Primary Immunodeficiencies (PID)

10 Recommendations for Clinicians: When you suspect a PID, please follow use the following recommendations for a better diagnosis orientation.

Shereen M. Reda, Brian Eley, James Shipeta, Maroufou J. Alao, L. Jeddane Nahla Erwa, A. Aziz Bousfiha

An ASID 2015 production. www.asid.ma

1. When a PID is suspected, first exclude HIV infection.
2. If the patient experiences two or more pneumonias during a 12-month period: think about Antibody Deficiencies and measure serum IgG, IgA and IgM levels.
3. If pan-hypogammaglobulinemia is present: consider Bruton’s disease if B cells (CD19)<2%; and CVID if CD19+ > 2%. If Selective IgA deficiency is present [only diagnose this condition after the age of 4 years], evaluate IgG sub-classes levels + anti-pneumococcal antibody titers.
4. In conditions with opportunistic infections [e.g. interstitial pneumonia due to CMV or Pneumocystis jirovecii], persistent diarrhea and/or persistent oral thrush: think about T-cell defects [Combined immunodeficiencies; CID]. They are called severe combined immunodeficiencies (SCID) if the total lymphocyte count is <3000/mm3 in children under 2 years of age [CD3 lymphopenia]. If there is no lymphopenia (>3000), consider CID caused by a functional defect. In both SCID and CID, evaluate lymphocyte subpopulation counts (CD3, CD4, CD8, CD19, CD16 and HLA-DR). The MHC II deficiency (CD4 lymphopenia + HLA-DR=0) is the most common CID in North Africa.
5. In case of neonatal onset, including liver abscess or delayed umbilical cord separation (>3 weeks), or later bacterial infections including supplicative lymphadenitis or aspergillosis, consider congenital defects of phagocyte number, function or both, and request a CBC [Congenital Neutropenia], NBT test or oxidative burst test [Chronic Granulomatous Disease] and CD18 / CD11 expression on lymphocytes [Leukocyte Adhesion Deficiency].
6. Immunodeficiency is a feature in several clinical syndromes including: ataxia + chest infections + telangiectasia = Ataxia Telangiectasia; thrombocytopenic purpura + eczema + chest infections = Wiskott-Aldrich syndrome; grey hair + hemophagocytic lymphohistiocytosis = Griscelli syndrome; hypocalcemia + cardiac defects = DiGeorge syndrome.
7. Infections with atypical mycobacteria [including BCG] and/or invasive/recurrent infection due to Salmonella spp: consider Mendelian Susceptibility to Mycobacterial disease (MSMD) or CID and ask for lymphocyte subpopulation counts. If these are normal, explore the IFN-γ/IL-12/IL-23 pathway.
8. If IgG, IgA and IgM levels, lymphocyte subpopulation counts and NBT or oxidative burst test are normal, explore Complement deficiencies (CH50 and AP50 assays), Hyper-IgE syndromes [IgE levels>2000 IU/mL or >10 fold that of normal reference range], Innate Immune defects [predisposition to infections such as herpes simplex encephalitis, chronic mucocutaneous candidiasis, invasive pneumococcal disease, human papillomavirus infection or disseminated vaccine-strain measles] or Auto-inflammatory syndromes such as FMF, MVK deficiency, Marshall or TRAPS.
9. Always compare CBC, immunoglobulin [Ig] levels and lymphocyte counts to age-related norms.
10. As the diagnosis of PID is based on clinical manifestations, even if the investigations are normal, a PID cannot be excluded. In these situations, please consult an expert.