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Two Cases of Tuberculosis Manifesting as Cutaneous Solitary Mass in Patients with Adult T-Cell Leukemia/Lymphoma

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Abstract

Tuberculosis (TB) is a major public health problem worldwide and a large number of fatal cases are still reported. Immunocompetent individuals are naturally susceptible to TB, and immunocompromised patients have a greater risk of infection. Although patients with adult T-cell leukemia/lymphoma (ATL) are in an immunosuppressed condition, there is only one reported case of TB accompanied with ATL in the English-language literature in the field of dermatology. Here, we report two patients with chronic-type ATL infected with TB manifesting as cutaneous solitary masses. Case 1 was a 58-year-old woman diagnosed with lumbar abscess with pulmonary TB. Case 2 was an 84-year-old woman diagnosed with tuberculous lymphadenitis in the left cervical region. It is important to raise the differential diagnosis of TB and perform tissue culture for acid-fast bacilli as well as Interferon-Gamma release assay test when dermatologists encounter mass lesions in patients with ATL.

Keywords

Tuberculosis, Tuberculous Lymphadenitis, Immunosuppression, Adult T-Cell Leukemia/Lymphoma, Regulatory T-Cell

1. Introduction

Adult T-cell leukemia/lymphoma (ATL) is a mature CD4-positive T-cell lymphoma caused by infection with human T-cell lymphotropic virus type-1 (HTLV-1). Most cases of ATL belong to HTLV-1-endemic areas in southwestern Japan, Central Africa and the Caribbean Basin [1] [2].

It is well known that patients with ATL are more susceptible to various infections.

Non-specific skin manifestations have been investigated for infections such as leprosy, scabies and superficial mycoses, which can frequently be complicated with ATL, resulting from immunosuppression caused by tumor progression [3]-[6]. With regard to tuberculosis (TB), one review suggests that patients with ATL have an increased risk of TB compared with the general population without ATL [7]. However, no epidemiological evidence, or even a case series, has yet been reported on this issue.

Here, we report two cases of TB manifesting as cutaneous solitary masses in patients with ATL, and discuss the pathoetiology about the relation between ATL and TB.

2. Case

2.1. Case 1

A 58-year-old woman had been treated with antibiotics for lobular pneumonia which had not been identified the infected organism in a municipal hospital since early August 2010. Although her general symptoms improved with antibiotic treatment, she required careful observation by her attending physician because of residual pulmonary opacity. In late August 2010, she had an uncomfortable feeling at her waist. Then, she was referred to our outpatient clinic. Physical examination revealed an elevated subcutaneous mass with slight tenderness in the lumbar region (**Figure 1(a)**). T1-weighted magnetic resonance imaging of the lumbar lesion demonstrated a well-defined, low-intensity area measuring ~7 cm, suggesting a large abscess in the subcutaneous/intramuscular lesion (**Figure 1(b)**). A test incision revealed widespread yellowish necrotic tissue in the subcutaneous tissue (**Figure 1(c)**), and no pus discharge. Culture of the necrotic tissue generated acid-fast bacilli, and DNA testing identified *Mycobacterium tuberculosis*. The interferon-Gamma release assay (IGRA): Quanti-FERON-TB, was also positive. Detailed questions confirmed that she had had a family member with pulmonary TB. Computed tomography revealed a pulmonary shadow on the S6 area in the left lung, suggesting active TB (**Figure 1(d)**). The results of hematological examination were as follows: total lymphocytes in white blood cells, 5760/μL; atypical lymphocytes, 4630/μL (>5% total lymphocytes); soluble interleukin-2 receptor, 5047 U/mL; and lactate dehydrogenase, 211 IU/L. And serum albumin and BUN were within normal range. Serologically, anti-HTLV-1 antibody was positive. Based on these findings, we diagnosed this case as pulmonary and subcutaneous TB in association with chronic-type ATL. Combined chemotherapy with isoniazid (INH), ethambutol (EB), rifampicin (RIF) and pyrazinamide (PZA) was started, and all lesions of TB were improved by 6 months after treatment.

