



## Letter to editor

### Immunocompetence in adults: more than HIV negative

Immunocompetencia en adultos: más que VIH negativo

Andres Felipe Zea-Vera

Departamento de Microbiología, Facultad de Salud, Universidad del Valle. Cali, Colombia

Zea-Vera AF. Immunocompetence in adults: more than HIV negative. *Colomb Med (Cali)*. 2016; 47(3):176.

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#### Dear editor

I read a case report about Tuberculosis and fungal co-infection in a previously healthy patient published in *Colomb Med (Cali)* by Fontalvo *et al.*<sup>1</sup>, (<http://colombiamedica.univalle.edu.co/index.php/comedica/article/view/2271>) and I would like to address some related comments. Frequently clinicians report adult cases of patients with opportunistic infections as disseminated tuberculosis and/or fungal infections in patients consider as immunocompetent based mainly in the absence of human immunodeficiency virus infection (HIV negative). Immunocompetence is more complex than absence of HIV infection and involves a normal capacity to develop an immune response following the exposure to an antigen or broadly a normal immune response, but usually immunocompetent is define as the opposite of immunodeficiency. In the report authors said "Our aim is to report the case of an immunocompetent patient diagnosed with *Mycobacterium tuberculosis* and *Candida albicans* co-infections" but my deliberation is Do we make in the clinical practice all the efforts to consider a patient as immunocompetent?

Mycobacterial, fungal and other opportunistic infections force the clinician to rule out a large list of conditions associated with secondary immunodeficiency as infectious agents (HIV, Herpesvirus, HTLV), drugs (steroids, immunosuppressants, biologics, chemotherapy), metabolic diseases (diabetes, renal failure, cirrhosis), malignancies (leukemia, lymphomas and solid tumors) and environmental conditions (radiation, heavy metals)<sup>2</sup> but even adult patients can have late onset primary genetic immunodeficiency disorders as chronic granulomatous disease, X-linked agammaglobulinemia, interleukin-12 receptor deficiency or interferon-gamma (IFN- $\gamma$ ) and interleukin-23/interleukin-17 pathway defects<sup>3</sup> explaining their pattern of infection or the presence of opportunistic microorganism. When a patient with opportunistic infections is assessed cellular immune response evaluation is mandatory, not only CD4+ and CD8+ T lymphocytes absolute quantification (not evaluated in this case report) but also qualitative T cell responses (v.g lymphoproliferation, cytokine production) as well as B cell and natural killer (NK) cells evaluation. Opportunistic infections in adult patients can also be a presentation of autoantibodies that inhibit cytokines including (but not only) anti interferon-gamma (anti IFN- $\gamma$ ) self-antibodies in previously healthy adults presenting with severe Mycobacterial infections<sup>4</sup> or antibodies to interleukin-17 (IL-17) and IL-22 that are associated with chronic candidiasis<sup>5</sup> this group of autoantibodies are now recognized as phenocopies or acquire immune disorders resembling primary genetic immunodeficiency diseases<sup>6</sup>. From my point of view the term immunocompetent should be use more carefully.

Interestingly the patient presented had mild macrocytic anemia (hemoglobin 10.7 g/dL and mean corpuscular volume 103  $\mu\text{m}^3$ ). This feature is found frequently in patients with anti-cytokines autoantibodies and is related with self-antibodies to gastric parietal cell and to intrinsic factor producing pernicious anemia<sup>7</sup>. Patients with adult onset immunodeficiency due to anti IFN- $\gamma$  autoantibodies could be more susceptible to autoimmune disorders, requiring a higher suspicious index.

The intent of this letter is to generate a wake-up call for better evaluation of patients with recurrent or opportunistic infections.

#### Conflicts of interest:

None to disclaim

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#### Corresponding author:

Andres Felipe Zea-Vera. Departamento de Microbiología, Facultad de Salud, Universidad del Valle. Sede San Fernando, Cali, Colombia. Calle 4B No 36-00. E-mail: andres.zea@correounivalle.edu.co

## Authors Response: Tuberculosis and pulmonary candidiasis co-infection present in a previously healthy patient

Respuesta de los autores: Coinfección de tuberculosis y candidiasis pulmonar en paciente previamente sana

Dear Editor:

Article ref: <https://www.ncbi.nlm.nih.gov/pubmed/27546933>

In response to the note<sup>1</sup> about the case described<sup>2</sup>, we fully agree that immunodeficiency is not only the relationship with HIV infection, and that there are pathologies and different immunological and genetic conditions associated with it<sup>3-5</sup>; the main ones were discarded in the patient.

