

ACTINOMYCES NAESLUNDII IN PATIENTS WITH HEMATOLOGICAL MALIGNANCIES

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Abstract- Mycotic infections have been commonly encountered in patients with hematological malignancies. The current study seeks the prevalence of actinomycete infection in patients suffering from blood cells malignancies. A hundred and fifty patients with some kinds of blood cells dyscrasia who underwent the bone marrow aspiration were recruited. In addition to the diagnostic work up, samples were examined for the presence of actinomycete infections. Twenty one samples were positive for actinomycete infections. All of them were infected by *Actinomyces naeslundii*. All the positive patients were categorized in malignant groups, acute myelocytic leukemia, chronic myelocytic leukemia, and lymphoma and myelodysplastic syndrome. High incidence of actinomycete infections in the present study population was interesting. These results can also be suggestive of a pre-malignancy role for the actinomycosis.

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INTRODUCTION

Different species of actinomyces are usually associated with tumors and leukemia or initiate tumors in the patients. Chaumentin *et al.* reported disseminate actinomycosis resembling a pulmonary carcinoma (1). In another report, Guerri *et al.* reported two cases of the actinomycosis associated with non-Hodgkin lymphoma (NHL); one with persistent lymphadenopathy of the abdominal region

which was resistant to antibiotic therapy. The other with hepatic metastasis with high-grade NHL was diagnosed by using laparotomy and liver metastatic metastasis (2). Billingham and Griener reported actinomycosis from a patient with myeloblastic leukemia. Mycotic infections have been identified post-mortem in as many as 39% leukemic patients (3). In the recent studies there are an increasing reports of actinomycosis in the patients with hematological malignancies. Mobedi *et al.* observed a relative high prevalence of the disease among the leukemic patients (4). Also, the diagnosis of the actinomycosis is relatively difficult and its clinical recognition is of utmost importance since the appropriate therapies may lessen the morbidity and prolong the useful live. Actinomycosis and the

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relative species are indigenous to oral, bowel, and vaginal flora inhabitant as well periodontal pockets, carious teeth, and tonsillar crypts as well gastrointestinal tract. These organisms are not particularly virulent requiring disruption of mucosal barriers by trauma, infections or surgical injuries for invasion of the underlying tissues (5). Actinomycosis is an infectious disease that is slowly progressive, painless, indurated, which can produce multiple abscesses and cutaneous fistulae. The acute and less frequent form is a rapidly progressive, tender, and fluctuant mass, suggestive of an acute dental infection. Actinomycotic infections at all sites are characterized by a long-latency period, and a delay in the diagnosis. On pathological examinations, abdominal disease is characterized by micro-abscess formation with progression to the formation of chronic sinuses and fistulae. The surrounding woody induration is characteristic and once encountered clinically, is not quickly forgotten. Infected patients present low-grade fever, mild anemia, abdominal pain, or nausea and vomiting. Intermittent bowel obstruction or ureteral compromise may be seen (5).

Despite the presence of sulfur granules being almost pathognomic of actinomycosis, the main stay of diagnosis must be based on the microbiological procedures or histological examinations. Burckhardt *et al.* proposed the possible roles of the actinomyces viscosus as cell mitogens which is important in autoimmune diseases including rheumatoid arthritis (6).

In another experience, Schroeder and Page observed the functional properties of human fibroblast exposed to actinomyces viscosus which was caused by hosts cell reactions (7). Actinomyces was isolated from cystic worm by Shahbazi who reported that 80% of patients with hydatid cysts had actinomyces antibodies on their sera by using immunoelectrophoresis methods (8).

MATERIALS AND METHODS

In this evaluation, patients with hematological malignancies who had been referred to the Oncology Wards of Imam Khomeini and Shariati Hospitals were assessed. Sampling was done in 150 males and females, not been treated for their disease by bone

marrow aspiration. Tissue specimens, were transferred to sodium thioglycolate anaerobic media, after which they were been placed in an aerobic jar with gas pack and then incubated at 37 Centigrade degree for 10 days, and samples were checked and the positive samples were derived from negative samples. Then negative samples were placed in incubator for another 30 days, after which, negatives were excluded and deleted. The positive samples then were passed in a new sodium thioglycolate anaerobic medium, and also all the positive specimens were cultured in Brain Heart Infusion Agar (BHI) plate. After that, plates were incubated again in sodium thioglycolate anaerobic media with gas pack for 10 days. After gram staining, plates were assessed with direct examination. After observing the gram-positive actinomyces strains, urea test and gelatin hydrolysis test were done for confirming the diagnosis of actinomyces. Moreover, catalase test was done to confirm it to be anaerobic. All the specimens were catalase negative and urea test and gelatin hydrolysis tests were negative, too. After diagnosis confirmation, xylose and mannitol fermentation tests were done for differentiation of strains of actinomyces. After 72 hr of incubation at 37 Centigrade degree in mannitol and xylose media, stable red color of media indicated that all the specimens were *Actinomyces naeslundii*.

