Alopecia Areata as a Manifestation of Systemic Lymphoma: Report of Two Cases

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Established Fact

- Alopecia areata (AA) usually affects young and generally healthy individuals, and first appearance in older subjects is considered uncommon.

Novel Insights

- When rapidly progressing AA appears for the first time in patients older than 40, the possibility of a malignancy-related phenomenon should be considered in the right clinical context.
- The development of AA in patients with systemic lymphoma highlights the importance of circulating lymphocytes in the induction of hair loss.

Key Words

Alopecia areata · Alopecia · Hair · Lymphoma · Cancer · Hematology

Abstract

Alopecia areata is a common autoimmune disorder leading to hair loss. It usually affects individuals under the age of 40, and first appearance in older subjects is considered uncommon. Here, we report 2 cases of rapidly progressing alopecia areata, which appeared for the first time in adults. Patient 1 had alopecia universalis, which preceded the identification of hepatosplenic T-cell lymphoma, a rare form of lymphoma. Patient 2 suffered from the ophiasis type of alopecia areata, presenting for the first time following chemotherapy for non-Hodgkin B-cell lymphoma. These 2 cases highlight the need to screen for malignancies in patients who present with rapidly progressing alopecia areata for the first time after the age of 40.

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Introduction

Alopecia areata (AA) is a common autoimmune disease, which affects the hair follicles and leads to hair loss, either in a patchy pattern, affecting the whole scalp (alopecia totalis) or the whole body hair [alopecia universalis (AU)]. It is most common in individuals under the age of 30, with less than 20% of the patients developing the disease after 40 years of age [1]. While it is obvious that the disorder has a strong genetic basis [2], its exact pathogenesis is still not entirely clear, and the precise triggers leading to immune imbalance and loss of hair are most of the time obscure [3]. Only a limited number of case reports have described the development of AA in association with malignant disorders, and it has never been described in patients with systemic T-cell lymphomas.

Here, we describe 2 cases of AA developing in association with a hematological malignancy: one of them man-

Fig. 1. **a** Complete hair loss on the scalp of a patient with hepatosplenic T-cell lymphoma, accompanied by patches of hypopigmentation on the parietotemporal areas of the scalp. **b** Severe nail deformity, including onycholysis, onychorrhexis and leukonychia.

Fig. 2. Loss of hair on the occipital scalp of a patient previously treated with chemotherapy for a non-Hodgkin lymphoma.

ifesting as a rapidly progressing AU in a patient with hepatosplenic T-cell lymphoma, and the other appearing after chemotherapy in a patient with a non-Hodgkin B-cell lymphoma.

Case Reports

Patient 1

Patient 1 was a 42-year-old male who was generally healthy with no regular medications. The patient developed hair loss on the parietotemporal areas of the scalp. He applied an irritating cream, which he received without prescription, on the areas of hair loss on both sides of the scalp. This treatment did not lead to hair regrowth but resulted in loss of pigment on the areas where the irritating compound was applied. The hair loss continued to spread, resulting in complete loss of hair within 3 months. In addition, the patient developed severe deformities of the toenails and fingernails. Three months after the patient had identified the hair loss he was admitted due to fever and diagnosed as suffering from severe pancytopenia. Computed tomography examination demonstrated enlarged spleen (27.5 cm) and enlarged liver (22 cm). Bone marrow biopsy revealed T-cell lymphoproliferative disease with an intrasinusoidal growth pattern. The patient underwent splenectomy, and histopathological examination of the spleen was consistent with hepatosplenic T-cell lymphoma. Perioperative liver biopsy confirmed liver involvement.

On examination, the patient had complete loss of hair on the scalp and body, including eyelashes and eyebrows (fig. 1a). He had patches of hypopigmentation symmetrically located on the parietotemporal scalp and on the occipital scalp posterior to the ears (fig. 1a). Nail examination revealed severe onychodystrophy of all 20 nails, including onycholysis, onychorrhexis and leukonychia (fig. 1b). Skin biopsy taken from the parietotemporal scalp was consistent with AA.

Patient 2

Patient 2 was a 69-year-old female who was diagnosed as suffering from non-Hodgkin B-cell lymphoma in March 2014. The patient underwent splenectomy and was treated with rituximab

plus cyclophosphamide, doxorubicin, vincristine and prednisone (R-CHOP). Therapy was completed in December 2014. Three months later, the patient noticed hair loss on her occipital scalp, with a reticular pattern that coalesced to an ophiasis pattern within 3 weeks. On examination, the patient had nonscarring hair loss on the occipital scalp, forming an ophiasis pattern of hair loss (fig. 2). No hair loss was observed in other areas of the body or scalp. A skin biopsy taken from the occipital scalp was consistent with AA.

Discussion

Here, we present 2 cases of AA appearing in association with hematological malignancies. Hepatosplenic T-cell lymphoma is a rare and highly aggressive type of lymphoma, mostly of the gamma-delta type [4]. Gamma-delta T-cell lymphocytes are expressed in very small amounts in the human hair follicle, and are therefore not considered to play a major role in securing the immune privilege [5]. However, it is reasonable to assume that the clonal T-cell proliferation seen in lymphomas can lead to immune imbalance and propagation of an immune attack on the hair follicle [6]. To the best of our knowledge, Patient 1 is the first reported case of AA associated with hepatosplenic T-cell lymphoma and systemic T-cell lymphomas in general. Patient 2 experienced the onset of AA only after the completion of chemotherapy. It is well established that AA can flare after tapering of systemic steroid treatment [1]. Since the R-CHOP protocol includes administration of prednisone, it is plausible that her AA was masked by the treatment, only to be revealed following its cessation.

Patient 1 presented to our attention with several patches of hypopigmentation. These lesions were attributed in the beginning to concurrent vitiligo, which is known to appear in association with AA, and sometimes even in the same location as the hair loss [7]. However, further enquiry revealed that the pigment loss developed specifically in the locations where a strong irritating local treat-

ment was applied. Therefore, the loss of pigment could be attributed to postinflammatory hypopigmentation [8]. This phenomenon should be taken into consideration when examining AA patients, since induction of inflammation by irritating substances is a well-established treatment modality for AA [9]. Nevertheless, the possibility of vitiligo cannot be ruled out, since vitiligo has been shown to develop, although rarely, following local immunotherapy [10].

In both cases presented in the current report, the hair loss appeared in people older than 40 and presented as a rapidly progressing disease, manifesting as the more recalcitrant types of AA, either as ophiasis in Patient 2 or as AU with significant involvement of the nails in Patient 1. It should be taken into consideration that the severity of AA when first appearing in adults is usually mild in nature, and more than half of the adult patients with AA have less than 10% involvement of the scalp [11]. Indeed, rapid development of AA has been previously reported in cases of AA manifesting as a paraneoplastic phenomenon [12]. Furthermore, in a cohort of 73 patients with first onset of AA at the age of 50 years and above, 8% had a history of malignancy before or after the onset of AA [11]. Taken together, these reports raise the question of whether or not patients older than 40 who present for the first time with a rapidly progressing AA should be screened for malignancy with proper blood and imaging tests. This assumption needs to be validated by additional studies.

Statement of Ethics

A written consent was obtained from Patient 2. Unfortunately, Patient 1 passed away.

Disclosure Statement

The authors have no conflicts of interest to disclose.

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