Specific cutaneous involvement of a mixed-type mature plasmacytoid dendritic cell tumor in chronic myelomonocytic leukemia

Kronik myelomonositer lösemide mikst tip matur plasmositoid dendritik hücreli tümörün spesifik kutanöz tutulumu

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Abstract

A 68-year-old man with chronic myelomonocytic leukemia (CMML), proven by bone marrow biopsy, presented to our clinic with pruritic indurated papules on his scalp, trunk and gluteal regions that have been present for two years. Purpuric, infiltrated miliary papules and petechiae were predominantly observed on his trunk, abdomen, back and legs. Histopathological examination revealed atypical monocytic cells with convoluted, irregularly shaped chromat with histiocytes. He was finally diagnosed with CMML with specific cutaneous involvement of mixed-type mature plasmacytoid dendritic cell tumor. Immunohistochemical tests showed positive CD4, CD56, and CD123 mature plasmacytoid dendritic cells, positive CD1a indeterminate dendritic cells, and positive CD68 monocytic cells. Mixed-type mature plasmacytoid dendritic cell tumor is known as a clinicopathological subtype of CMML that has the best prognosis, involving non-aggressive lesions. We conclude that identification of clinicopathologic subtypes in CMML will guide clinicians on chemotherapy protocols and estimation of survival.

Keywords: Chronic, dendritic cells, leukemia, myelomonocytic

Öz

Altmış sekiz yaşında kemik iliği biyopsisi ile tanısı doğrulanmış kronik myelomonositer lösemili (KMML) erkek hasta saçlı deride, gövde ve gluteal bölgelerde 2 yılı var olan pruritik, endure papüller nedeniyle başvurdu. Ağırlıklı olarak gövde, karın, bel ve bacak bölgelerinde yer alan purpurik, infiltrative miliary papules and peteşiler görüldü. Histopatolojik incelemede kıvrımlı, düzensiz şekilli kromatinli atipik monositik hücreler ve eşlik eden histiyositler görüldü. Hasta sonuç olarak KMML’nin matur plazmositoid dendritik hücreli tümör mikst tipinin spesifik deri tutulumu tanısı aldı. İmmünohistokimyasal testlerde CD4 (+), CD56 (+), CD123 (+) matur plazmositoid dendritik hücreler, CD1a (+) belirsiz dendritik hücreler, CD68 (+) monositik hücreler saptandı. Mikst tip matur plazmositoid dendritik hücreli tümör KMML’nin en iyi prognozu ve agresif olmayan lezyonların görülüğü klinikopatolojik alt tipi olarak bilinmektedir. KMML’nin klinikopatolojik alt tiplerinin belirlenmesinin klinik ve sağkalım tahmininde rol oynayacağını sonucuna vardık.

Anahtar Kelimeler: Kronik, dendritik hücreler, lösemi, myelomonositik

Introduction

Cutaneous involvement is seen in 6-10% of lymphocytic and myeloid leukemias and 10-50% of monocytic leukemia cases1. The differential diagnosis of a leukemic skin lesion located on the trunk includes a vast majority of cutaneous diseases, such as cutaneous malignancies, metastasis of visceral malignancies, Kaposi sarcoma, drug eruption, viral exanthem, syphilitic exanthem, pityriasis rosea, urticarial vasculitis, Sweet’s syndrome, cutaneous pseudolymphoma, and cutaneous lymphomas2. Chronic myelomonocytic leukemia (CMML) is characterized by an absolute monocytosis greater than 1x109/L in the peripheral blood that persists for at least three months. The diagnosis of CMML depends on
Case Report

