral view of patient K.Y. Note the 2.5 mm space between the maxillary left central and lateral incisors. The lateral incisor was slightly mobile and had a 5 mm pocket lingually.



Figure 4. Intraoral view of patient K.Y. No gingivitis or gingival ulceration is apparent.

The sibling was referred to the same pediatrician for complete examination and consecutive CBC s each week for four weeks. The physical examination revealed no significant findings. The results of the CBC s are listed in Table 2. The first CBC indicated a mild decrease in the neutrophil count (26%), the second a significant decrease in the WBC count (4600 WBC/mm³) and a mild decrease in neutrophil count (28%), the third CBC was within normal limits and the fourth revealed a significant decrease in the neutrophil count (20%).

Treatment

Based on dental and medical laboratory findings, both children were diagnosed as having cyclic neutropenia. Initial treatment consisted of monthly dental visits for prophylaxis, scaling and oral hygiene instruction. Parental education regarding future treatment options is presently underway.

Discussion

Since cyclic neutropenia may be uniquely manifest in the oral cavity, the pedodontist often has the first opportunity to diagnose this disease. As illustrated in these cases, the fundamental diagnostic tool is the serial



Figure 5. Periapical radiograph of patient K.Y. Bone loss is seen around the left lateral incisor.

hematologic study to determine whether a cyclic phenomenon is occurring with the blood values. The initial hematological and biopsy reports on A.Y. ruled out hypophosphatasia, histiocytosis X and were inconclusive for cyclic neutropenia. Only in the last in a series of four blood studies did evidence of the neutropenia emerge. The blood values in K.Y. also illustrate the difficulty in detecting a cyclic neutropenia without a series of hematological examinations.

Summary

Since treatment options may vary, and occasionally involve drastically different treatment approaches, accurate diagnosis of periodontal problems in children is critical. These cases emphasize the need to routinely perform repeated weekly blood studies in patients with recurrent oral ulcers and marked alveolar bone loss until the diagnosis of cyclic neutropenia is confirmed or ruled out.

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	Date	HCT	WBC	STABS	SEGS	LYMPH	MONO	EOSIN	BASO
Table 2. CBC Laboratory Report (K.Y.)	3/12/80	—	8400	0	26	59	0	15	0
	3/30/80	—	4600	2	28	68	2	0	0
	3/27/80	—	8150	3	37	55	2	3	1
	4/14/80	—	7350	0	20	69	1	9	1