Neoplastic diseases in a pediatric population: a survey of the incidence of oral complications

Anthony A. Kamp, DMD, MSD

Abstract

A survey of 186 pediatric patients with neoplastic disease at Riley Children's Hospital in Indiana was conducted to determine the distribution, frequency, and types of oral problems encountered during their hospitalization. Thirty-one per cent of the patients had some form of oral complications during the course of their hospitalization. Ten per cent of the patient population had existing dental treatment needs prior to cancer treatment. The oral problems most frequently seen were mucositis, fungal or candidal infections, gingival bleeding, herpetic lesions, and apthous ulcerations. Different frequencies of oral complications were found to exist between differing types of malignancy and the types of therapy. Not all patients receiving chemotherapy developed oral complications. The pediatric dentist should therefore be aware of the different clinical and biological characteristics of each neoplastic disease, and the various types and phases of treatment in the assessment of his patients.

Neoplastic diseases in children occur with a frequency of about 10 in 100,000 and are the second leading cause of death in children younger than 14 years of age (Silverberg and Lubera 1987). The leukemias and lymphomas constitute approximately 40% of pediatric neoplastic diseases, with solid tumors making up the remaining percentages (Tubergen 1984). Pain, oral infection, mucositis, gingival bleeding, ulcers, stomatitis, and caries have been reported as the result of the direct toxicity of antineoplastic drugs on the mucosal epithelium or secondary to the effects of immunosuppression.[1] The goal of cancer therapy is to increase patient comfort, longevity, and ultimately cure the patient. With current advances in early diagnosis and therapy, more than 40% of children with cancer now survive for at least five years after treatment (Silverberg 1986; Krakoff 1987).

[1] DelRegato 1939; King et al. 1968; Dreizen 1974; Dreizen et al. 1975; Bruya and Madeira 1975; Rotman et al. 1977; Braham 1977; Sonis et al. 1978; Epstein 1986.

Treatment of pediatric neoplastic disease is multidisciplinary and ideally involves the pediatric dentist in the supportive care of oral complications. The oral mucosa can become a major site of systemic infection and pain in cancer patients. Knowledge and understanding of the multiplicity and the incidence of oral complications is essential in facilitating appropriate dental management. Prevention and early detection of existing dental needs are important in providing optimum care.

Materials and Methods

A retrospective analysis of pediatric oncology patient records was undertaken. Oncology pediatric patients admitted to James Whitcomb Riley Hospital for Children, Indianapolis, Indiana, were surveyed from July, 1985, to October, 1986. During the 14 months of the study, 186 pediatric oncology patients were followed during their hospitalization by the pediatric dental residents on service with the hematology/oncology department. Patients on service varied from initial diagnosis and treatment to maintenance and consolidation therapy. There were 96 males (52%) and 90 females (48%). The mean age was seven years with a range of 10 months to 20 years. There were 27 different clinical diagnoses of neoplastic disease made in the survey group.

Information concerning the patients was obtained by pediatric dental residents making rounds with the hematology/oncology physicians. The dental resident, as part of the oncology team, completed a "pediatric oncology patient profile" on each patient on the service. Data for the profile were obtained by bedside visual examination, cultures as necessary, information supplied by the attending physicians, and the hospital patient chart. The patient profile contained specific information: name, sex, date of birth, diagnosis, date of diagnosis, treatment protocol, oral conditions (baseline), date of observation, vital signs, and laboratory results, medications and chemotherapy drugs given, comments and oral problems.

Results

Fifty-eight pediatric patients, or 31% of those in the survey, had at least one oral complication during their hospitalization secondary to their treatment (Table 1). A variety of neoplastic diseases comprised the sample pediatric population. The leukemias made up 40% of the sample population (Table 2). Hodgkin's and non-Hodgkin's disease were seven per cent of the sample population (Table 3). Cancers of the nervous system comprised 12% (Table 4). Bone cancers, osteosarcoma and Ewing's sarcoma, comprised nine per cent of the sample population (Table 5). Rhabdomyosarcoma and leiomyosarcoma comprised eight per cent (Table 6), while Wilm's tumors of the kidney comprised 10% (Table 1). Ten per cent of the patients had untreated dental caries unrelated to their cancer therapy (Table 7).

