Case Report

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Trismus as an Orofacial Manifestation of Acute Lymphoblastic Leukemia

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Leukemia is a malignant disease characterized by uncontrolled clonal proliferation of white blood cells. It is classified depending on clinical course of disease (acute or chronic) and the primary hematopoietic cell line affected (myeloid or lymphoid). Leukemia is often associated with orofacial manifestations, such as oral bleeding, petechiae, oral ulceration, gingival enlargement, mucosal pallor and mental nerve neuropathy. However, trismus has been rarely reported as a sign of leukemia. We present a case of trismus caused by acute lymphoblastic leukemia and emphasize the importance of orofacial manifestations in the early diagnosis of leukemia.

Key Words: Acute lymphoblastic leukemia; Orofacial manifestations; Trismus

INTRODUCTION

Leukemia is a malignant neoplasm characterized by an excessive proliferation of immature white blood cells and their precursors. It is classified depending on clinical course of disease (acute or chronic) and the primary hematopoietic cell line affected (myeloid or lymphoid).[1] Leukemia is often associated with orofacial manifestations, and these manifestations may occur due to direct leukemic cell infiltration of tissues, or be secondary to underlying anemia, thrombocytopenia, neutropenia and impaired granulocyte function. It has been suggested that orofacial manifestations of leukemia include oral bleeding, petechiae, oral ulceration, gingival enlargement, mucosal pallor, mental nerve neuropathy, facial palsy and infections.[2] However, trismus has been rarely reported as a sign of leukemia.[3]

Early diagnosis and prompt treatment of leukemia is essential because leukemia, especially acute form, may be rapidly fatal if left untreated. Moreover, it has been indicated that early detection of oral manifestations of leukemia may lead to reduction in the frequency and severity of complications.[4]

We present a patient whose orofacial manifestation of trismus represented the first sign of leukemia.

CASE REPORT

A 12-year-old male was referred to Kyungpook National University Dental Hospital by a local clinician due to severe limitation of mouth opening and pricking pain on chin area. He had been undergoing orthodontic treatment since 1-month ago. Mouth opening limitation and numbness on chin were developed 4 days ago without apparent initiating event. He reported the occurrence of facial swelling for the past 2 days. In addition, he has no history of systemic disease, trauma and temporomandibular joint (TMJ) sound.

Clinical examination revealed the swollen bilateral parotid and submandibular glands. Mouth opening was severely restricted with maximum assisted mouth opening range of 12 mm. Patient reported tenderness during palpation of bilateral TMJs, masseter muscles, parotid and submandibular glands. There was no TMJ sound on mandibular movement. Neither dyspnea nor dysphagia was observed. Light touch test using a cotton swab indicated hypoesthesia in chin and

lower lip area. There were no pathologic findings including infection, fracture or any other abnormalities on panoramic radiograph (Fig. 1).

Tentative diagnosis of acute sialadenitis was initially made based on the swelling and tenderness of salivary glands. Routine laboratory tests were conducted to exclude the possibility of hematologic malignancy which often manifests with sudden numbness on chin area. In addition, facial computed tomography (CT) with enhancement was performed to exclude the possibility of solid tumor. While facial CT demonstrated no remarkable pathologic findings, complete blood count revealed a marked increase in white blood cells and a marked decrease in platelets and lowered red blood cell count, hemoglobin and hematocrit (Table 1). The differential analysis of leukocytes revealed the abnormal population of leukocytes including segmented neutrophils (8.9%), monocytes (2.1%), basophils (2.4%) and large unstained cells (47.7%). As acute leukemia was strongly suspected, the patient was immediately referred to pediatric hematology for further evaluation. The final diagnosis of B-lymphoid lineage acute lymphoblastic leukemia (ALL) was made on the basis of bone marrow test. The patient received chemotherapy following the Children's Oncology Group protocol AALL0232 and matched unrelated donor peripheral blood stem cell transplantation. The patient reported resolution of trismus and no pain 4 months after transplantation.

DISCUSSION

Trismus is defined as a motor disturbance of the trigeminal nerve, especially a masticatory muscle spasm, with difficulty in mouth opening. It was known that trismus had variety of potential causes including infection, trauma, dental treatment, TMJ disorders, radiotherapy, chemotherapy, tumor and miscellaneous disorders, which range from the simple and non-progressive to potentially life-threatening conditions.[3,5] Therefore, a potential problem in diagnosing patients with trismus is the risk of misdiagnosing the patient with the occult malignancy in stomatognathic system.[5,6]

Leukemia is the most common malignant neoplasm of the white blood cells. It is characterized by an uncontrolled proliferation of immature white blood cells, resulting in suppression of normal hematopoiesis by accumulation of leukemic cells in the bone marrow. The disease can be classified according to the type of white blood cell involved, either lymphoid or myeloid and the clinical course, either chronic or acute.[1] While chronic leukemia characterized by relatively well differentiated leukocytes is slow in onset and runs an indolent course, acute leukemia involving poorly differentiated blast cells is abrupt in onset and aggressive.[7]

