

Original Article

Odontogenic Infections and Septicemia in Immunocompromised Patients with Hematologic Malignancies

—Assessment of the need for root canal treatment in patient with leukemia—

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Abstract

Myelosuppressive chemotherapy for acute leukemia develop several oral infections.

The purpose of this study is to evaluate possibility of systemic infection from apical periodontitis during treatment for acute leukemia.

The subjects consisted of 6 patients with acute leukemia who had treated between January 1997 and October 1998 were reviewed retrospectively. This population included 5 male patients and a female patient ranging age from 37 to 64 years, of whom 5 chronic apical periodontitis and 1 acute transformation of chronic apical periodontitis.

Several clinical criteria were used to determine whether infectious complications developing.

The results were as follows :

1. The mean number of days that the patients had a temperature greater than 37.5 °C and had leukocyte counts were less than 1000/ μ l were 8.5 days.
2. The mean number of days that the patients had a neutrophil counts less than 500/ μ l were 7.3 days.
3. No patient revealed odontogenic acute reaction after the chemotherapy.
4. All patients were administered several antibiotics which possess wide range of antibacterial activity.

Taken together, these results suggest that asymptomatic apical periodontitis does not increase the incidence of infectious complication during antileukemic chemotherapy with the administration of antibiotics which possess wide range of antibacterial activity

I. Introduction

It is well known that oral infection is dangerous to life if it is left to take its own course for immunocompromised patients.

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In recent years, remarkable progress has been made in the treatment of patients with haematologic malignancies. A survival ratio is increased by the prolonged administration of several chemotherapeutic agents. However, the recent development of chemotherapy in the treatment of cancer and leukemia requires that all practitioners involved have a thorough knowledge of the sometimes life-threatening side-effects of chemotherapeutic agents. Infection is the most frequent complication and a major cause of death in patients with profound and prolonged granulocytopenia.²

Septicemia is found in about 20% of the febrile episode of patients with hematologic malignancies.¹

The primary focus, however, is known in only about 60% of septicemias.^{3,4,5,6,7} As a possible origin of septicemia in cases with unknown primary focus, the role of the oral microflora has been emphasized.⁶

Apical periodontitis is a bacterial infection originating in the apex. Many cases of dental periapical abscess present annually worldwide. Such abscesses have been associated with either frank dental carious lesions with concomitant pulp tissue exposure or with advanced periodontal lesions; however, some are without obvious antecedent pathology.^{8,9} The lesions can, if left untreated, lead to cellulitis, bacteremia, septicemia or abscesses at distant sites.^{8,10,11}

The purpose of this study is to investigate the possible relationship between apical periodontitis and septicemia in patients with leukemia.

II. Material and methods

The subjects consisted of 6 patients with acute leukemia who had been referred from department of hematology in our hospital for pre-chemotherapeutic dental assessment between January 1997 and October 1998 were reviewed retrospectively.

The following features were noted for each patient : age, gender, tooth status, nature of pain, previous pain, swelling or pain on pressure of periapical area of the gingiva, history of previous root canal treatment, radiographic findings and status of root canal such as the presence of clear, haemorrhagic or purulent exudates.

All adult patients (more than 15 years of age) with hematologic malignancies (acute myeloid leukemia [AML], acute lymphoblastic leukemia [ALL], chronic myeloid leukemia [CML], chronic lymphatic leukemia [CLL]) were consecutively and prospectively included in the study if they developed a body temperature of 38.5°C or more for two consecutive hours and had received treatment with antineoplastic drugs within the previous 28 days. Individual patients could be included with more than one febrile episode. Age, sex, underlying disease, administration of antineoplastic drugs, and use of antibiotics were recorded. A history was obtained and a physical examination was performed by the same investigator on each day to detect signs and symptoms of oral or extraoral infections.

Clinical and radiological findings, in addition to other complementary tests are of special importance in the diagnosis of the apical periodontitis. Amongst the most important clinical data we include the presence of pain and its characteristics, in particular its intensity, duration, spontaneous nature and continuity. The irreversibility of pulpar involvement is determined by

the presence of severe and repeated spontaneous long-lasting pain. Brief pains induced by changes in temperature, particularly by cold, are the hallmarks of the reversible forms of pulpitis.