The frequency of oral complications in this population group was found to vary depending on the type of malignancy and type of therapy (Tables 2-6). The percentage for those having oral complications is as follows: acute lymphoblastic leukemia, 34%; acute myelocytic leukemia, 64%; Wilm's tumor, 11%; Rhabdomysarcoma, 31%; neuroblastoma, 15%; acute myelocytic leukemia, 64%; Burkitt's lymphoma, 50%; Hodgkin's disease, 0%; non-Hodgkin's lymphoma, 25%; osteosarcoma, 13%; and Ewing's sarcoma, 83%.

Of the oral complications observed, 52% were described as a mucositis; 38% fungal or candida infections; 19% gingival bleeding; nine per cent herpetic lesions; and three per cent apthous ulceration. A total of 70 occurrences of oral complications were observed in the 58 patients. Although not a complication of therapy, 10% of the pediatric patients had existing dental caries.

Ninety-one per cent of the patients received chemotherapy as part of their treatment course, either alone or in combination with other forms of therapy. However, because of the multimodality and multiagent chemotherapy treatment utilized, it is difficult to assess the stomatoxicity of any specific antineoplastic agent in this survey. Indeed, combination chemotherapy is now the standard of care, and the regimens are complex and cyclical (Krakoff 1987).

Discussion

Oral complications from the treatment of neoplastic diseases are common and are very significant as they can account for patient discomfort and compromised food intake. Also, oral infections may represent a direct threat to the life of the patient (Sonis and Sonis 1979). The incidence of oral complications has been reported to range from approximately 20 to 90% in various studies.[2] This study found an incidence of 31% for pediatric patients. This lower incidence of oral complications may in part be due to a larger pediatric patient popula-

[2] Guggenheimer 1977; Sonis et al.1978; Sonis and Sonis 1979.

TABLE 1. Frequency of Oral Complications by Major Site of Malignancy

Malignancy	*Total Patients with Diagnosis*	*% of Total with Malignancy*	*Number of Patients with Diagnosis with Oral Complications*	*Number of Patients with Diagnosis, % with Oral Complications*
Leukemia	76	40.5	34	45
Lymphoma	23	12.5	6	26
Nervous system	23	12.5	2	9
Bone	17	9	7	41
Wilm's tumor	19	10	2	11
Other organ sites	28	15	7	25
Total	186	99.5	58	31

TABLE 2. Frequency of Oral Complications by Type of Leukemia

Malignancy	*Total Patients with Diagnosis*	*% of Total with Malignancy*	*Number of Patients with Diagnosis with Oral Complications*	*Number of Patients with Diagnosis, % with Oral Complications*
Acute lymphocytic leukemia	53	28	18	34
Acute myelocytic leukemia	17	9	11	64
Acute promyelocytic leukemia	2	1	1	50
Leukemia lymphoma syndrome	3	2	3	100
Erythroblastic leukemia	1	0.5	1	100
Total	76	40.5	34	45

TABLE 3. Frequency of Oral Complications by Type of Lymphoma

Malignancy	*Total Patients with Diagnosis*	*% of Total with Malignancy*	*Number of Patients with Diagnosis with Oral Complications*	*Number of Patients with Diagnosis, % with Oral Complications*
Hodgkin's disease	9	5	0	0
Non-Hodgkin's lymphoma	4	2	1	25
Lymphoblastic lymphoma	1	0.5	0	0
Nonlymphoblastic lymphoma	3	2	2	67
Burkitt's lymphoma	6	3	3	50
Total	23	12.5	6	26

tion surveyed than that of previous studies. Sonis and Sonis (1979) reported a 90% incidence of oral complications in 49 pediatric oncology patients. However, the Sonis et al. (1978) analysis of a larger sample size of 93 adult patients with neoplastic disease noted approximately 40% having some form of oral complications. The Riley Hospital patient population also included a larger number of neoplastic disease diagnoses. Sonis and Sonis's (1979) patient population included only eight separate diagnoses of neoplastic disease with leukemia representing 67% of diagnoses. The leukemias, however, constituted approximately 40% of the total Riley Hospital pediatric neoplastic diseases. The present study group also represented patients in various phases of treatment, immunosuppression, and myelosuppression.

