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Late Onset Combined Immune Deficiency (LOCID) Revealed by a Haemolytic Anaemia in a Child: A Case Report

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Abstract

Variable Common Immune Deficiency (VCID) is a very heterogeneous condition both clinically and immunologically. It is a group of molecular abnormalities responsible for a defect in antibody production leading to hypogammaglobulinemia often associated with autoimmune and/or lymphoproliferative manifestations. Late Onset Combined Immune Deficiency (LOCID) is a type of Variable Common Immune Deficiency (VCID) defined by a defect in antibody production (IgG and IgA ± IgM type), profound CD4 T-cell lymphopenia and frequent opportunistic infections. LOCID has been considered as a distinct entity from VCID due to its particular clinical and immunological profile.

Keywords

Haemolytic Anaemia, LOCID, Immune Deficiency, Child

1. Introduction

Variable Common Immune Deficiency (VCID) is a humoral immune deficiency described as the most common primary immune deficiency (PID) [1] characterized by heterogeneity of the clinical picture, the symptoms can be attenuated or acute, mainly infectious, other manifestations can be encountered in particular autoimmune, cutaneous, lymphoproliferative and digestive. We report a case of a child revealed a LOCID type immune deficiency following an autoimmune haemolytic anaemia, this type of association is rare and described in literature in 5% of cases.

2. Observation

A 12-year-old male child from a non-consanguineous marriage, with a history of

repeated respiratory infections since the age of 6 years, as well as multiple transfusions since the age of 3 years, initially admitted with an acute haemolytic anaemia with a positive coombs test and a positive IAR, then put under corticosteroids with a transfusion of compatible blood, and then lost to follow-up for a year. The evolution was marked by the installation of acute haemolytic crises with a delay in height 125 cm and weight 19 kg at −3 SD, splenomegaly at 12 cm and hepatomegaly at 5 cm.

The blood tests showed a positive Coombs test with warm anti-D IgG antibodies, a normal haemoglobin electrophoresis, a normal globular resistance test and a normal G6PD activity assay, hypogammaglobulinaemia found on three serum protein electrophoreses carried out at approximately two-year intervals, a collapse of IgG (<3.20 g/L for a normal value correlated to the patient's age of between 6.2 and 11.5 g/L) and IgA (0.46 g/L for a normal value correlated to the patient's age of 1.03) with IgM and IgE levels within the norms and a normal HLADR expression study. The biological evolution was marked by the installation of a constant lymphopenia over 07 years of follow-up varying between 220 and 940 cells/mm^3 with a decrease in CD3, CD19, CD4 and NK fractions (natural killers). In summary of these clinical and biological data, the diagnosis of an autoimmune haemolytic anaemia secondary to a variable common immune deficiency LOCID phenotype was confirmed. The child is on a monthly Ig transfusion program with a good clinical evolution thereafter.

3. Discussion

VCID is a humoral immune deficiency described as the most common PID with a prevalence ranging from 1/10,000 to 1/100,000 [2], and it ranks first in almost all national registries worldwide (Europe, USA, Latin America, Near and Middle East, South East Asia). In Australia more than 3/4 of the immunodeficiencies results from antibody deficiencies, of which VCID accounts for half, thus describing the highest rate in the world, while the lowest rate is recorded in Morocco (6.8% - 7.44%).

This disorder usually appears only in adulthood but sometimes the clinical signs start at an earlier age; in a European study the median age of discovery of the first clinical signs was 35 years [3], in the series of A. Tahiat *et al.* [4] the clinical signs appear at a lower age with an average of 13.5 years.

The diagnostic delay is usually several years (2 to 19 years), a mean diagnostic delay of 9.4 years was noted in the series of A. Tahiat *et al.*, joining the European and Italian series which described respectively a delay of 7.5 and 8.9 years [3], [5].

In the series by A. Tahiat *et al.*, infectious complications were found in 97% of cases, in line with the other series published in the literature; these infectious complications can affect the ears, nose, sinuses, bronchi and lungs. The most common agents encountered are: haemophilus influenzae, pneumococcus and staphylococcus.

