

Forgotten immunodeficiencies: a case of Primary Selective Immunoglobulin M deficiency

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Case history

A 62 year old female was referred because of persistent elevated inflammatory parameters. She had been treated for chronic lumbar pain with a morphine pump, leading to **recurrent infections** and finally removal of the pump. Furthermore her clinical history reveals peripheral vascular insufficiency treated with endovascular surgery and stent placement but complicated by a chronic wound on the right foot and recurrent Staphylococci infections (MSSA and MRSA), requiring long courses of antibiotics. She is also known with several allergies towards disinfectants and atopic dermatitis.

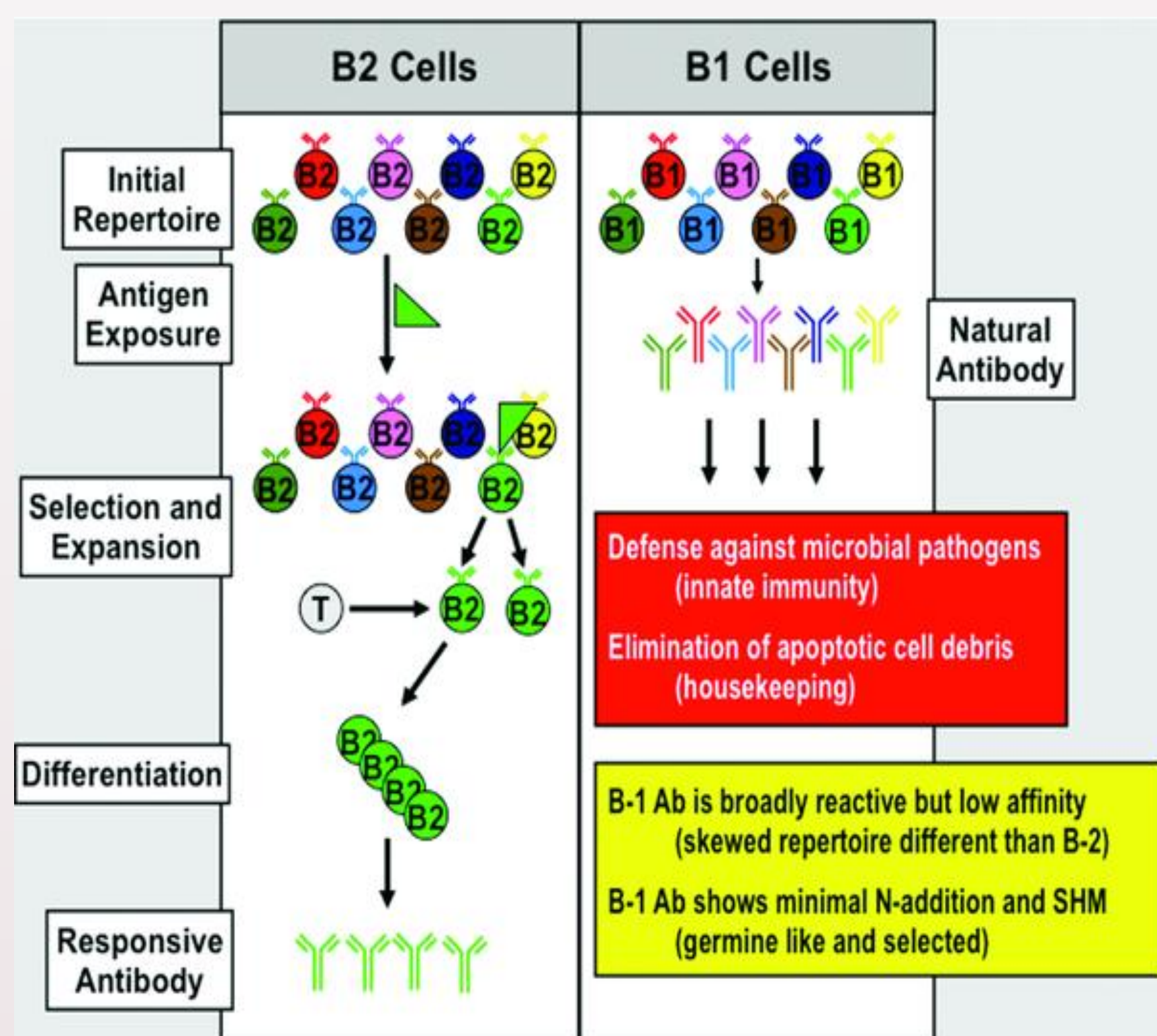
Diagnosis

A broad laboratory screening revealed increased inflammation parameters (sedimentation 44 mm/u, CRP 24.8mg/l), normal leucocytes count and formula, normal liver and kidney function but a remarkable **dysglobulinemia** characterized by an IgM of 0.179g/l (normal range 0.46-3), confirmed after repeating the test. IgG and IgA showed normal values and as expected the IgE values were also elevated (119kU/l) confirming the associated **allergic diathesis**. Further screening for associated auto-immune disease, acquired immunodeficiency syndrome (HIV), hematological disorders and lymphocyte analysis revealed no associated abnormalities.