2.2. Case 2

An 84-year-old woman had been visiting an internist regularly for chronic-type ATL without any medication. Her condition of ATL had been stable for the past few years without any indications of poor prognosis on her peripheral blood. She had no familial or past history of TB. One day, she noticed a left cervical nodule measuring ~1 cm in diameter. The nodule had enlarged gradually despite oral cephem antibiotics. She was

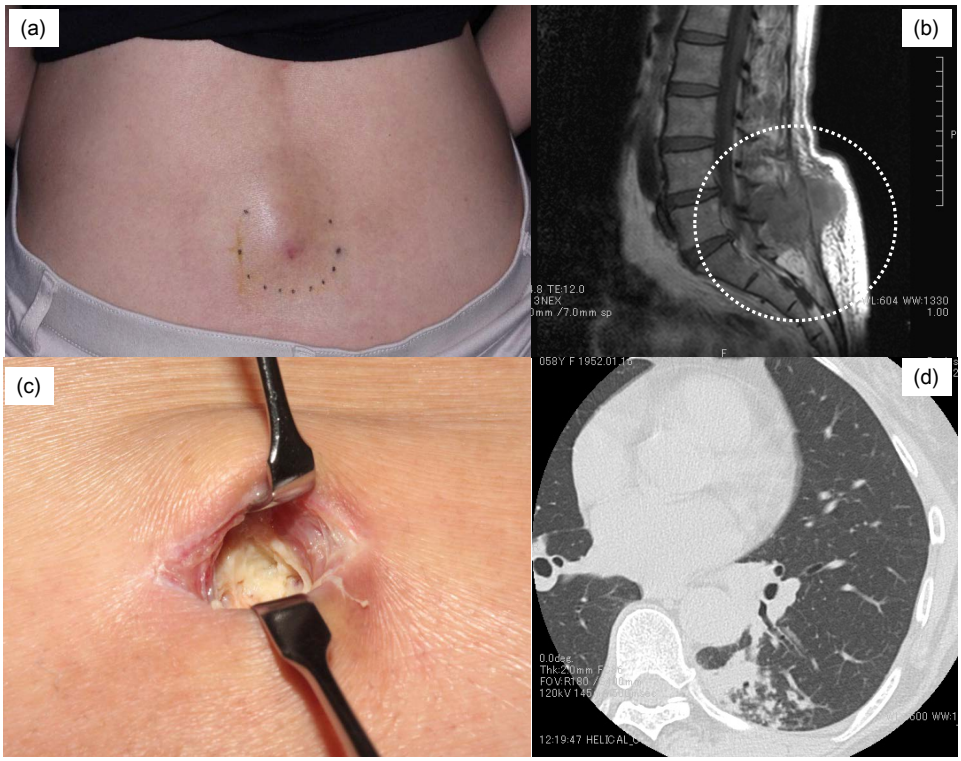

Figure 1. Clinical appearance (a, c), results of magnetic resonance imaging and computed tomography (b, d) in Case 1. (a) Mass lesion with slight tenderness in the lumbar region was observed. (b) Well-defined, low-intensity area measuring ~7cm, suggesting a large abscess developing from the subcutaneous/intramuscular lesion. (c) Widespread yellowish necrotic tissue was seen in the subcutaneous tissue. (d) Pulmonary infiltrates with satellite lesion in S6 of the left lung, suggesting active tuberculosis.

referred to our outpatient clinic with suspicion of skin involvement of acid-fast bacillus infection.

At the first visit, she had no respiratory symptoms such as cough and sputum. She presented with a hard brownish nodule measuring 3 cm in diameter with symptoms on the left aspect of the neck (**Figure 2(a)**). Culture taken from the lesion generated acid-fast bacilli confirmed as *M. tuberculosis* by polymerase chain reaction. No acid-fast bacilli or other organisms were detected in her sputum. The result of IGRA, T-spot TB was negative. Imaging revealed swollen lymph nodes around the left cervical lesion without any other active focus of TB (**Figure 2(b)**), and we confirmed diagnosis of tuberculous lymphadenitis. We started combination chemotherapy (RIF, PZA, INH, EB), and 1 year after the lesion has almost disappeared.