Severe and recurrent pulmonary infections can lead to bronchial shaft sequelae with bronchiectasis. The latter was observed in 31% of cases in the series by A. Tahiat *et al.* and in 34% of an Italian series [5].

Other infections are described in the literature such as meningitis, pneumococcal septicaemia, joint infections, urogenital infections [6] [7] and viral infections with enterovirus or herpes virus [8]. Opportunistic infections with Mycobacteria spp, Pneumocystis jirovecii, or Cryptococcus neoformans are rarely described.

Chronic diarrhea is also described as a sign of the disease in 27.6%, and may be secondary to infection, lymphoid follicular hyperplasia or villous atrophy [9].

Other manifestations may reveal this type of immune deficiency, in particular autoimmune manifestations [10]; these may be autoimmune cytopenias constituting the main manifestations of autoimmunity during VCID, thrombocytopenic purpura which is described in nearly 15% of cases, autoimmune haemolytic anaemia which is found in 5% of cases.

A combination of the latter two abnormalities is possible, constituting Evans syndrome which is described in the literature with an incidence of 4%.Other autoimmune diseases may be found in VCID such as vitiligo, psoriasis, Hashimoto's thyroiditis, pernicious anaemia, celiac disease, rheumatoid arthritis, juvenile idiopathic arthritis, systemic lupus erythematosus, Sjogren's syndrome and primary biliary cirrhosis [11].

In Morocco, a study carried out at the Marrakech University Hospital on 41 children with an immune deficiency showed autoimmunity in 4 cases (14%).

Splenomegaly and/or adenopathy may accompany VCID, this tumor syndrome may be secondary to benign lymphoproliferation, lymphoma or another malignant lymphoproliferative syndrome [12]; A. Tahiat *et al.* described this syndrome in 21% of cases. From an immunological point of view, confirmation of the diagnosis is based on the study of serum protein electrophoresis by showing hypogammaglobulinaemia of less than 5 g/l with the determination of each class of immunoglobulin, which is essential to assess the extent of the Ig G deficiency and to look for a total Ig A deficiency as well as IgM deficiency which may be associated.

LOCID is described in the literature as an entity with distinct characteristics from those of VCID, including a high rate of consanguinity (29%), a higher prevalence of certain clinical abnormalities (splenomegaly, granuloma, gastrointestinal disease, and lymphoma), chronic use of antibiotics, and the need for frequent hospitalizations despite immunoglobulin substitution.

According to the literature, LOCID is defined by opportunistic infections with or without profound TCD4 lymphopenia.

In a French DEFI study, LOCID cases constituted 8% of the cases with VCID, the latter having more and infection despite Ig substitution.

Therapeutic management is based on the evaluation of the sequelae of complications, particularly bronchial dilatation and bronchial colonisation by anti-

biotic-resistant germs, and is essentially based on the administration of polyvalent immunoglobulins by intravenous or subcutaneous access. In autoimmune cytopenias, immunoglobulins are administered in high doses of around 1 g/kg. Corticosteroid therapy can also be effective in high doses (IV bolus followed by moderate doses per os) for a prolonged period of several weeks. Rituximab is administered at 375 mg/m^2/week for 4 weeks and is effective in the management of refractory and recurrent forms of the disease. In studies published in the literature, the use of immunoglobulins is more important, particularly in Europe, South Africa, Kuwait and Qatar.

In a Moroccan study conducted by the MARRAKECH University Hospital, the most common treatment used was cotrimoxazole-based antibiotics in 65.8% of patients, followed by intravenous immunoglobulins in 14.6%, while bone marrow transplantation was used in only 4.87% of patients [13].

