CLINICAL IMAGE

Coexistence of ataxia-telangiectasia syndrome and idiopathic CD4 lymphopenia: diagnostic difficulties in a complex immunodeficiency case report

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We present a case of a 28-year-old woman admitted to the immunology department with suspected immunodeficiency.

The patient was diagnosed with cerebral palsy at the age of 7 but no early childhood medical documentation was available. The previous medical history included finger osteitis, chronic skin ulcerations, bone necrosis, and limb deformation (FIGURE 1A). The whole skin nodule in histopathology demonstrated granulomatous inflammation "around the foreign body" type. Immunological investigations revealed B- and $CD4^+$ T-cell depletion (FIGURE 1B) and decreased IgG2 and IgG4 concentrations. Cases of early deaths were reported in the closest family history. Based on these findings, a complex immunodeficiency syndrome with pyoderma gangrenosum was diagnosed and immunoglobulin supplementation (20–30 g every 4 weeks) was initiated together with oral steroids. Between 2014 and 2017 the skin ulcerations were resolving (FIGURE 1C).

In 2017 generalized lymphadenopathy occurred. Following the suspicion of a lymphoproliferative disorder, a detailed early childhood history was retaken. The patient's mother pointed to the start of the gait abnormalities at the age of 3 years; the cerebral palsy was diagnosed in the school period, so the motility problems were not further investigated even though they continuously progressed. Detailed neurological examination revealed dysarthria, cerebellar ataxia in the right limbs, ataxic gait, and eye telangiectasias (FIGURE 1D). Genetic studies revealed 1 metaphase with t(7,14)(q35,g11) mutation in karyotype testing, cell damage percentage of 31% in bleomycin test, and a deletion in the *ATM* gene confirming ataxia-telangiectasia syndrome (FIGURE 1E). However, next generation genome sequencing also documented a deletion in the *UNC119* gene (p.Gly22Val) resulting in reading frame alteration and leading to idiopathic $CD4^+$ lymphopenia syndrome. The neck lymph node histopathology demonstrated non-Hodgkin peripheral T-cell lymphoma; some B-immunoblasts were positive for Epstein–Barr virus RNA (FIGURE 1F). The patient received the CHOP chemotherapy regimen with reduced vincristine dosage due to the worsening of ataxia. The final evaluation of the response to treatment revealed a complete remission of the disease. Autologous stem cell transplantation was not considered due to a chronic bacterial infection of the wounds. One year later the disease relapsed. Due to the active infection of limb ulcers, only palliative oral chemotherapy was recommended with cyclophosphamide and prednisone. Five months later the patient died.

Ataxia-telangiectasia (A-T) is an autosomal recessive disorder caused by mutations in the *ATM* gene.[1] Its product coordinates the cellular mechanisms of DNA double strand repair.[2] Prevalence of A-T is estimated at 1:40 000 to 1:100 000 and it typically presents with progressive ataxia, variable immunodeficiencies, such as T- or B-cell lymphopenia, hypogammaglobulinemia or defective cell-mediated immunity, oculocutaneous telangiectasia, radiosensitivity, and increased incidence of cancer.[3-5]