Radiological studies also provide findings that are relevant for diagnosis, in that they confirm or rule out the presence of caries that are potentially responsible for pulpar infection, as well as the existence of radiolucent periapical lesions, possibly corresponding to considerably more advanced stages of involvement of the tissues around the tooth. On the basis of intraoral radiographic examination, an apical periodontitis was defined as a widening of the periodontal ligament space greater than 1.5mm located at the apex of an endodontically treated tooth. Some apical periodontitis were not treated because of insufficient time for treatment between screening and chemotherapy or recognizing almost no subjective symptom.

A total of 6 patients, each with a single lesion, who met the eligibility criteria were identified. Of these 5 did not receive treatment and one was treated with endodontic treatment because of acute apical periodontitis.

The follow-up observation was conducted only during the hospitalization. Patients were examined once a week by the dentist. The outcomes measured were as follows, (1) the number of days febrile (when the patients temperature was greater than 37.5 °C and the white blood cell count was less than 1,000/ μ l), (2) the number of days when the absolute neutrophil count was less than 500/ μ l, and (3) local signs and symptoms associated with odontogenic infection, such as swelling, pain, and sensitivity. (4) selection and the administration period of antibiotics.

III. Results

Patient characteristics are described in Table I.

This population included 5 male patients and a female patient with 5 acute myeloid leukemia (AML) and 1 acute lymphoblastic leukemia (ALL) ranging age from 37 to 64 years, of whom 5 chronic apical periodontitis and 1 acute transformation of chronic apical periodontitis with radiological evidence of bone destruction. (Table 1) The patient with acute transformation of chronic apical periodontitis was treated 5 days before chemotherapy for leukemia. There were no documented reports of oral complications or complaints such as swelling, pain, or sensitivity associated with teeth with apical periodontitis. No organisms suggestive of oral flora were isolated from the blood of patients.

The mean number of days that the patients had a temperature greater than 37.5°C, and leukocyte counts of less than 1000/ μ l were 2 to 24 days in average of 8.5 (Table 2).

The mean number of days that the patients had neutrophil counts of less than 500/ μ l were 6 to 9 in average of 7.3 (Table 2).

No special abnormality attributed to inflammation of the periapical tissue was recognized during and after chemotherapy. The blood culture examination revealed no abnormalities.

All patients were administered several antibiotics that possess a wide range of antibacterial activity such as carbapenems for 10 to 30 days in average of 22 days (Table 3).

Table 1 Patients and characteristics

Case	Age	Sex	Diagnosis	Dental problem	
				Dental diagnosis	Decayed tooth
1	45	M	AML*	CAP *	1
2	56	M	AML*	CAP *	1
3	64	M	AML*	CAP *	1
4	55	M	AML*	CAP *	1
5	37	F	AML*	CAP *	1
6	61	M	ALL**	AAP **	1

* AML : acute myelocytic leukemia, ** ALL : acute lymphocytic leukemia

* CAP : chronic apical periodontitis, ** AAP : acute apical periodontitis

Table 2 Fever and leucopenia after leukemic chemotherapy

Case	Fever (Days)	Leucopenia (Days)
1 (AML)	10	6
2 (AML)	5	9
3 (AML)	7	7
4 (AML)	2	7
5 (AML)	3	6
6 (ALL)	24	9

Table 3 Kinds and dosage periods of antibiotics

Case	Administration of antibiotics	Period (Days)
1 (AML)	9 (AMK, CPR, MINO, IPM, ABPC, FCZ, VCM, CTM, GM)	27
2 (AML)	1 (IPM)	15
3 (AML)	4 (AMK, IPM, MINO, ABPC)	30
4 (AML)	4 (AMK, IPM, MINO, ABPC)	20
5 (AML)	2 (PAPM, AMK)	10
6 (ALL)	3 (PAPM, AMK, CPR, NTL)	30

