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Anaplastic lymphoma kinase-negative primary systemic anaplastic large cell lymphoma mimicking a ruptured epidermal cyst of the scalp: a case report and literature review

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Case Report and Literature Review

The incidence of anaplastic large cell lymphoma is 0.25 cases per 100,000 people. It usually causes lymphadenopathy and B symptoms; however, diverse cutaneous manifestations can also be observed. We report a rare case of anaplastic large cell lymphoma of the scalp, which presented similarly to a ruptured epidermal cyst. A 77-year-old woman visited the outpatient clinic complaining of scalp masses that had appeared 2 months before. One week before her visit, she had undergone incision and drainage at a local clinic but showed no improvement. Before surgery, facial magnetic resonance imaging revealed two suspicious ruptured cystic masses. Surgical excision was performed with a 1-cm free margin from the soft mass. Histopathology confirmed anaplastic lymphoma kinase-negative anaplastic large cell lymphoma. After wide excision and skin grafting for wound reconstruction, followed by consultation with a hemato-oncologist and radiation oncologist, chemotherapy was planned to prevent recurrence. Differentiating anaplastic lymphoma kinase-negative anaplastic large cell lymphoma of the scalp from a ruptured epidermal cyst-like mass proved challenging. We recommend considering the possibility of anaplastic large cell lymphoma if an epidermal cyst-like mass does not respond to antibiotics or conventional dressing, as illustrated by our rare case.

Abbreviations: ALCL, anaplastic large cell lymphoma; ALK, anaplastic lymphoma kinase; CT, computed tomography; MRI, magnetic resonance imaging

Keywords: Anaplastic large cell lymphoma / Anaplastic lymphoma kinase / Case reports / Epidermal cyst

INTRODUCTION

Anaplastic large cell lymphoma (ALCL) is a heterogeneous group of non-Hodgkin lymphomas, accounting for only 2% of cases [1]. Given its rarity, the exact incidence of ALCL is unknown. According to retrospective analyses, the incidence of this disease is 0.25 cases per 100,000 people in the United States [2]. ALCL incidence has a bimodal age distribution, peaking in adolescence and around 60 years [3].

ALCL is classified into four distinct forms. This distinction is important because anaplastic lymphoma kinase (ALK)-positive ALCL has significantly better clinical outcomes than ALK-negative ALCL [4]. Usually, ALCL causes lymphadenopathy and B symptoms (fever, night sweats, and unexplained weight loss); however, it can also cause diverse cutaneous manifestations. It

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can mimic eczema, pyoderma gangrenosum, Behçet's disease, and skin infection [5,6]. Despite the diverse cutaneous features of ALCL, no report on ALCL mimicking the epidermal cyst exists. Additionally, typical ALCL symptoms were absent, which made diagnosis difficult. Thus, this case reports a rare case of ALK-negative ALCL of the scalp that mimicked an infected epidermal cyst-like mass.

CASE REPORT

A 77-year-old Korean woman with a history of hyperlipidemia and thyroid cancer visited our outpatient clinic complaining of tender masses of the scalp present for 2 months (Fig. 1A). She had a tender scalp, along with erythema near the masses. Initially, the patient was treated with oral antibiotics, although without improvement. One week before her visit, she had undergone incision and drainage of two scalp sites at a local clinic.

Given that the masses were deemed most likely to be a ruptured epidermal cyst, we performed a wound culture of the lesions and planned to treat them with gauze dressings. Intravenous and oral cephalosporins were administered empirically. Despite the absence of bacterial growth on the wound culture, the patient reported persistent pain near the wound site, prompting surgical excision.

Facial magnetic resonance imaging (MRI) was preoperatively performed to evaluate worsening headaches. At first, the MRI revealed two adjacent masses in the scalp area, which were suspected to be ruptured cystic masses according to the radiologist's opinion. However, it was later revised with the opinion that malignancy should also be considered (Fig. 1B). Although a punch biopsy was first considered, we decided to perform a total resection, which might be needed in the future to relieve pain, since the patient complained of extreme pain.

The incision with a 1 cm free margin from the soft masses were performed. After careful dissection, deep layer involvement of masses into the periosteum was found. It was removed en bloc including the periosteum layer until the skull bone grossly seemed to be clear from the lesion (Fig. 1C). Considering the possibility of malignancy, we deferred defect coverage until histological diagnosis.

