

CD30 (+) ANAPLASTIC LARGE CELL LYMPHOMA PRECEDED BY ACQUIRED ICHTHYOSIS

EDİNSEL İKTIYOZU İZLEYEN CD30 (+) ANAPLASTİK BÜYÜK HÜCRELİ LENFOMA

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ABSTRACT

Primary cutaneous CD30 (+) anaplastic large cell lymphoma (PCALCL) and lymphomatoid papulosis (LyP) form the spectrum of primary cutaneous CD30 (+) lymphoproliferative disorders with favourable prognosis. Spontaneous regression of the skin lesions is characteristic of LyP, but a minority of LyP patients may progress to cutaneous anaplastic large cell lymphoma (CALCL) in which skin lesions longer regress and extracutaneous dissemination often occurs.

Acquired ichthyosis is a known paraneoplastic sign of lymphoproliferative malignancies with histopathologic findings that are nonspecific. Although Hodgkin's lymphoma are associated with acquired ichthyosis, only few cases of PCALCL have been reported to be associated with this condition.

In this article, we report an unusual case of ALCL in a 27-year-old man was preceded by acquired ichthyosis.

Key words: Acquired ichthyosis, CD30 (+) anaplastic lymphoma, treatment

ÖZET

Primer kutanöz CD30 (+) anaplastik büyük hücreli lenfoma (PCALCL) ve lenfomatoid papülozis (LyP) primer kutanöz CD30 (+) lenfoproliferatif hastalıkların iyi gidişli formlarıdır. Spontan olarak deri lezyonlarının gerilemesi LyP için karakteristiktir, ama olguların kutanöz anaplastik büyük hücreli lenfomaya (CALCL) gidiş gösteren küçük bir kısmında deri lezyonları daha uzun sürede gerilediği gibi ekstrakutanöz yayılım da sıklıkla görülebilmektedir. Edinsel iktiyoz lenfoproliferatif tümörlerin paraneoplastik bulgusu olarak bilinir. Hodgkin lenfoması ile edinsel iktiyoz birlikte görülebilmesine rağmen, literatürde çok az sayıdaki olguda PCALCL'nin edinsel iktiyozla birlikteliği bildirilmiştir.

Bu sunumda, ALCL'ye edinsel iktiyozun eşlik ettiği 27 yaşındaki erkek olgu sunulmaktadır.

Anahtar kelimeler: Edinsel iktiyoz, CD30(+) anaplastik lenfoma, tedavi

INTRODUCTION

The CD30 antigen is a type 1 transmembrane glycoprotein. It is commonly expressed on activated B and T cells; however, certain lymphoproliferative disorders express the CD30 antigen as well. Primary CD30 (+) cutaneous T-cell lymphomas (CTCLs) represent a spectrum of non-Hodgkin's lymphomas. Other lymphoproliferative disorders that may express the CD30 antigen include large cell transformation of mycosis fungoides (MF), systemic ALCL, cutaneous NK/T-cell lymphoma, and Hodgkin's disease (3,4).

PCALCL and LyP are characterized by CD30 (+) large atypical cells predominantly of T-cell origin. There are clear differ-

ences between the clinical presentation and histologic pattern in these two diseases, but both diseases are characterized by long benign course (9).

Acquired ichthyosis usually begins in adult life and constitutes a cutaneous sign pointing toward a wide range of underlying causes, mostly malignancies. It has also been reported, although rarely, in association with lymphoproliferative disorders of the skin, including LyP, CD30 (+) ALCL, and secondary to MF (1,2,6).

A rare case of CD30(+) ALCL associated with acquired ichthyosis regressing totally after chemotherapy is presented here.

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CASE

A 27 years-old male patient was admitted to our out-patient clinic with the complaint of multiple firm nodules on his right calf. The lesions appeared four months ago and progressed. History revealed that he had ichthyosis since he was ten years-old. In addition, he described chronic, recurrent papulonecrotic or papulonodular lesions for the last seven years. He also described that these lesions were self healing with atrophic scars in a month.

He had received no medical or surgical therapy. His parents were not relatives and there was no history of ichthyosis in the family.

