

Cytomegalovirus Pneumonitis as a Presentation of Severe Combined Immunodeficiency in an Infant: A Case Report

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Abstract

Cytomegalovirus (CMV) is a major cause of congenital infection and morbidity in immunocompromised patients; CMV pneumonia remains rare in immunocompetent infants and should raise suspicion of an underlying immune deficiency. We report the case of an 11-month-old infant, with no relevant past medical history, admitted for febrile respiratory distress complicating a chronic respiratory disorder evolving over two months, previously misdiagnosed and treated as pneumonia and then as infantile asthma. Chest radiography and computed tomography showed bilateral interstitial infiltrates with absence of the thymic shadow. Because of the lack of improvement under empirical antibiotic therapy, positive CMV serology and blood PCR led to treatment with Ganciclovir, with marked clinical improvement. Immunological work-up revealed hypogammaglobulinemia and a lymphocyte immunophenotyping pattern consistent with severe combined immunodeficiency (low CD19 B-cells and CD4 T-cells, normal NK cells). Cotrimoxazole antibiotic prophylaxis and immunoglobulin replacement therapy were started. CMV infection should be investigated in any infant presenting with atypical, chronic, or treatment-resistant interstitial pneumonia, and its identification should systematically prompt screening for an underlying primary immunodeficiency, the early diagnosis of which determines prognosis.

Keywords: Cytomegalovirus; Pneumonia; Severe Combined Immunodeficiency; Infant; Primary Immunodeficiency; Ganciclovir

Introduction

Cytomegalovirus (CMV) is a ubiquitous virus belonging to the Herpesviridae family, transmitted by various biological fluids. It is the leading cause of congenital viral infection and is a major cause of acquired sensorineural hearing loss and neurodevelopmental delay in children [1,2].

In immunocompetent subjects, the infection is most often asymptomatic or paucisymptomatic. On the other hand, in immunocompromised people, particularly in the case of cellular immunity deficiency, CMV can be responsible for severe visceral damage, particularly pulmonary [1,2].

CMV pneumonitis remains rare in immunocompetent infants, but its occurrence should suggest an underlying immune deficiency. We report the case of an infant in whom CMV pneumonitis revealed a severe combined immunodeficiency [1,3].

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Materials and Methods

This is a descriptive clinical observation of an infant hospitalized with febrile respiratory distress.

The data collected included:

- Clinical data
- Biological examinations
- Chest imaging
- Microbiological investigations
- Immunological assessment.

The diagnosis of CMV infection was based on:

- CMV Serology
- Blood CMV PCR.

Case Observation

We report the case of an 11-month-old male infant with a history of delayed umbilical cord fall, full-term birth from a non-consanguineous marriage, vaginal delivery with good adaptation to extrauterine life, and up-to-date vaccination according to the NIBP. The child was admitted for the management of febrile respiratory distress complicating chronic respiratory discomfort that had been evolving for 2 months, for which he had been treated successively for pneumonitis and then for infant asthma, after several outpatient consultations.

The clinical presentation at admission was associated with fever at 39°C, tachycardia at 160 beats/min, respiratory distress with signs of subcostal pulling and thoraco-abdominal swaying, 91% desaturation in the ambient air, and bilateral snoring and sibilant rattles on pulmonary auscultation. Consciousness was normal and the rest of the examination was unremarkable.

Chest X-ray showed bilateral interstitial syndrome with multiple foci, as well as absence of thymic shadow, confirmed by cervical ultrasound. Chest CT scan revealed infectious lung disease and pectus carinatum-like chest malformation.

The phthisiological assessment, carried out as part of a tuberculosis test, was negative, and the blood culture did not identify any germ. The patient was initially put on probabilistic antibiotic therapy. In the absence of clinical and radiological improvement, serology and CMV PCR were positive, which led to treatment with Ganciclovir, with a clear clinical improvement.

In view of this clinical picture, an initial immunological assessment was requested, including a negative HIV serology and a weight assay of immunoglobulins showing hypogammaglobulinemia, thus suggesting a primary immune deficiency. The assessment was completed by lymphocyte immunophenotyping showing a low level of CD19 B lymphocytes and CD4 T lymphocytes, with a correct level of NK lymphocytes, pointing to a severe combined immunodeficiency. The patient was put on antibiotic prophylaxis based on cotrimoxazole, and an infusion of immunoglobulins was scheduled.

Discussion

Cytomegalovirus pneumonitis is a rare manifestation in immunocompetent children, but represents a major cause of morbidity and mortality in immunocompromised subjects. Indeed, CMV is an opportunistic pathogen whose replication and dissemination are



Figure 1: Chest X-ray showing foci of bilateral lung disease with sequelae images.

closely linked to the alteration of cellular immunity, in particular CD4 T lymphocytes. Several studies have shown that severe forms occur preferentially in patients with a primary or acquired immune deficiency, particularly after transplantation or chemotherapy [1,2,7].

Pathophysiologically, CMV infection can correspond to a primary infection, viral reactivation or reinfection. Reactivation is the mechanism most frequently involved in immunocompromised patients, favored by a failure of immune control. The virus persists in a latent state in mononuclear cells and can reactivate in the event of immunosuppression, leading to severe visceral damage, particularly pulmonary [1,3].

Clinically, CMV pneumonitis is most often manifested by a picture of febrile respiratory distress with hypoxemia, sometimes associated with a subacute or chronic course resistant to conventional antibiotic therapies. This non-specific presentation makes diagnosis difficult; CMV should be considered in the presence of any atypical or persistent interstitial lung disease, especially in the absence of response to probabilistic treatment [2,4].

Radiological data are generally non-specific, dominated by diffuse interstitial syndrome, bilateral infiltrates or ground-glass opacities. These abnormalities, although not pathognomonic, should alert the clinician in a compatible context, especially in patients at risk of immunosuppression [4].

Diagnosis is currently based on sensitive virological techniques, in particular the detection of viral DNA by PCR, which is the reference method for confirming active infection and monitoring viral load. pp65 antigenemia is also a useful diagnostic tool, although less used at present. Serology remains of limited interest in immunocompromised patients due to sometimes altered humoral responses [3,5].

Therapeutic management is based on the administration of antivirals, mainly intravenous Ganciclovir as a first-line treatment, with a possible follow-up to Valganciclovir. These treatments have significantly reduced CMV-related mortality in at-risk populations. However, resistance may occur, justifying in some cases the use of alternatives such as Foscarnet [5].

In our observation, the severity of the pulmonary involvement and the confirmation of CMV infection led to the performance of an immunological assessment, revealing a severe combined immunodeficiency. This diagnostic approach is in line with current recommendations, which recommend the systematic search for an underlying immune deficiency in the face of any severe, unusual or prolonged CMV infection in children [2,6].

Conclusion

Cytomegalovirus pneumonitis, although rare in immunocompetent children, must be systematically considered in the presence of any atypical, chronic interstitial lung disease or one that is resistant to usual probabilistic treatments, particularly in young infants. Our observation illustrates the interest of a rigorous diagnostic approach combining virological confirmation and systematic immunological assessment, which has revealed an underlying severe combined immunodeficiency. The early diagnosis of this deficiency directly conditions the child's prognosis, by allowing the rapid initiation of antibiotic prophylaxis, immunoglobulin substitution and, ultimately, curative management such as hematopoietic stem cell transplantation. This observation is a reminder that a severe opportunistic infection in infants should always be investigated for an underlying primary immune deficiency.

Consent

Written informed consent was obtained from the patient's parents for the publication of this observation and associated images.

Conflicts of Interest

The authors do not declare any conflicts of interest.

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