RESULTS

Of the overall 150 patients which had been assessed, 21 patients had been positive for actinomyces, all of them were infected by *A. naeslundii*. All 150 patients were divided into benign and malignant groups. All the positive patients were among the malignant group.

Actinomyces naeslundii were isolated from all 21 malignant reticuloendothelial patients. They were leukemic (chronic myelocytic leukemia [CML], acute myelocytic leukemia [AML], idiopathic thrombocytopenic purpura [ITP], and myelodysplastic syndrome [MDS], lymphoma, aplastic anemia, and myelofibrosis) (Table 1). Negative groups were among non-malignant anemic patients.

Table 1. Types of lymphoreticular tumors in patients with actinomycosis in two hospitals*

| Hospital | Aplastic anemia | MDS | Myelofibrosis | ITP | Lymphoma | CML | AML | Total |
|---------------|-----------------|-----|---------------|-----|----------|-----|-----|-------|
| Shariati | 1 | 1 | 2 | 2 | 3 | 1 | 3 | 13 |
| Imam Khomeini | 0 | 0 | 1 | 1 | 2 | 2 | 2 | 8 |
| Total | 1 | 1 | 3 | 3 | 5 | 3 | 5 | 21 |

*Data are given as number.

Abbreviations: MDS, myelodysplastic syndrome; CML, chronic myelocytic lymphoma; AML, acute myelocytic leukemia.

Table 1 shows the prevalence of the malignant versus the benign diseases in the patients. As shown in table 2, from all 21 positive patients, numbers of infected females were 13 and infected males were 8. Fifteen patients were between 41-60 years, five were between 20-40 years, and the remaining one patient was in 60-80 age-group.

DISCUSSION

Actinomyces are amongst the most important microorganisms inhabiting in the upper respiratory tract. They are commonly found in areas including tonsillar crypts, tooth carries, as well as alimentary tract. It includes species of the *A. israelii*, *A. naeslundii*, *A. eriksonii*, and the normal flora of human buccal cavity, and tonsillar crypts are of limited invasive ability. It is also suggested that they can not elicit disease without the aid of trauma to tissues. The present study presents a descriptive investigation of 21 cases of the disease in patients with hematological malignancies during a 2-year-period. Five patients presented with AML, three patients had CML, five have lymphoma, and three had ITP, three had myelofibrosis, one had myelodysplastic syndrome, and one had aplastic anemia. All cases were presented before any treatment regime had begun. The specimens were obtained from the bone marrow aspiration, and all

the patients with positive culture had hematological malignancies, and all negative patients had benign disease. These results are consistent with the hypothesis of some which studies suggest that actinomycosis may cause malignancies by attaching and altering the characteristic of cell nucleus.

Actinomyces belongs to family Actinomycetales and was first described almost 200 years ago. Currently, actinomyces are considered to be bacteria, previously reported as fungi or some forms between the two species. A major difficulty in establishment of actinomycotic infection diagnosis is to obtain positive cultures. The most important problem relating to microbiologic examination is concomitant aerobic and anaerobic bacterial overgrowth. These micro-organisms are extremely delicate especially if they are exposed to air for prolonged periods, because of the slow growth pattern, as well the necessity of a careful anaerobic culturing atmosphere.

Treatment of the actinomycosis usually involves long-term and high dosage of antibiotic therapy associated with surgical removal and the drainage of the infectious foci, if present.

Several antibiotics have been used for treating the disease including tetracycline, clindamycin, erythromycin, chloramphenicol, and penicillin which are the preferred ones. However, there are some controversies about the dosage and the duration of antibiotic therapy (9, 10).

Table 2. Sex, occupation and age group of patients with *actinomyces naeslundii* positive lymphoreticular tumors*

| Age group | Female | Male | | | Total |
|-----------|------------------|---------|-----------------|-----------------|-------|
| | All house keeper | Farmers | Electric worker | Chemical worker | |
| 20-40 | 4 | 0 | 0 | 1 | 5 |
| 41-60 | 9 | 2 | 3 | 1 | 15 |
| 61-80 | 0 | 1 | 0 | 0 | 1 |
| Total | 13 | 3 | 3 | 2 | 21 |

*Data are given as number.

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Conflict of interests

We have no conflict of interests.

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