On dermatologic examination, multiple pinkish-purple colored, firm nodules were observed on his right calf (Figure 1). Some of the nodules showed ulceration in the center. Generalized acquired ichthyosis (Figure 2) and multiple hyperpigmented and atrophic macules have also been noted (Figure 3). Physical examination was within normal limits. Laboratory tests and chest x-ray were normal. Bone marrow biopsy, peripheral blood count and morphology, CT examination of the chest and abdomen showed normal results.

Histopatologic examination of a nodular lesion demonstrated diffuse proliferation of large sized atypical lymphoid cells in the dermis. Most of these cells displayed irregular and large nuclei with prominent nucleoli, and large cytoplasm (Figure 4). Immunphenotyping using a large antibody panel revealed that large neoplastic cells were positive for CD 30 (Figure 5) and epithelial membrane antigen (EMA) antibodies. They were negative for CD 20, CD 68, and ALCL tyrosine kinase (ALK-1). CD 3 was positive only in a minority of the neoplastic cells. According to the findings diagnosis of the CD 30 (+) CALCL was made.

Biopsy of the ichthyosiform skin revealed lamellar orthokeratosis, acantosis, and melanophages in upper dermis which was compatible with acquired ichthyosis.

The patient was treated with low-dose methotrexate (12.5

mg/week) for three weeks. Lesions regressed totally (Fig 6). On the follow-up of 37 months no new lesion was detected, but ichthyosiform appearance persisted.

DISCUSSION

The spectrum of CD 30 (+) cutaneous lymphoproliferative disorders includes LyP, PCALCL and borderline CD 30 (+) lesions (1,2,5). Prognostic subsets have been difficult to identify due to lack of uniform clinicopathologic criteria. Borderline cases where histologic features are LyP-like, but clinically behave as lymphoma or cases where histologic features are consistent with PCALCL, but clinically behave as LyP (3,4,7).

LyP's primary lesions are typically an erythematous, dome-shaped papule or nodule that spontaneously regressed over a few weeks with atrophy, hyperpigmentation, or both. PCALCL's primary lesions are typically larger than LyP's. Lesions may undergo spontaneous regression as seen with LyP. A minority of LyP patients (10-20%) progress to ALCL (3,8). In our case, the atrophic scars and necrotic self-healing lesions are suggestive of LyP, but histopathologic findings of these lesions could not be shown. Therefore, it is not clear that, whether the lesions recurring intermittently and regressing spontaneously for 7 years are LyP or not and that they progressed to ALCL.

Characteristics that distinguish a subset of systemic ALCL from PCALCL include more frequent expression of ALK-1 protein, and EMA (3,7). Despite the fact that EMA positivity can be suggestive of systemic disease, we were not able to demonstrate any systemic disease in our case.

Acquired ichthyosis has been described in lymphoproliferative disorder, such as multiple myeloma, LyP, and Hodgkin's disease(1,2,6). Reviewing the literature, we found that only a few cases of ALCL which have been described to be associated with acquired ichthyosis. Although transforming growth factor β produced by tumor cells has been implicated in the pathogenesis of these hyperproliferative paraneoplastic skin



Figure 1. Appearance of the patient's calf on admission.



Figure 2. Note the generalized acquired ichthyosis on the thigh.



Figure 3. Note the hyperpigmented and atrophic macule on the distal forearm.

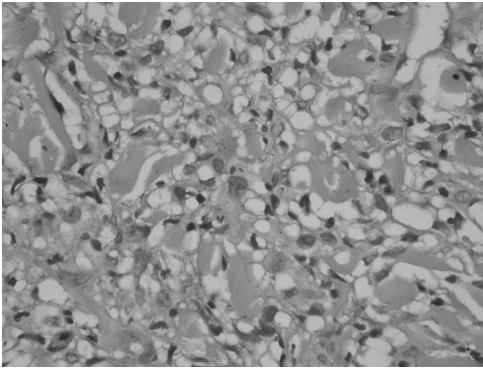


Figure 4. Neoplastic infiltration in the deep dermis. Large atypical cells with pleomorphic nuclei and abundant cytoplasm are seen between collagen fibers. A reactive small lymphoid population is also present (H.E. x 400).