4. Conclusion

LOCID or Late Onset Combined Immune Deficiency (LOCID) is a type of Variable Common Immune Deficiency (VCID) that can be defined by a defect in antibody production (IgG and IgA ± IgM type), profound CD4 T-cell lymphopenia and opportunistic infections, and can be considered a distinct entity from CVID due to its particular clinical and immunological profile and its higher morbidity and mortality.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Notarangelo, L., Casanova, J.L., Conley, M.E., Chapel, H., Fischer, A., Puck, J., *et al.* (2006) Primary Immunodeficiency Diseases: an Update from the International Union of Immunological Societies Primary Immunodeficiency Diseases Classification Committee Meeting in Budapest 2005. *Journal of Allergy and Clinical Immunology*, **117**, 883-896. https://doi.org/10.1016/j.jaci.2005.12.1347

[2] Chapel, H. and Cunningham-Rundles, C. (1999) Update in Understanding Common Variable Immunodeficiency Disorders (CVIDs) and the Management of Patients with these Conditions. *British Journal of Haematology*, **145**, 709-727. https://doi.org/10.1111/j.1365-2141.2009.07669.x

[3] Chapel, H., Lucas, M., Lee, M., Bjorkander, J., Webster, D., Grimbacher, B., *et al.* (2008) Common Variable Immunodeficiency Disorders: Division into Distinct Clinical Phenotypes. *Blood*, **112**, 277-286. https://doi.org/10.1182/blood-2007-11-124545

[4] Tahiat, A., *et al.* (2014) Variable Common Immune Deficiency (VCID): Clinical and Immunological Characteristics of 29 Algerian Patients. *Pathologie Biologie*, **62**, 377-381.

[5] Quinti, I., Soresina, A., Spadaro, G., Martino, S., Donnanno, S., Agostini, C., *et al.* (2007) Long-Term Follow-up and Outcome of a Large Cohort of Patients with Common Variable Immunodeficiency. *Journal of Clinical Immunology*, **27**, 308-316.

https://doi.org/10.1007/s10875-007-9075-1

[6] Steuer, A., Franz, A., Furr, P.M., Taylor-Robinson, D., Webster, A.D. and Hughes, G.R. (1996) Common Variable Immunodeficiency Presenting as a Mycoplasma Hominis Septic Arthritis. *Journal of Infection*, **33**, 235-237. https://doi.org/10.1016/S0163-4453(96)92441-X

[7] Bonilla, H.F., Chenoweth, C.E., Tully, J.G., Blythe, L.K., Robertson, J.A., Ognenovski, V.M., *et al.* (1997) Mycoplasma Felis Septic Arthritis in a Patient with Hypogammaglobulinemia. *Clinical Infectious Diseases*, **24**, 222-225. https://doi.org/10.1093/clinids/24.2.222

[8] Rudge, P., Webster, A.D., Revesz, T., Warner, T., Espanol, T., Cunningham-Rundles, C., *et al.* (1996) Encephalomyelitis in Primary Hypogammaglobulinaemia. *Brain*, **119**, 1-15. https://doi.org/10.1093/brain/119.1.1

[9] Hermaszewski, R.A. and Webster, A.D. (1993) Primary Hypogammaglobulinaemia: A Survey of Clinical Manifestations and Complications. *Quarterly Journal of Medicine*, **86**, 31-42.

[10] Cunningham-Rundles, C. and Bodian, C. (1999) Common Variable Immunodeficiency: Clinical and Immunological Features of 248 Patients. *Clinical Immunology*, **92**, 34-48. https://doi.org/10.1006/clim.1999.4725

[11] Pavic, M., Sève, P., Malcus, C., Sarrot-Reynauld, F., Peyramond, D., Debourdeau, P., *et al.* (2005) Variable Common Immune Deficiency with Autoimmune Manifestations: Study of Nine Observations; Interest of Specific Immunophenotyping of Circulating B-Lymphocytes in Seven Patients. *La Revue de Médecine Interne*, **26**, 95-102. https://doi.org/10.1016/j.revmed.2004.11.001

[12] Sander, C.A., Medeiros, L.J., Weiss, L.M., Yano, T., Sneller, M.C. and Jaffe, E.S. (1992) Lymphoproliferative Lesions in PATIENTS with Common Variable Immunodeficiency Syndrome. *The American Journal of Surgical Pathology*, **16**, 1170-1182. https://doi.org/10.1097/00000478-199212000-00004

[13] Talibi Alaoui, Z. (2017) Les Deficit Immunitaires Primitifs chez L'Enfant. Ph.D. Thesis, University of Cadi Ayyad, Marrakech.