The frequency of oral complications was found to vary between the types of malignancies and types of therapy. Not all patients receiving chemotherapy develop oral complications. However, those patients who do develop complications may develop multiple oral problems. Therefore, the pediatric dentist must be aware of the different clinical and biological characteristics of each neoplastic disease, and the various types and phases of treatment in the assessment of his patients.

The clinical presentation of oral complications can be altered due to a patient's immunosuppression; therefore, lesions should be cultured to obtain a diagnosis. Because of the multimodality and multiagent chemotherapy, it is difficult to assess the stomatoxicity of any specific antineoplastic agent in this survey. Berkowitz et al. (1987) reported that approximately 20% of pre-bone marrow transplantation pediatric patients had existing dental caries prior to transplantation therapy. Decalcification of dental enamel can arise secondary to anticancer therapy as a result of acquired xerostomia or the consumption of sucrose-based medications (Berkowitz et al. 1987; Lowe 1986). As the oral cavity may act as an entrance for systemic infection in the myelosuppressed patient, untreated caries could pose a serious health threat in oncology patients.

TABLE 4. Frequency of Oral Complications for Neoplasms of the Nervous System

Malignancy	*Total Patients with Diagnosis*	*% of Total with Malignancy*	*Number of Patients with Diagnosis with Oral Complications*	*Number of Patients with Diagnosis, % with Oral Complications*
Neuroblastoma	13	7	2	15
Medulloblastoma	6	3	0	0
Brainstem glioma	2	1	0	0
Malignant schwannoma	1	0.5	0	0
Bilateral retinal blastoma	1	0.5	0	0
Total	23	12	2	9

TABLE 5. Frequency of Oral Complications for Neoplasms of the Skeletal System

Malignancy	*Total Patients with Diagnosis*	*% of Total with Malignancy*	*Number of Patients with Diagnosis with Oral Complications*	*Number of Patients with Diagnosis, % with Oral Complications*
Osteosarcoma	8	4	1	13
Osteoblastic osteosarcoma	3	2	1	33
Ewing's sarcoma	6	3	5	83
Total	17	9	7	41

TABLE 6. Frequency of Oral Complications for Other Major Sites

Malignancy	*Total Patients with Diagnosis*	*% of Total with Malignancy*	*Number of Patients with Diagnosis with Oral Complications*	*Number of Patients with Diagnosis, % with Oral Complications*
Histocytosis X	5	3	1	33
Hepatoblastoma	3	2	2	66
Rhabdomyosarcoma	13	7	4	31
Leiomyosarcoma	2	1	0	0
Sarcoma of rectum	1	0.5	0	0
Adenocarcinoma of rectum	2	1	0	0
Malignant terotoma	1	0.5	0	0
Ovarium germinal cell tumor	1	0.5	0	0
Total	28	15	7	25

TABLE 7. Frequency of Oral Complications

Type of Complication	*Number*	*%*
Mucositis	30/58	52
Candidiasis or other fungal	22/58	38
Gingival bleeding	11/58	19
Herpetic lesions	5/58	9
Apthous ulceration	2/58	3
Caries	18/186	10

Antineoplastic drugs can cause oral complications as a direct cytotoxic effect on the mucosa and an indirect effect as a result of immunosupression.[3] The oral mucosa is particularly susceptible to chemotherapy drugs due to the normal level of rapid cellular activity. Adriamycin,® cystosine arabinoside, methotrexate, vincristine, actinomycin D, and bleomycin, are all agents that can produce significant stomatitis (Greenberg 1983; Vieti and Ragab 1975). Directly induced stomatitis usually is observed within four to seven days following administration of the antineoplastic drugs and is usually self-limiting, with healing occurring approximately two to three weeks from the initiation of therapy, barring secondary infection (Lockhart and Sonis 1979; McGaw and Belch 1985). Indirect stomatitis is usually observed some 12-16 days following the initiation of chemotherapy when the functional white blood count is at its lowest levels (Lockhart and Sonis 1979; Bodey 1971). Clinically, the effects of neutropenia are often most marked in the marginal gingiva, where it presumably allows exacerbation of pre-existing levels of dental plaque and periodontal disease (Peterson and Sonis 1983).