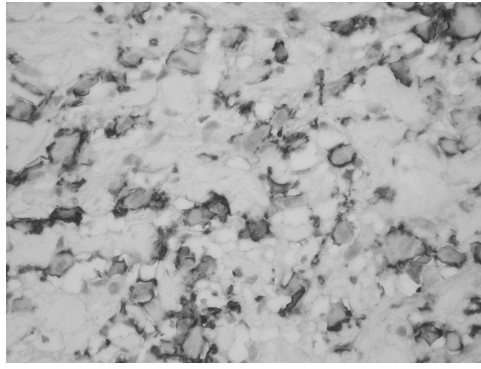


Figure 5. Neoplastic cells showed membrane positivity for CD 30 (anti-CD 30 x400).



Figure 6. Appearance of the regressed lesions after methotrexate administration.

lesions, the relationship between acquired ichthyosis and lymphoproliferative diseases still remains to be explained (6,7).

Acquired ichthyosis may appear either before or at the same time with occurrence of lymphoma lesions and it has been reported that the acquired ichthyosis regresses with lymphoma treatment in most cases (1). However in our case, contrast to the literature PCALCL was regressed completely with therapy, but ichthyosis persisted.

Our patient had generalized ichthyosis since he was 10 years-old. Therefore, ichthyosis in this case could be described definitely as either acquired ichthyosis or as late onset congenital ichthyosis since both forms of ichthyosis show similar histological characteristics.

In conclusion, we consider that this case of PCALCL progressed from LyP and was preceded by acquired ichthyosis. The link between acquired ichthyosis and ALCL seen in the presented case is worth considering.

REFERENCES

1. Hodak E, Amitay I, Feinmesser M, Aviram A, David M. Ichthyosiform mycosis fungoides: An atypical variant of cutaneous T-cell lymphoma. *J Am Acad Dermatol* 2004; 50:368-74
2. Kato N, Yasukawa K, Kimura K, Yoshida K. Anaplastic large-cell lymphoma associated with acquired ichthyosis. *J Am Acad Dermatol* 2000; 42(5 Pt 2):914-20.
3. Liu HL, Hoppe RT, Kohler S, Harvell JD, Reddy S, Kim YH. CD 30 + cutaneous lymphoproliferative disorders: The Stanford's experience in lymphomatoid papulosis and primary cutaneous anaplastic large cell lymphoma. *J Am Acad Dermatol* 2003; 49:1049-58.
4. Mori M, Manuelli C, Pimpinelli N, Mavilia C, Maggi E, Santucci M, Bianchi B, Cappugi P, Gianotti B, Kadin ME. CD 30-CD 30 ligand interaction in primary cutaneous CD 30 (+) T-cell lymphomas: A clue to the pathophysiology of clinical regression. *Blood* 1999; 94:3077-83.
5. Rabhi M, Ennibi K, Harket A, Al Bouzidi A, Labraimi A, Charari J, Toloune F. Acquired ichthyosis disclosing non-Hodgkin's malignant lymphoma. *Intern Med* 2007; 46:397-9.
6. Rizos E, Milionis HJ, Pavlidis N, Elisaf MS. Acquired ichthyosis: A paraneoplastic skin manifestation of Hodgkin's disease. *Lancet Oncol* 2002; 3:727.
7. Sasaki K, Sugaya M, Fujita H, Takeuchi K, Torii H, Asahina A, Tamaki K. A case of primary cutaneous anaplastic large cell lymphoma with variant anaplastic lymphoma kinase translocation. *Br J Dermatol* 2004; 150:1202-7.
8. Schiemann WP, Pfeifer WM, Levi E, Kadin ME, Lodish HF. A deletion in the gene for transforming cutaneous T-cell lymphoma. *Blood* 1999; 94:2854-61.
9. Tomaszewski MM, Lupton GP, Krishnan J, May DL. A comparison of clinical, morphological and immunohistochemical features of lymphomatoid papulosis and primary cutaneous CD30 (Ki-1)-positive anaplastic large cell lymphoma. *J Cutan Pathol* 1995; 22:310-8.