

How the INF- γ release assay (IGRA) may suggest a PID?

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Background

INF- γ release assay (IGRA) is primarily used to screen for latent tuberculosis. However, the test may display indeterminate results, which is generally due to a low response to positive control (Mitogen). This can be related to immunodeficiency conditions that negatively impact the production of IFN- γ .

Purpose:

We sought to demonstrate how an indeterminate INF- γ release assay profile can reveal a possible primary immunodeficiency disorder (PID).

Methods:

The population of this study was selected from 584 cases who initially underwent an IGRA showing 162, 409 and 13 positive, negative and indeterminate cases respectively. After ruling out the other causes of indeterminate IGRA profiles, such as pre-analytical errors (n=4) and acquired immunodeficiency conditions (n=6), 3 cases for whom clinical data were in favor of PID benefited from T, B and NK (BD Multitest 6-color) immunophenotyping by flow cytometry (BD FACSCanto II) using CD45-PerCP-Cy5.5/CD3-FITC/CD4-PE-Cy7/CD8-APC-Cy7/CD19-APC/CD16 and CD56-PE panel.



Results:

The three selected cases were 15 months, 25 years old and 18 months, and all of them had a medical history of unexplained and recurrent infections. The subpopulation phenotyping results showed: T lymphopenia, suggesting a cellular deficiency (Case-1); NK cell lymphopenia that may suggest a MSMD (Case-2) and B lymphopenia in favor of a humoral deficit (Case-3).

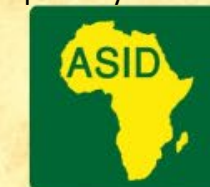
Cases	Phenotyping results	Reference values
Case1	T lymphopenia : - TCD3 = 980/mm ³ - TCD4 = 723/mm ³ - TCD8 = 250/mm ³	- 2100-6200 - 1300-3400 - 620-2000
Case 2	NK cell lymphopenia : NK CD16/56 = 10/mm ³	70-480
Case 3	B lymphopenia : CD19=668/mm ³	720-2600

The first case is in favor of CID, for which memory and naïf T cell analysis was normal and is still under investigation in order to

rule out other possible CID etiologies. For the second case, we first proceeded with the DHR test which was normal, and INF- γ /IL12 investigation is scheduled once reagents are available. Also, a follow up of NK cells with its subsets is planned. For the third case, the quantification of immunoglobulins was normal and further CD19 and immunoglobulin assessment is programmed after six months.

Conclusion:

Indeterminate INF- γ release assay profile represents a possible primary immunodeficiency disorder revealing circumstance. On basis of clinical data, such profile should be initiate a rational diagnostic approach including subpopulations phenotyping, immunoglobulin assay, IFN- γ /IL12 investigating and others in order to establish or eliminate the diagnosis of primary immunodeficiency.



PID-IEI IN AFRICA:
WHERE AND HOW TO FIND THEM?

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