3. Discussion

ATL often manifests with non-specific skin lesions for some infections such as leprosy, scabies and superficial mycoses, in addition to the specific tumoral skin lesions [3]-[6]. As previously investigated, tumor cells of ATL typically express CD4, CD25 and often fork head box P3, which are matched with a phenotype of probable origin, regulatory

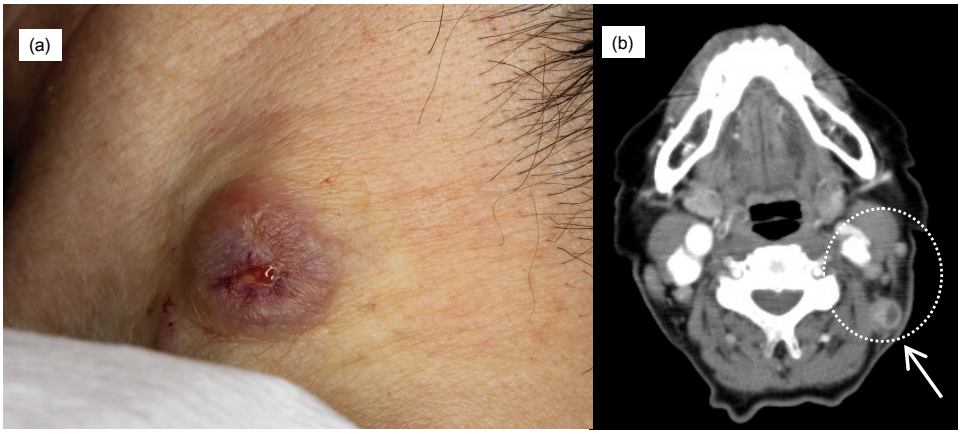

Figure 2. Clinical appearance (a) and computed tomography (b) in Case 2. (a) The lesion presented as a hard brownish nodule measuring 3 cm in diameter with no signs on the left cervical region. (b) Multiple lymph node swellings were found in the left cervical region.

T (Treg) cells. Although the exact etiology of increased susceptibility to some infections in patients with ATL has not yet been clarified, it has been speculated that tumor cells and/or nontumoral Treg cells might contribute to the immunosuppression [2] [4] [5].

Immunity mediated by T helper 1 cells has been shown to be responsible in *M. tuberculosis* infection [8]-[10], and the mediator, interferon gamma, produced by peripheral blood mononuclear cells has been quantified by IGRA (Quanti-FERON-TB Gold test and T-spot TB) for screening of TB. The T-spot TB test was negative in Case 2, suggesting that her T helper 1 immunity was impaired. IGRA has high sensitivity to detect *M. tuberculosis* infection, however, it should be kept in mind that IGRA measures host response as evidence of infection. Therefore, it can be negative in immunosuppressed patients, and Kobashi *et al.* have reported that IGRA shows false-negative results more frequently in immunosuppressed patients [11].

With regard to the relation between Treg cells and TB, one report states that patients with TB have more Treg cells in their peripheral blood compared with healthy controls [12]. Another study demonstrated that Treg-cell-depleted mice infected with TB have a low bacterial load in the lungs after aerosol infection [13]. These findings indicate that activation of Treg cells helps progression of TB, and it could be interpreted that patients with ATL have a greater risk of being infected with TB.

Although there are many reports of TB complicated with immunosuppression, such as acquired immunodeficiency syndrome, to the best of our knowledge, there is only one reported Japanese case of cutaneous TB with ATL in the English-language literature [14]. That case was a 65-year-old man with multiple reddish plaques and erythema around the head who was diagnosed with multifocal lupus vulgaris. And there have been no reported cases of TB manifesting as cutaneous solitary mass in patient with ATL except for true-cutaneous tuberculosis and tuberculid. With more cases accumulated, we may be able to clarify the incidence and predominant type of cutaneous involvement of TB and clinical type of ATL.

4. Conclusion

We emphasize here that TB is one of the important differential diagnoses when dermatologists encounter tumoral lesions in patients with ATL, and one should perform an acid-fast bacillus culture as well as IGRA test.

Conflict of Interest

None declared.

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