Pathogenesis

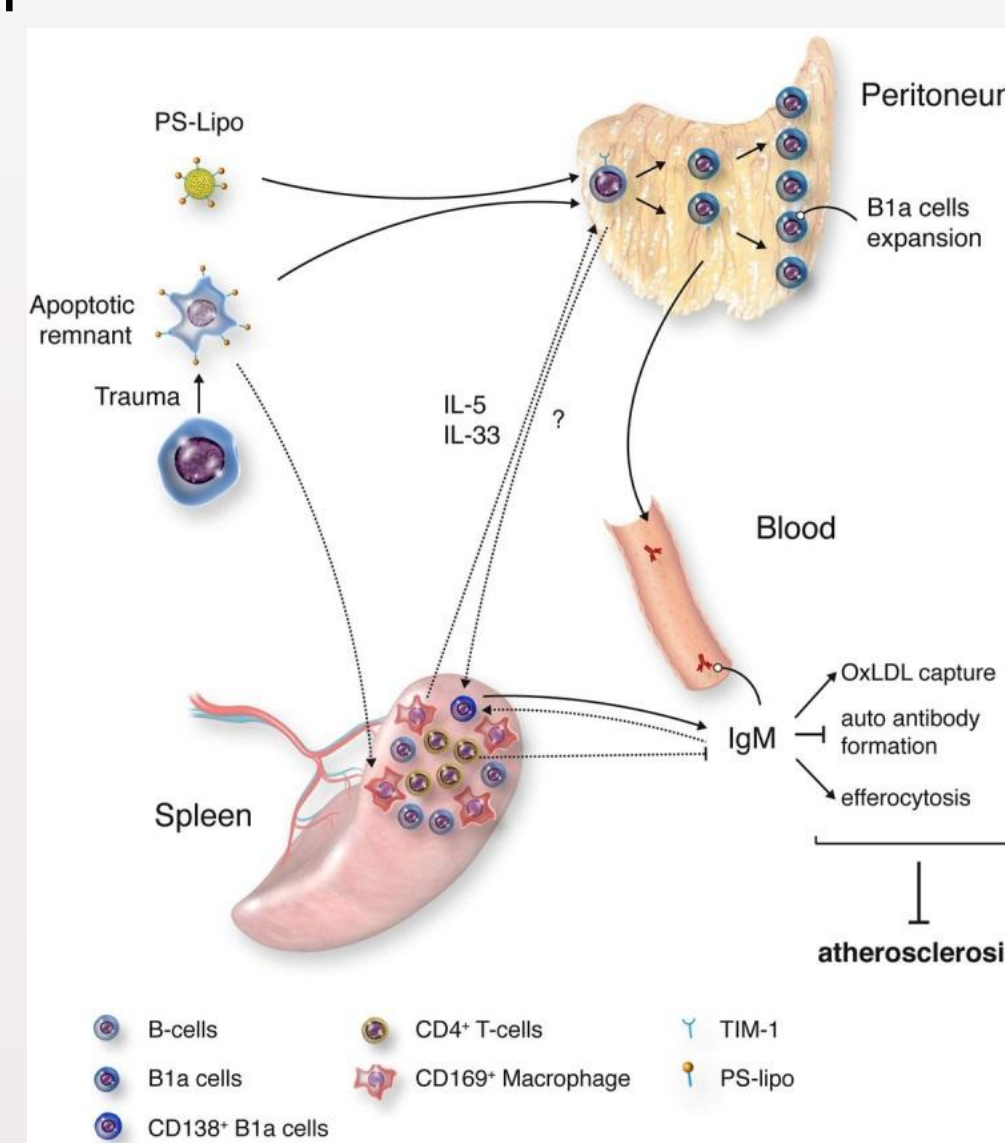
Antigen mediated germinal center **B2-cell** expansion and isotype switching (IgA, IgE, IgG)

Polyreactive, non germinal center **B1-cell** secretion of "natural" IgM antibodies



Naturally antibodies = **without any antigen exposure**. Recognize "oxidation-specific" epitopes, as found in oxidative processes involved in metabolism, aging, and inflammation.

Localised on both pathogens (viral and bacterial) and aging/apoptotic host cells .



Role in:

- early defense:** before more specific antibodies can be produced
- housekeeping:** removal of cellular debris, homeostasis of inflammation: anti-atherosclerosis, less auto-immunity and allergy

Follow-up and management

- Screening for **auto-immune disease, lymphoproliferative disease and allergic diathesis** 1x/y
- DD between primary and secondary IgM deficiencies
- Treatment as suggested after splenectomy (because of the lack of direct opsonisation).
 - Low threshold to start antibiotics but no prophylaxis: on demand treatment is recommended in Belgium
 - No indication for IVIG because of low concentration of IgM and their short half life.

Conclusion

Deficiency in serum IgM may explain a paradox of diminished responsiveness to foreign antigens (therefore susceptibility to infections) and increased inflammation (because of lack of homeostasis) resulting in auto-immunity (and possibly malignancy) in patients with Selective IgM deficiency.

References

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