Histopathological examination confirmed a diagnosis of ALK-negative ALCL (Fig. 2). Additionally, it confirmed that

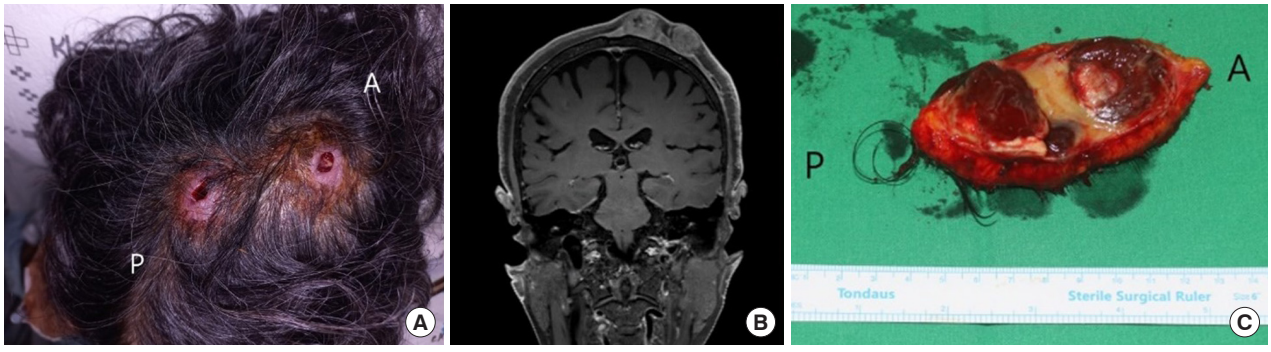

Fig. 1. A 77-year-old woman with presumed ruptured epidermal cyst-like masses on the scalp. (A) Incision and drainage of two scalp sites. (B) Facial magnetic resonance imaging showing two suspicious masses of the scalp. Initially, masses were suspected to be ruptured cystic masses but were later revised, considering the possibility of malignancy by a radiologist. (C) An intraoperative photograph of the excised masses. It was widely excised with a 1 cm free margin. Gross photograph showing protrusion into the periosteum. A, anterior; P, posterior.

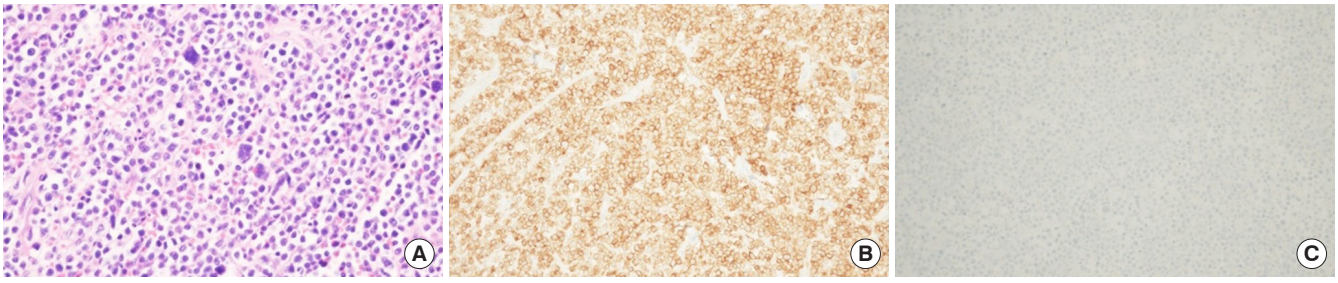

Fig. 2. Histologic and immunohistochemical staining of the specimen from a 77-year-old woman's scalp mass. (A) A histological section showing an extensive dermal infiltrate composed predominantly of medium to large lymphocytes with anaplastic morphology (hematoxylin and eosin, ×400). (B) Immunohistochemical studies demonstrating that large lymphoid cells were diffusely positive for CD30 and negative for anaplastic lymphoma kinase (ALK) (×200). (C) Immunohistochemical studies confirming that large lymphoid cells were diffusely negative for ALK (×200).