A 68-year-old man presented to our clinic with pruritic, indurated cutaneous lesions on the scalp, trunk and gluteal regions that have been present for the last two years (Figure 1a). Laboratory findings were typical of leukemia and bone marrow biopsy confirmed the diagnosis of CMML. Immunohistochemical studies of the bone marrow biopsy material provided negative results for the diagnosis of CMML. Immunohistochemical studies of the bone marrow biopsy material provided negative results for the BCR-ABL1 gene and the JAK2 V617F mutation. Blood analysis revealed the presence of leukoerythroblastosis, an absolute monocytosis (2.3x10^9/L) and leukocytosis. Splenomegaly was also noted. The patient’s medical history included hypertension, for which he was taking diuretics. He reported that he was working in the barrel chemicals industry and had been in contact with a suspicious hair dye a few months earlier. He was started on hydroxyurea after consultation with the hematology department. The leukocytosis was reduced with remarkable clinical improvement also in cutaneous lesions. After a few months, he presented to our clinic again with widespread lesions all over his trunk, arms, abdomen and legs. Dermatological examination revealed new widespread, purpuric, infiltrated miliary papules, petechiae and palpable purpuric lesions predominantly located on his trunk, abdomen, lumbar region and posterior compartment of the legs (Figure 1b-1d). The patient’s condition did not improve after topical corticosteroid and anti-histaminic treatments. Considering a differential diagnosis of leukemic skin infiltration or leukocytoclastic vasculitis, punch biopsy material was taken from one of the papular lesions on the leg and trunk. Histopathological examination showed atypical monocytic cells with thin, convoluted, irregularly shaped chromatin and nucleus accompanied by reactive lymphocytes, eosinophils and histiocytes (Figure 2a). Vascular proliferation and extravasated erythrocytes were also noted.

In immunochemical analysis, we first examined CD4 as a T-cell marker and CD68 as a monocytic cell marker. The presence of plasmacytoid dendritic cell markers, such as CD123, TCL1 and CD303 and indeterminate dendritic cells markers such as CD56, CD1a, Langerin, and S100 were also analyzed. Positive CD4, CD56, CD303 and CD123 mature plasmacytoid dendritic cells (MPDC), CD1a indeterminate dendritic cells, and CD68 monocytic cells were seen (Figure 2b). S100 was positive, but Langerin was negative. The coexistence of CD56, CD303, TCL1 and CD123 MPDCs with CD1a indeterminate dendritic cells was notable. The patient was finally diagnosed with CMML with specific cutaneous involvement of mixed-form MPDC tumor (MPDCT). Six months of hydroxyurea treatment resulted in remarkable improvement in skin lesions, and the pruritus almost completely resolved.

Discussion

Cutaneous involvement in leukemia is mostly seen in the acute myeloid and chronic lymphocytic forms. The prevalence is 2.1 to 30% and independent from factors, such as age and sex. The diagnosis of leukemia cutis is often made either simultaneously with or after the diagnosis of systemic leukemia. While 55-77% of patients with leukemia cutis have already been diagnosed with leukemia, 22-38% of cases present with simultaneous onset of systemic symptoms and cutaneous findings. In approximately 7% of cases, cutaneous lesions are seen many years before the manifestation of the disease. Leukemia cutis often presents with solitary or disseminated lesions on the head and neck or the trunk. Generalized distribution can also be seen, especially in acute leukemia. In differential diagnosis, sarcoidosis, acute febrile neutrophilic dermatosis, cutaneous B-cell lymphoma, cutaneous positive CD30 (Ki-1) anaplastic large cell lymphoma, pseudolymphoma, and urticarial vasculitis should be considered and eliminated. The specific cutaneous lesions of CMML are seen very rarely with a prevalence of 10%. In some cases, CMML can be transformed to acute myeloid leukemia that is also accompanied by the lesions of myeloid leukemia cutis.
and myeloid cells. Bone marrow cytology assessment has revealed a rare distinct neoplasm, cutaneous indeterminate dendritic cell histiocytosis (ICDN), have been described in the literature. IDCN was shown to present as a mostly cutaneous proliferation of histiocytoid cells, predominantly in adults. As characteristic for IDCN, the patients were found to be positive for CD1a, negative for Langerin, and variably positive for S100, and the condition was strongly associated with the presence of a second hematopoietic malignancy.