IV. Discussion

The goal of dental screening is to reduce the morbidity and mortality that may arise from oral complications associated with antileukemic chemotherapy. The most significant clinical condition of all bacterial infections of periapical origin is the so-called chronic or acute apical periodontitis. It is usually the result of purulent pulpitis that spreads into the periapical space and therefore, it appears in the course of pulpar disease. In acute apical periodontitis there is an accumulation of pus inside the apical space of the tooth in question. Local or systemic disease secondary to a localized chronic dental infection is termed dental focal infection. Clinically, dental focal infection is probably rather rare, by virtue of the efficiency of host defense. However, infective endocarditis, acute bacterial myocarditis, brain abscess, uveitis,

and iridocyclitis are comparatively well known. The focal infection theory has remained controversial because of the lack of clear evidence regarding the causal relationship between oral infections and general health.

No study has shown that bacteremia spontaneously occurs in cases of infected root canals associated with a chronic periradicular lesion. Peters also reported nontreatment of asymptomatic postendodontic periapical radiolucencies does not increase the incidence of infectious complications during bone marrow transplantation.¹² Many drugs that are used to treat leukemia can also cause oral lesions; in addition, patients may have complications from bone marrow transplantation. Bacteremia can occur in cases of acute periradicular abscesses and during the root canal treatment. Although it has been demonstrated that the microbial species present in blood of patients undergoing endodontic therapy can cause bacteremia but not that microorganisms from the root canal cause damage in remote sites of the body.

The purpose of antibiotic therapy is to aid the host defenses in controlling and eliminating microorganisms that temporarily have overwhelmed the host defense mechanisms. The most important decision in antibiotic therapy is not so much which antibiotic should be used but whether antibiotics should be used at all.

The majority of infections of endodontic origin are treated without the need for antibiotics. Because of the absence of blood circulation within a necrotic and infected pulp, antibiotics cannot reach and eliminate microorganisms present in the root canal system. On the other hand, antibiotics can help to impede spreading of the infection and the development of secondary infections in compromised patients such as patients with hematologic malignancies. Therefore, antibiotics can be a valuable adjunct for the management of some few cases of endodontic infection.

Most recommendations for the approach to abnormal findings on routine screening examinations are based on case reports, personal preference and on limited anecdotal experience. There is a need to identify which strategies are optimal to prevent or to minimize oral complications during periods of profound immunosuppression. Retrospective chart reviews have their limitations but are frequently the only way to study some clinical problems. Because of ethical constraints, randomized and clinical trials are not always possible. The question of whether treatment of asymptomatic apical periodontitis affects outcome in patients who undergo profound myelosuppression associated with antileukemic chemotherapy was desirably studied retrospectively because conducting a randomized clinical trial was considered inappropriate. As a result it was possible to identify patients through retrospective chart review and measure their outcome.

In this study, these results suggest that nontreatment of asymptomatic postendodontic periapical radiolucencies does not increase the incidence of infectious complications during antileukemic chemotherapy with antibiotics that possess a wide range of antibacterial activity.

Further studies are warranted to establish the true relationship between myelosuppression and periradicular response to bacterial infection.

V. References

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血液悪性腫瘍患者における歯性感染症に関する研究 —白血病患者に対する根管治療の必要性について—

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要 約

我々は、根尖性歯周炎が白血病の化学療法後に生じる骨髄機能の低下時に、生体にどのような影響を及ぼしたかをレトロスペクティブに調査し、化学療法前の根管治療の必要性について検討した。

(結果) 発熱の日数及び、好中球減少の日数は各々8.5日と7.3日と1週間を越え、やはり感染のリスクが高いことが明らかとなった。化学療法に先立ち根管治療を要した症例が1例あった。他の5例は症状はなく、全症例が化学療法

前には症状が認められなかった。化学療法後の急性症状は、全症例で認められなかった。抗生剤は全例で、広範囲の抗菌力を有する薬剤が投与され、このことが急性炎症の発現を防止した一因と考えられた。

(結論) 自覚症状がない根尖性歯周炎は、抗菌スペクトラムの広い抗生物質の点滴静注を併用することで化学療法前に必ずしも治療しなくても重篤な感染症を発症しない可能性が示唆された。

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