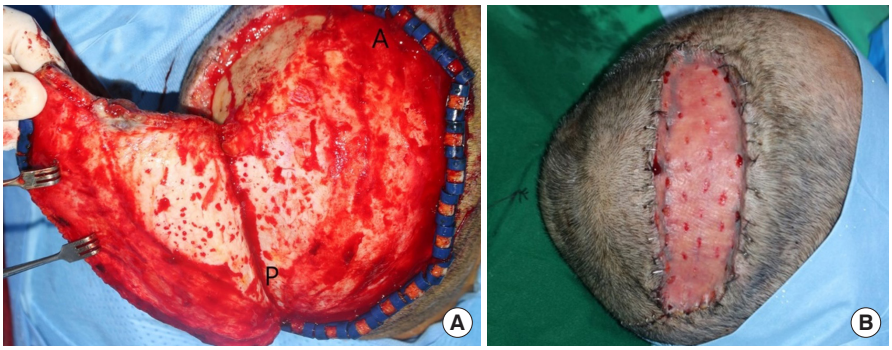

Fig. 3. Intraoperative and postoperative photographs of the reconstruction stage of the exposed scalp bone. (A) Intraoperative image. The reconstruction was performed using a rotation flap on the exposed scalp bone and split-thickness skin grafting on the donor site. (B) Postoperative day 5 image. The condition of the flap condition and the split-thickness skin graft was good. There were no complications such as recurrence or headache. A, anterior; P, posterior.

the peripheral margin was clear, but deep margin involvement was noted. On additional tumor evaluation, chest computed tomography (CT) and positron emission tomography-CT revealed evidence of lung metastasis in both lung fields. Due to an extracutaneous lesion, the patient was diagnosed with a primary systemic ALK-negative ALCL. Regarding deep scalp tissue involvement, multidisciplinary consultations with the hemato-oncology and radiation oncology departments led to the decision to administer chemotherapy after scalp reconstruction without the additional removal of skull lesions.

After the excision, the scalp defect measured 10×4 cm, rendering direct closure impossible. Additionally, when performing the excision, the masses were removed with the periosteum. Therefore, a direct skin graft over the defect was not feasible. We planned to elevate the rotation flap at the subgaleal layers for defect coverage and cover the donor sites using a split-thickness skin graft. A rotational flap was carefully elevated to avoid damage to the pedicle. Upon inserting the flap into the defect area, the tension was manageable.

Therefore, we approximated the flap with rotation. Donor of rotated flap area was covered by split-thickness skin (0.0125 inches) harvested from the left posterior thigh (Fig. 3A). On postoperative day 5, the condition of the flap and split-thickness skin graft was good (Fig. 3B). At the 6-month follow-up, there were no complications, such as headache or recurrence. For additional treatment of primary systemic ALK-negative ALCL, chemotherapy with a BV-CHP regimen (brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone) was administered 1 month after surgery. The patient did not complain of any complications.

LITERATURE REVIEW

ALCL was identified by Stein in 1985 and named in the Revised European American Lymphoma classification. It is a heterogeneous group of non-Hodgkin lymphomas, accounting for only 2% of cases [1]. Given its rarity, the exact incidence of ALCL is unknown. However, according to retrospective analyses of major centers in the United States, ALCL incidence is low at 0.25 cases per 100,000 people nationwide [2]. It has a bimodal age distribution, peaking in adolescence and around 60 years, with a male preponderance (male-to-female ratio: 1.5:1) [3].

The main signs and symptoms are lymphadenopathy and B symptoms (fever, night sweats, and unexplained weight loss), although different symptoms can be observed depending on the affected site. Bone marrow invasion can be associated with anemia and thrombocytopenia. Other symptoms, such as dyspnea and cough, can be observed when ALCL affects the lungs. Cutaneous ALCL manifestations are diverse, possibly mimicking eczema, pyoderma gangrenosum, Behçet's disease, and skin infection [5-7].

ALCL is classified into four distinct forms based on its molecular characteristics and clinical features: primary systemic ALK-positive ALCL, primary systemic ALK-negative ALCL, breast implant-associated ALCL, and primary cutaneous ALCL [2]. Primary systemic ALCL and primary cutaneous ALCL are morphologically similar but clinically distinct, with primary cutaneous ALCL being confined to the skin. In turn, primary systemic ALCL is defined by present extracutaneous involvement [8].

Primary systemic ALCL can be categorized into ALK-positive or ALK-negative ALCL. *ALK* is located on chromosome 2p23. If ALCL is associated with a translocation involving *ALK*, the disease is classified as ALK-positive ALCL. Otherwise, it is classified as ALK-negative ALCL. ALK-negative ALCL is common in adults, whereas ALK-positive ALCL is common in young patients. The distinction between these forms is important because ALK-positive ALCL has a significantly better clinical

prognosis, with a 5-year overall survival of 80% compared to a 5-year overall survival of 48% in ALK-negative disease [4].

