

Folliculotropic Mycosis Fungoides Associated with Autoimmune Hepatitis

Dear Editor,

the association between lymphomas and autoimmune manifestations, as well as the prevalence of the cases of coexistent lymphomas and autoimmune conditions, has not been completely established (1-3). Since cutaneous T-cell lymphoma (CTCL) cases are rare, any hypothesis can only be based on case reports or small case series.

We present the case of a male patient with folliculotropic mycosis fungoides (FMF) and synchronous autoimmune hepatitis (AIH) with extremely high levels of cancer antigen 19-9 (CA 19-9). The patient was under the supervision of a multidisciplinary team consisting of dermatologists, hepatologists, and hematologists. The patient died 15 months after the diagnoses of FMF and AIH were established and 3.5 years after the first skin changes. Based on our knowledge and search of medical databases, this is the first case of AIH in a patient with CTCL, i.e. with MF.

A 53-year-old male patient was admitted to our Dermatology Clinic in September 2014 after being

briefly treated with acitretin. During hospitalization, he was diagnosed with FMF, autoimmune hepatitis, and newly developed diabetes mellitus. At the time of hospital admission, about 70 percent of the surface of the skin was affected, infiltrated with numerous cysts on the face, neck, and upper thorax. The patient also presented with alopecia affecting most of the scalp, loss of eyebrows and eyelashes (Figure 1), and complained of intensive itching. The clinical presentation suggested the diagnosis of FMF, which was later confirmed based on histological (Figure 2) and immunohistochemical (Figure 3) findings. The histochemical staining method PAS-Alcian did not reveal mucin deposits. Immunohistochemical findings revealed tumor cells to show aberrant T-immunophenotypes - CD3⁺, CD2⁺, CD5⁻, CD7⁻, CD4⁺, CD8⁻, CD30⁻. Due to elevated serum conjugated bilirubin and extremely high levels of hepatocellular and cholestatic liver enzymes, the patient was transferred to the Gastroenterology Department. Diagnosis of AIH



Figure 1. Clinical findings: cystic and comedo-like lesions on the head and neck, partial loss of hair, eyebrows, and lashes, yellow sclera

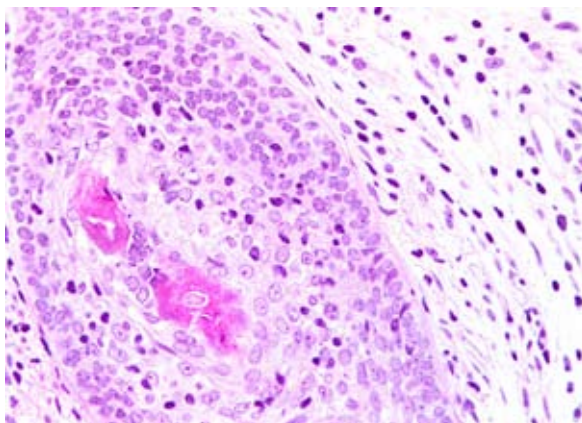


Figure 2. Histological features: folliculotropic infiltrate and intrafollicular collection of atypical lymphocytes (hematoxylin and eosin, original magnification $\times 40$).

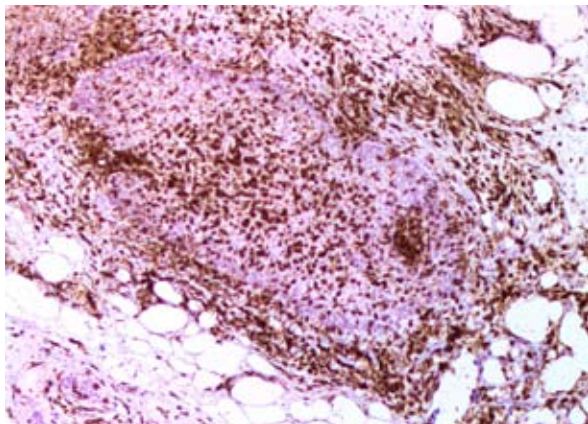


Figure 3. Immunohistochemical features: tumor cells show folliculotropism with diffuse expression of CD4 (immunohistochemistry CD4, original magnification $\times 10$)

was established based on the liver biopsy (highly active autoimmune hepatitis) and the exclusion of viral etiology, drug-induced hepatotoxicity, and inherited metabolic disorders of the liver. CA 19-9 level was extremely high (4475.0; RR < 37.0 $\mu\text{g/L}$). In March 2015, CA 19-9 decreased to 365.3. In April 2015, erythroderma and small isolated tumors on the trunk and extremities developed. The patient was treated with RE-PUVA and radio-therapy. In June 2015, due to systemic symptoms, the patient was started on PUVA with IFN α . In November 2015, erythroderma persisted together with larger and ulcerated tumors. The patient was treated at the Hematological Department with two cycles of cyclophosphamide, vincristine, doxorubicin, and methylprednisolone. From March 2015, the patient was continuously treated with ursodeoxycholic acid, prednisolone, azathioprine, analog insulin, and allopurinol. MSCT revealed lymphoma infiltrates in the liver, spleen, and peritoneum (gross tumors). The immunophenotypic analysis of the cells in ascites revealed atypical lymphocytes with convoluted nuclei - LCA $^{+}$, CD3 $^{+}$, CD20 $^{-}$. The patient died in December 2015 due to sepsis with febrile neutropenia. Before death, he suffered from candidiasis and toxic liver damage due to fluconazole.

FMF is an aggressive MF variant with infiltration of lymph nodes, visceral involvement at an earlier stage, and decreased life expectancy (4). Autoimmune hepatitis (AIH) is still an unclear progressive liver disease of unknown etiology which features hypergammaglobulinemia, detectable autoantibodies, and interface hepatitis (5). Being exposed to xenobiotic (acitretin) with consequent liver damage could lead to the formation of self-antigens to which

the patient's immune system might have sensitized, and the autoimmune attack continued (6). Slightly elevated CA 19-9 levels in autoimmune hepatitis were reported by other authors (7-9). It should be noted that the liver involvement with atypical lymphocytes can be diffuse without any detectable nodules on a CT scan (4). Soluble liver antigen and liver-pancreas antibodies, together with CA 19-9, need to be implemented as routine diagnostic tools to rationalize the usage of tumor markers in day-to-day practice as well in diagnosis of AIH (10).

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