ALL is the most common cancer among children with the peak incidence between the ages of 2 and 5 years.[1,3] It accounts for 75% of all newly diagnosed leukemia and 25% of all malignancies in childhood.[8] ALL is diagnosed based on the morphology and immunophenotype of the lymphocytes found.[9] While the pathogenesis of ALL remains unclear, it was suggested that a genetic predisposition lies in the base of the disease, which is further triggered by environmental factors. Though advances of diagnostic and therapeutic modalities have increased the survival rate from less than 10% in the 1960s to 90% today, the importance of

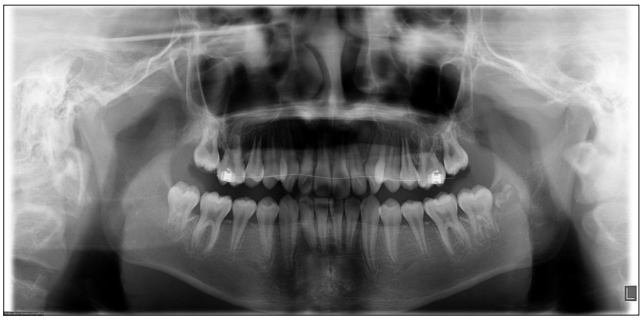

Fig. 1. Panoramic radiograph showed no remarkable pathologic findings.

Table 1. Hematological findings

Test	Value		Normal value range
White blood cells ($\times 10^3/\mu L$)	16.24	↑	4.8-10.8
Red blood cells ($\times 10^6/\mu L$)	3.88	↓	4.6-6.2
Hemoglobin (g/dL)	11.2	↓	13.0-18.0
Hematocrit (%)	31.0	↓	40.0-50.0
Platelets ($\times 10^3/\mu L$)	16	↓	130-400
Segmented neutrophils (%)	8.9	↓	40-74
Lymphocytes (%)	38.5		19-48
Monocytes (%)	2.1	↓	3.4-9.0
Eosinophils (%)	0.4		0-7
Basophils (%)	2.4	↑	0-2
Large unstained cells (%)	47.7	↑	0-4

early diagnosis and prompt treatment is still emphasized to date.[10]

Orofacial manifestations are commonly accompanied by leukemia and, more frequently by acute form of leukemia.[1,7] Thrombocytopenia and anemia caused by the suppression of normal hematopoiesis may result in oral changes, such as mucosal pallor, petechiae, ecchymoses and gingival bleeding. Direct infiltration of leukemic cells may induce gingival enlargement and mental nerve neuropathy, subsequently leading to numbness or paresthesia in chin area as reported in this patient. Hou et al.[4] evaluated the oral manifestations as an early clinical sign of leukemia and found that fever was the most common symptom in leukemia patients, followed by lymph node enlargement, laryngeal pain, oral bleeding, oral ulceration, gingival swelling, petechiae, mucosal pallor, tooth mobility, toothache and paresthesia. However, trismus has been rarely reported as a sign of leukemia.[3] This patient was also referred for the evaluation of the mouth opening limitation and mandibular pain, initially diagnosed as temporomandibular disorders by general practitioner. Because the dentist is frequently the first medical person to encounter various orofacial manifestations of leukemia, it is important to better understand the oral manifestations of leukemia. Diagnostic checklist was devised to reduce the risk of delayed or misdiagnosis of malignancy in cases of trismus by Beddis et al.[6] The checklist is made up of 6 items (opening less than 15 mm, progressively worsening trismus, absence of history of clicking, pain of non-myofascial origin [neuralgia etc.], swollen lymph glands, suspicious intra-oral soft tissue lesion), and any 'yes' answers in the checklist necessitates further assessment for excluding the possibility of malignancy or referral to an oral and maxillofacial surgery consultant. In the present case, 'yes' answers on the checklist were given to 'opening less than 15 mm', 'absence of history of clicking' and 'pain of non-myofascial origin'.

Radiographic findings might be also useful in revealing the pathologic alterations in orofacial area by leukemia. Fat-rich yellow bone marrow is less vulnerable to invasion of leukemic cells than red bone marrow, which predominantly consists of bone marrow in young child.[11] It was suggested that radiographic findings in pediatric patients with acute leukemia presented with bone resorption, loss of cancellous bone, thinning of the crypts of developing teeth, loss of lamina dura, disappearance of mandibular canal border and enlargement of the mental foramen.[11] However, panoramic radiograph showed no remarkable pathologic findings in this patient.

Although the precise mechanism how leukemia contributes to the development of trismus is unknown, leukemic cells are known to infiltrate skeletal muscles, such as temporalis and sternocleidomastoid muscle.[12] Therefore, it was reasonable to assume that trismus was probably attributed to direct infiltration of leukemic cells into the masticatory muscles of this patient.

To the best of the authors' knowledge, no dental treatment of trismus caused by ALL has been universally established. In this case, jaw symptoms of the patient improved with ALL treatment even though no treatment of temporomandibular disorders was performed. Thus, it can be inferred that prognosis of jaw problem in ALL patient is closely related to response to leukemia treatment. Further investigation is required for setting up protocols for assessment and treatment of trismus caused by ALL.

ALL is possible to present with various and non-specific orofacial manifestations which may resemble musculoskeletal or inflammatory conditions. This case report indicates the significance of differential diagnosis in childhood patients presenting with atypical manifestations including mouth opening limitation and pricking pain on chin area as the first sign of ALL.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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