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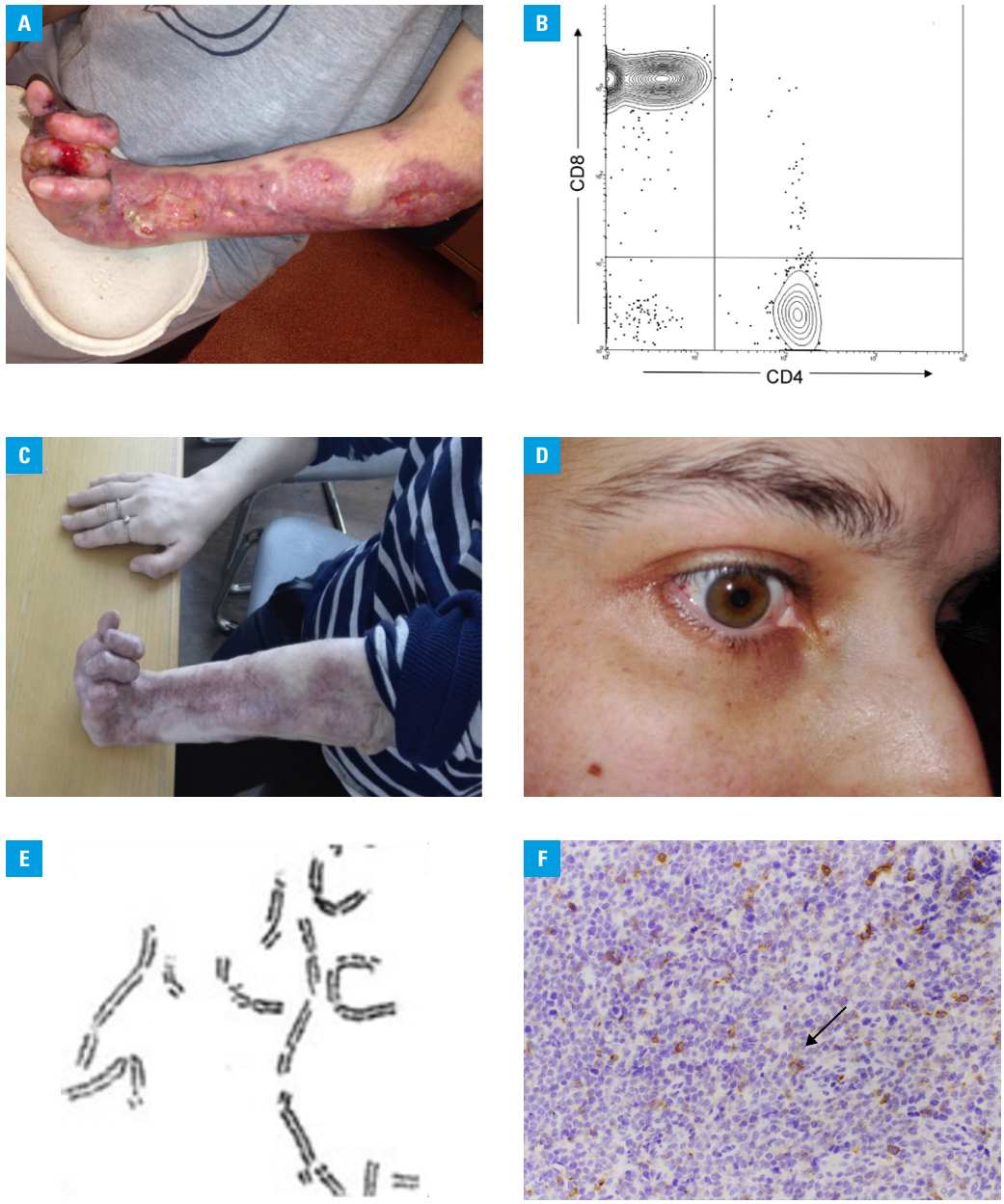

FIGURE 1 **A** – active skin ulcerations; **B** – lymphocyte flow cytometry showing a decreased number of $CD4^+$ T cells; **C** – cured skin ulcerations; **D** – eye telangiectasias; **E** – bleomycin-induced DNA breaks; **F** – CD30 staining showing few scattered positive cells, some with Hodgkin and Reed/Sternberg-like morphology (arrow; magnification × 40)

The first symptoms of A-T occur in early childhood, so this diagnosis should be considered as the gait or hand coordination impairment occurs in preschoolers. Cerebral palsy is the main mimic at the initial stage of the disease but telangiectasia, normal mental development, and a broad spectrum of immunodeficiencies might be significant diagnostic indicators. An early diagnosis is essential since X-ray exposure avoidance is critical in neoplastic prophylaxis. Presenting skin lesions is not typical for A-T, and referred rather to the idiopathic $CD4^+$ T-cell lymphopenia in that patient.

ARTICLE INFORMATION

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