The severity and duration of oral complications caused by antineoplastic drug therapy have been shown to be correlated with pre-existing levels of dental plaque, periodontal disease, and oral hygiene habits (Lindquist et al. 1978; Hickey et al. 1982). The potential oral sequelae associated with cancer chemotherapy drugs can be prevented, reduced, or alleviated with careful and continuous dental care.[4] Personal oral hygiene instructions in dental plaque control and their periodic reinforcement are essential to prevent oral complications (Bottomley et al. 1977).

Oral hygiene care should be individualized for each patient since each experiences different levels of immunosuppression and myelosuppression and ability to tolerate tissue manipulation (Lowe 1986; Yasko and Greene 1987). Routine daily brushing with a soft-bristle toothbrush and use of dental floss are recommended when the patient is not hematologically compromised or debilitated by infection or therapy (Peterson and Sonis 1983; Wright et al. 1985). The patient's white blood counts should be greater than 2000/mm^3 with 20% of the differential as polymorphonuclear leukocytes, and platelet counts greater than 20,000/mm.[3]

Unfortunately, the profound neutropenia and thrombocytopenia that these patients experience during their course of therapy may preclude conventional preventive dental measures in light of the risks of bacteremia or bleeding.[5] Oral hygiene methods must minimize trauma to the oral soft tissues. Cleaning of the oral tissues can be done with 4 x 4-in gauze moistened with a mild solution of baking soda and water wrapped around a finger, or with a disposable sponge toothette. Bactericidal solutions of chlorhexidine gluconate have been found to be a suitable agent to prevent dental plaque accumulation and the development of gingivitis in compromised patients (McGaw and Belch 1985; Johnson and Rozanis 1979). Ferretti et al. (1987) have demonstrated that the use of chlorhexidine mouthrinse produced reductions in the oral microbial populations with a significant decrease in mucositis and Candida infections. The management of oral ulcerations from chemotherapy should include treatment to reduce pain and discomfort, minimize infection, and promote healing (Greenberg 1983).

Elective dental procedures and manipulation of the oral tissues should not be performed when the patient is receiving cancer chemotherapy. Neither is the myelosuppressed patient a candidate for elective procedures during periods of granulocytopenia with polymorphonuclear leukocytes less than 500/mm^3 and thrombocytopenia with platelets less than 20,000/mm^3 (Wright et al. 1985; Bottomley et al. 1977). A minimum interval of 10 days is recommended between dental procedures and the initiation of cancer chemotherapy (Berkowitz et al. 1987).

Attention to oral microbial control, meticulous personal hygiene, and palliative treatment of soft tissue lesions may significantly reduce the oral morbidity associated with cancer therapies (Wright et al. 1985). Sonis and Sonis (1979) reported that a 25% improvement in overall disease prognosis can be attributed to improved oral supportive care. Berkowitz et al. (1987) noted that daily dental hygiene helped to develop an optimistic outlook for their oncology patients and their parents.

Summary

A survey of 186 pediatric patients with neoplastic disease at Riley Children's Hospital in Indianapolis found that approximately 31% had some form of oral complication during the course of their disease or treatment. Ten per cent of the patient population had existing dental treatment needs. Different frequencies of oral complications exist between types of malignancy and the type of therapy. Therefore, the pediatric dentist must be aware of the different clinical and biological characteristics of each neoplastic disease, and the various types and phases of treatment in the assessment of his patients. Prevention and early detection of existing treatment needs are important in providing optimum care and comfort for the pediatric oncology patient.

[3] DelRegato 1939; King et al. 1968; Dreizen et al. 1974; Dreizen et al. 1975; Bruya and Maderia 1975; Rotman et al. 1977; Braham 1977; Epstein 1986.

[4] Peterson et al. 1980; Hickey et al. 1982; Wright et al. 1985; DePaola et al. 1986.

[5] Bottomley et al. 1977; Peterson and Sonis 1983; DePaola et al. 1984; McGaw and Belch 1985; Wright et al. 1985.

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At the time of writing, Dr. Kamp was a second-year pediatric dental resident at Riley Children's Hospital and University of Indiana School of Dentistry. Currently he is a pediatric dental officer in the United States Air Force. Reprint requests should be sent to: Dr. Anthony A. Kamp, 432 Medical Group/SGD, Box 2309, APO San Francisco 96519-5300.

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