In the patient of the presented clinical case, there is no family history of primary immunodeficiencies. And in her personal history, there were not found any data related to recurrent infectious processes, either in childhood or present, which does not lead to suspicion of diseases with primary immunodeficiencies, in which recurrent infections would be expected as in the case of recurrent pneumonia, lung, spleen and liver abscesses, cervical, axillary and inguinal lymphadenitis, or bone and skin infections, as in the case of chronic granulomatous disease<sup>6</sup>.

For other primary immunodeficiencies provided by the reader, such as the case of X-linked agammaglobulinemia, this is a congenital disease that affects males and involves B lymphocytes and plasma cells, which are not the primary immune line in tuberculosis<sup>7</sup>, nor does it correspond to our case.

On the other hand, inherited immune system defects, such as Mendelian susceptibility to mycobacterial diseases syndromes (MEMS), in which there are defects in the axis IL-12/IN- $\gamma$ , can be a major cause of fungal and mycobacterial associations, as in the patient of the clinical case; although it would be expected that these patients present, since their birth, a history of oral, skin and enteral fungal infections, with a very important fact, as it is the presence of axillary lymphadenitis and disseminated mycobacterial infection with the implementation of the BCG vaccine, and pigmented purpuric dermatosis<sup>8</sup>, data that were not found in our patient.

Within the recorded history, we found out that she was not receiving any medication related to immunosuppression. Studies to rule out metabolic, kidney and liver diseases were performed, including arterial blood gases, serum electrolytes, protein electrophoresis, coagulation tests, quantification of serum immunoglobulins, studies of renal function (urinalysis and urinary sediment, creatinine, BUN) and hepatic function (bilirubin, alanine transaminase, aspartate transaminase, alkaline phosphatase, serum albumin, prothrombin time), all of which were normal. Elisa test for HIV was negative. For the purpose of seeking collagen pathologies, antinuclear and anti-double-stranded DNA antibodies were performed, with negative results.

With respect to macrocytic anemia in the initial blood count at the admission of the patient, there were no data of personal or family history of anemia, and this condition was corrected during ambulatory evolution, suggesting a case of possible infectious condition.

Checks performed in the outpatient patient reveal that she is evolving satisfactorily. She is on medical supervision for internal medicine and infectious diseases under her health insurer, where he underwent blood count, serological determinations of IgA, IgG, IgE, CD4 and CD8, all of which were normal.

In this case, both clinical and para-clinical follow-up was definitive to determine associations with underlying conditions as predisposing factors for the coexistence of tuberculosis and pulmonary candidiasis.

However, clinical cases are an invitation to seek scientific explanations, to think on these clinical entities; in addition, they can give some guidelines to guide us in other similar situations, and to generate us concerns about the pathogenesis of primary immunodeficiencies, and the possible monogenic or other genetic defects to explain these susceptibilities.

Nevertheless, we have found very good and important the questioning and exhortation that the author does, and that we do and extend to all clinical colleagues: We must carefully use the term immunocompetence when we study a patient, and to perform an optimal evaluation to those who present with opportunistic infections.

The authors express their gratitude for this important contribution.

### Conflicts of interest:

None to declare

### Authors:

Dilia Mildret Fontalvo<sup>1,2</sup>, Gustavo Jiménez Borré<sup>3</sup>, Doris Gómez Camargo<sup>1,2</sup>, Neylor Chalavé Jiménez<sup>3</sup>, Javier Bellido Rodríguez<sup>3</sup>, Bernarda Cuadrado Cano<sup>1</sup>, Shirley Navarro Gómez<sup>1</sup>

<sup>1</sup>Departamento de Postgrado, Doctorado en Medicina Tropical, Universidad de Cartagena, Cartagena, Colombia.

<sup>2</sup>Grupo de investigación UNIMOL. Universidad de Cartagena, Cartagena, Colombia

<sup>3</sup>Unidad de Cuidados Intensivo Adultos, Departamento de Medicina Interna, Clínica Nuestra. Cartagena, Colombia

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