***Case report***

**Epidermodysplasia Verruciformis Revealing a Late Onset Combined Immunodeficiency (LOCID)**

## ABSTRACT :

We report a rare association of Late Onset Combined Immunodeficiency (LOCID) with epidermodysplasia verruciformis (EV) in a 23-year-old Moroccan woman. At age 7, the patient developed thousands of small verrucae and experienced recurrent respiratory and gastrointestinal infections. A skin biopsy confirmed the diagnosis of EV. Immunological evaluation revealed low absolute counts of CD3 T cells, CD3+CD4, CD3+CD8, CD19, and CD16+CD56, with persistent lymphopenia (390-940 cells/mm³). Hypogammaglobulinemia was ruled out. The diagnosis of EV secondary to LOCID was confirmed, and the patient is currently on a monthly immunoglobulin transfusion program with favorable clinical outcomes. LOCID, a subset of Variable Common Immune Deficiency (VCID), is characterized by defects in antibody production and profound CD4 T-cell lymphopenia, distinguishing it from Common Variable Immune Deficiency (CVID). Systematic T-cell phenotyping may enhance diagnostic accuracy and therapeutic strategies, providing critical insights for genetic diagnosis and management of associated infections.

**KEYWORDS :** Late Onset Combined Immunodeficiency, Epidermodysplasia verruciformis, immunoglobulin therapy, immunological disorders.

**Introduction**

Epidermodysplasia verruciformis (EV) is a rare genetic condition characterized by an abnormal susceptibility to human papillomavirus (HPV) infections, leading to widespread skin lesions resembling warts. Here, we report a unique case linking EV to a Late Onset Combined Immunodeficiency (LOCID) in a 23-year-old woman.

This association is rare and highlights the complexities of immunological disorders and their manifestations.

**Case Presentation**

A 23-year-old moroccan woman was diagnosed with Late Onset Combined Immunodeficiencie (LOCID), when at age of 7 years old, she presented thousands of multiple small verrucae disisiminated over her body, and continueted to develop repeated respiratory and gastro-intestinal infections. A skin biopsy was consistent with epidermodysplasia verruciformis.

The patient was issued from a consanguineous marriage, her parents were cousins. Both of them, were alive and well. The patient had five siblings, who were healthy.

The blood tests showed a low obsolute CD3 T cell, CD3+CD4, CD3+CD8, CD19 and CD16+CD56. The biological evolution was marked by the installation of a constant lymphopenia varying between 390 and 940 cells/mm3. Hypogammaglobulinaemia was not found on two serum protein electrophoreses. In summary of these clinical and biological data, the diagnosis of an EV secondary to a LOCID was confirmed. The patient is on a monthly Ig transfusion program with a good clinical evolution thereafter.



**Figure 1**: The patient with thousands of small verrucae

**Discussion**

Late Onset Combined Immune Deficiency (LOCID) is a subset of Variable Common Immune Deficiency (VCID) characterized by defects in antibody production (IgG and IgA, with or without IgM), profound CD4 T-cell lymphopenia, and increased susceptibility to opportunistic infections (1). Unlike Common Variable Immune Deficiency (CVID), LOCID is defined by its distinct clinical and immunological profile, as well as its higher morbidity and mortality rates (2).

The clinical presentation of LOCID can vary significantly among patients. The condition typically manifests in late childhood or adulthood, often after a history of recurrent infections. Patients may present with a range of symptoms, including chronic sinusitis, pulmonary infections, and gastrointestinal complications due to opportunistic pathogens (3). In our case, the patient’s early onset of skin lesions and recurrent infections suggests a more complex underlying immunological disorder.

Immunological evaluation in patients with LOCID often reveals a profound deficiency in T cell subsets. The findings in our patient included low levels of CD3 T cells, CD3+CD4, CD3+CD8, CD19, and CD16+CD56 cells. These abnormalities are consistent with the immunological profile seen in LOCID, where T cell lymphopenia is a hallmark feature (4).

Lymphopenia, as observed in our patient with counts ranging from 390 to 940 cells/mm³, can lead to significant clinical consequences, including increased susceptibility to infections and potential malignancies (5). The lack of hypogammaglobulinemia, as confirmed by serum protein electrophoresis, further distinguishes LOCID from other immunodeficiencies such as CVID, where hypogammaglobulinemia is a common finding (6).

The pathophysiology of LOCID is not fully understood, but it is believed to involve genetic mutations that affect lymphocyte development and function. Various genetic defects have been implicated, including mutations in genes responsible for T cell signaling and development (7). The association of LOCID with conditions like epidermodysplasia verruciformis raises questions regarding the role of genetic predisposition and environmental factors in the development of these disorders.

Management of LOCID typically involves supportive care, including prophylactic antibiotics and immunoglobulin replacement therapy. In our patient, the initiation of a monthly immunoglobulin transfusion program has been associated with a positive clinical response, highlighting the importance of tailored immunotherapy (8).

The role of immunoglobulin therapy in improving the quality of life and reducing the frequency of infections in patients with LOCID cannot be overstated. Regular monitoring and a multidisciplinary approach are essential to manage complications and optimize treatment outcomes.

Understanding the distinctions between LOCID and CVID is crucial for appropriate diagnosis and management. While both conditions may present with similar clinical features, systematic T cell phenotyping can aid in differentiating these disorders (9). Identifying specific T cell defects associated with LOCID can lead to more personalized therapeutic approaches and may offer insights into the underlying genetic mechanisms.

The genetic basis of LOCID remains an area of active research. Identifying genetic markers associated with LOCID could facilitate early diagnosis and provide insights into disease mechanisms (10). Genetic counseling may be beneficial for affected individuals and their families, particularly in consanguineous populations where the risk of inherited immunodeficiencies is elevated.

**Conclusion**

This case of a 23-year-old woman with epidermodysplasia verruciformis revealing a Late Onset Combined Immunodeficiency underscores the importance of recognizing the complex interplay between immunological disorders and their clinical manifestations. LOCID differs from classic CVID in its clinical and immunological characteristics, necessitating a systematic approach to diagnosis and management.

Further research is essential to elucidate the genetic underpinnings of LOCID and its associations with conditions like epidermodysplasia verruciformis. Identifying these relationships may improve our understanding of immunodeficiencies and lead to more effective therapeutic strategies.

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