Considering the diversity of ALCL manifestations, histopathologic findings are important to establish a diagnosis. ALK-positive and -negative ALCLs are morphologically indistinguishable, requiring immunohistochemistry with monoclonal antibodies [9].

There is no consensus on the treatment of ALCL because of its rarity, especially for systemic ALCL with limited options available [9]. Based on retrospective studies and subgroup analyses of aggressive lymphoma or peripheral T-cell lymphomas, surgical resection with chemotherapy is the treatment of choice. For decades, the combination of cyclophosphamide, doxorubicin, vincristine, and prednisone with or without etoposide (the CHOP regimen) has been the standard option for systemic ALCL [10]. However, a new method with the BV-CHP regimen (brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone) was introduced by Fanale et al. [11]. Afterward, Horwitz et al. [12] performed a phase 3, randomized, double-blind, double-dummy, placebo-controlled, active-comparator, multicenter study to compare the effects of the BV-CHP regimen. They showed that the BV-CHP regimen is more effective than the CHOP regimen for treating patients with CD30-positive peripheral T-cell lymphoma. Furthermore, Al-Rohil et al. [13] reported a case with the loss of CD30 expression after treatment with brentuximab vedotin in an ALCL patient.

DISCUSSION

In our patient, the primary lesion was on the scalp. However, the initial appearance was suspected to be an epidermoid cyst, which is a dermal nodule with a typical central punctum. It often appears on face, scalp, neck, and trunk, but can form anywhere on the body [14]. Thus, it was difficult to suspect a malignant tumor. Despite diverse cutaneous manifestations of ALCL, there is no report on ALCL mimicking a cystic mass. Considering the prevalence of ALCL, an epidermoid cyst would be suspected first in a similar situation, with lymphoma being a later priority due to its rarity [2,15].

Moreover, the patient did not have typical manifestations of ALCL, such as lymphadenopathy or B symptoms. The only symptom was the severe headache associated with an infected epidermal cyst-like scalp skin lesion. Even on MRI, there was only a finding that we interpreted as the ruptured epidermoid cyst at first. However, as this was revised later, we also suspected malignancy. Therefore, making a definite diagnosis before surgery was difficult. Considering that the patient did not respond to antibiotics and complained of intense pain relative to inflammation severity, we aimed to perform surgical treatment quickly. During surgery, we eventually confirmed that the undefined lesion was not an epidermoid cyst but a malignancy, which was ALCL.

Further evaluation detected lung metastases in both lung fields. Therefore, this patient was classified as having primary systemic ALCL. Furthermore, as *ALK* gene rearrangement was not found on the pathological examination, the patient was diagnosed with primary systemic ALK-negative ALCL [4,8].

We performed surgical treatment not only to obtain a definite histological diagnosis but also to achieve symptomatic control due to the patient's intensive headaches. Since the patient had primary systemic ALK-negative ALCL, chemotherapy using the BV-CHP regimen was selected, considering its effectiveness over the CHOP regimen, after the wide excision of the cutaneous lesion. The patient did not complain of any other complications, including recurrence or severe headache [10,12].

Establishing a definite diagnosis was difficult in our case because this ALK-negative ALCL of the scalp mimicked an infected epidermal cyst. However, there are reports diagnosing a cutaneous mass as a malignant tumor; hence, we should remember the possibility of malignancy [16]. Based on our experience with this patient, we suggest that if an epidermal cyst-like mass does not respond to antibiotics and conventional dressing, considering the possibility of malignancy, including ALCL, which shows various cutaneous features and can mimic a cystic lesion, is necessary. Early detection of ALCL is important because it can affect the timing of treatment and, thus, prognosis. Therefore, preoperative evaluations including radiological methods, such as CT or MRI, are required to differentiate infectious disease from malignancy such as ALCL in our case.

NOTES

Conflict of interest

Han Koo Kim is an editorial board member of the journal but was not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflicts of interest relevant to this article were reported.

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Ethical approval

This report was approved by the Chung-Ang University Hospital Institutional Review Board (IRB approval number: 2404-023-19521).

Patient consent

Written informed consent was obtained from the patient for the publication of this case presentation and any accompanying images.

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