In the current case, the patient was diagnosed with the mixed form of MPDCT based on the positive CD123, TCL1, CD303 and CD56, CD1a, and S100 findings according to the presence of plasmacytoid dendritic cell population. Among all subtypes, IDCN has the worst prognosis.

To date, only one patient with IDCN accompanied by Langerhans cells was reported to have IDCN with involvement of both skin and myeloid cells. Bone marrow cytology assessment has revealed that the dendritic cell-like population constituted 30% of the total cell count and immunophenotyping has shown the plasmacytoid dendritic cell population. Among all subtypes, IDCN has the worst prognosis.

In this paper, we presented a case of CMML involving the mixed form of IDCN, with a three-year history of stable CMML has been developed to develop splenomegaly and acute onset of skin lesions. Histopathological examination revealed a diffuse infiltrate of histiocytic cells morphologically resembling Langerhans-type cells (lacking histopathological features of frank atypia) and the immunophenotype of an indeterminate cell histiocytosis (positive S100, CD1a and Langerin). Furthermore, two additional cases of a rare distinct neoplasm, cutaneous indeterminate dendritic cell neoplasm (ICDN), have been described in the literature. ICDN was shown to present as a mostly cutaneous proliferation of histiocytoid cells, predominantly in adults. As characteristic for ICDN, the patients

Table 1. Differential diagnosis between different histopathological subtypes of chronic myelomonocytic leukemia

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Clinical presentation</th>
<th>Localization</th>
<th>Mean age (years)</th>
<th>Male/female ratio</th>
<th>Immunohistopathological findings</th>
<th>Prognosis</th>
<th>Survival time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myelomonocytic cell tumor</td>
<td>Multiple papules, papulonodular lesions</td>
<td>Generalized</td>
<td>71.5</td>
<td>5/1</td>
<td>CD68 (+), MPO (+/-), CD33 (+/-), CD13 (+/-), but the dendritic cell markers (CD1a, Langerin, S100, CD123, CD303 and TCL1) always negative</td>
<td>Good prognosis</td>
<td>13.9 months</td>
</tr>
<tr>
<td>Mature plasmacytoid dendritic cell tumor</td>
<td>Diffuse erythematous or maculopapular lesions without tumoral tissue or ulceration</td>
<td>Scalp/trunk</td>
<td>76.5</td>
<td>15/1</td>
<td>Positive dendritic cell markers CD123, TCL1 and CD303 but negative CD56, CD1a and S100</td>
<td>Moderate prognosis</td>
<td>20 months</td>
</tr>
<tr>
<td>Mature plasmacytoid dendritic cell tumor</td>
<td>Ucerated tumors on the scalp, infiltrated plaques, disseminated purplish papules and nodules</td>
<td>Generalized</td>
<td>71.5</td>
<td>3/1</td>
<td>Positive CD4, CD56, CD123 and TCL1 (+), and negative CD1a and S100</td>
<td>Aggressive</td>
<td>10.4</td>
</tr>
<tr>
<td>Blastic plasmacytoid dendritic cell tumor</td>
<td>Solitary or multiple nodular lesions, ulcerated tumoral lesions</td>
<td>Generalized</td>
<td>65</td>
<td>1/1</td>
<td>Positive CD68 and/or MPO, CD1a, and S100</td>
<td>The worst prognosis</td>
<td>6.8 months</td>
</tr>
</tbody>
</table>

MPO: Myeloperoxidase
Ethics

Informed Consent: Informed consent form was obtained from the patient.

Peer-review: External and internal peer-reviewed.

Authorship Contributions
Surgical and Medical Practices: P.Ü., Concept: P.Ü., Design: A.B.,
Data Collection or Processing: P.Ü., C.O., Analysis or Interpretation: P.Ü.,
A.B., M.O., C.D., Literature Search: P.Ü., Writing: P.Ü.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received
no financial support.

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