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How the INF-y release assay (IGRA) can suggest a PID

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Abstract

Purpose: INF-y 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-y. We sought to demonstrate how an indeterminate IGRA profile can reveal a possible 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 cell phenotyping, using flow cytometry (FacsCanto-II, BD).

Results: The three selected cases were 15 months, 18 months and 25 years old, and all of them had a history of unexplained and recurrent infections. The subpopulation phenotyping results showed: T lymphopenia (CD3=980, CD4=728, CD8=250/mm^3), suggesting a cellular deficiency (Case-1); B lymphopenia (CD19=668/mm^3) in favor of a humoral deficit (Case-2) and NK cell lymphopenia (CD16/56=10/mm^3) that may suggest a MSMD (Case-3). Additional investigations are underway for all these cases.

Conclusion: Indeterminate IGRA profile represents a possible PID revealing circumstance. On basis of clinical data, such profile should initiate a rational diagnostic approach including subpopulations phenotyping, immunoglobulin assay, IFN-y/IL12 investigating and others, in order to establish or eliminate a PID.