IMMUNE THROMBOCYTOPENIA AND IMMUNOGLOBULIN G4-RELARED DISEASE: IS THERE A CORRELATION?

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Immunoglobulin G4-related disease (IgG4-RD) is an immune-mediated fibroinflammatory condition associated with single or multi-organ swelling and subsequent fibrosis affecting multiple organs. In some rare cases it is seen an association of IgG4-RD and primary immune thrombocytopenia (ITP) with IgG4-anti platelet. ITP is an acquired immune mediated disorder characterized by isolated thrombocytopenia, defined as a platelet count (PLT) <100 x 10^9/L, and the absence of any underlying cause of the thrombocytopenia.

A 56 years old woman was admitted in Our Clinic in 2005 for PLT of 1 x 10^9/L and petechial rash, infective causes were excluded. ANA, ENA, ANCA, anti-phospholipid antibodies were within their normal range. A bone marrow evaluation excluded haematological diseases and showed adequate megakaryocytes. Considering it as an ITP the patient started Dexamethasone 40 mg for 4 days + IgIv 2 g/kg with a complete platelet recovery (CR).

In 2011, the patient had jaundice and initial diabetes requiring insulin, an abdomen CT (a-CT) scan showed a 10 cm mesenterial lesion and a swelling of the pancreas. The patient underwent an agoaspirate of pancreas and a Whipple procedure.

The histopathology was negative for malignancy, instead showed IgG4 autoimmune pancreatitis (AIP) with an infiltration of IgG4 secreting plasmacells with the serum IgG4 being > 250 mg/ml, so the patient initiated a first line therapy with steroids with a prompt serum response. An a-CT control in 2014 the pancreatic pseudotumor persisted, so Azathioprine was initiated for 1 year in the attempt to reduce the mass, with a little to no response.

On the first (2013) and second relapse (2018) of ITP a round of Prednisone (PDN) 1 mg/kg + IgIv was done attaining a CR. At the third relapse (2019), a second line therapy was initiated consisting in Rituximab 375 mg/mq/wk for 4 weeks with a CR for another year. Thereafter the patient started a TPO-RA therapy with Eltrombopag then switched to Romiplostim, with partial response. On January 2022, PLT was 0 x 10^9/L and Fostamatinib was seen as a good option, indeed the patient obtained a CR for a year, followed by a progressive reduction on the PLT, till reaching 8 x 10^9/L on April 2023, so we decided to try an association of small doses of PDN with Mycophenolate 1000 mg bid, followed by a slow steroid tapering. On October 2024 the platelet count is > 50 x 10^9/L, the patient has been steroid-free from July 2023. She had SARS-COV2 pneumonia on September 2023, but no alterations of the platelet count was seen.

DISCUSSION

To date, ten cases have been reported of IgG4-RD and ITP occurring concurrently in the same patient. However, the pathophysiological relationship between these conditions remains unclear, and no guidelines currently exist for the treatment of secondary ITP in this context. One hypothesis suggests that plasma cells in autoimmune pancreatitis (AIP) secrete IgG4 anti-GP IIb/IIIa antibodies targeting platelets, leading to their destruction.

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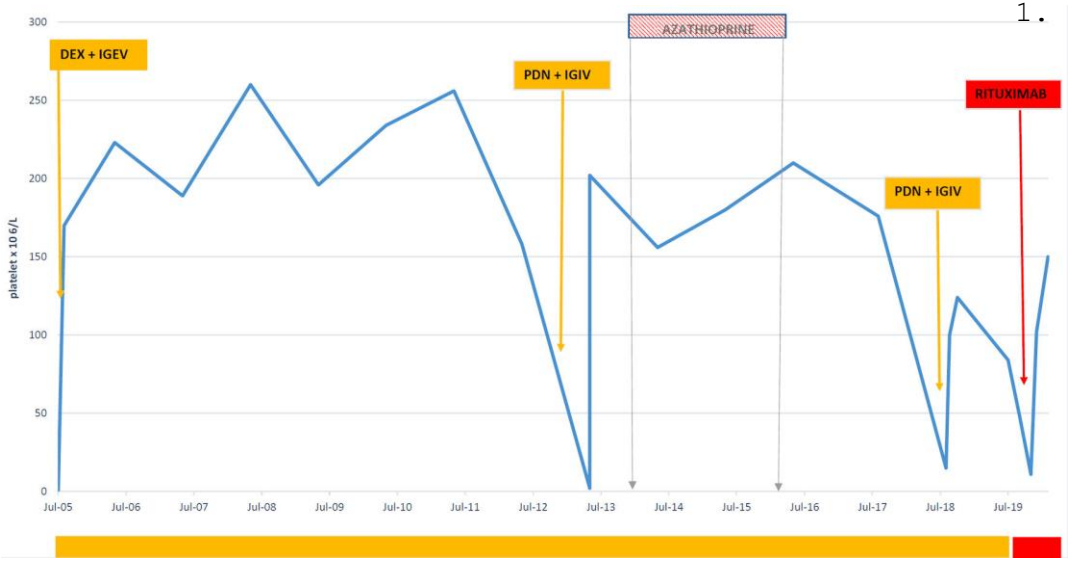

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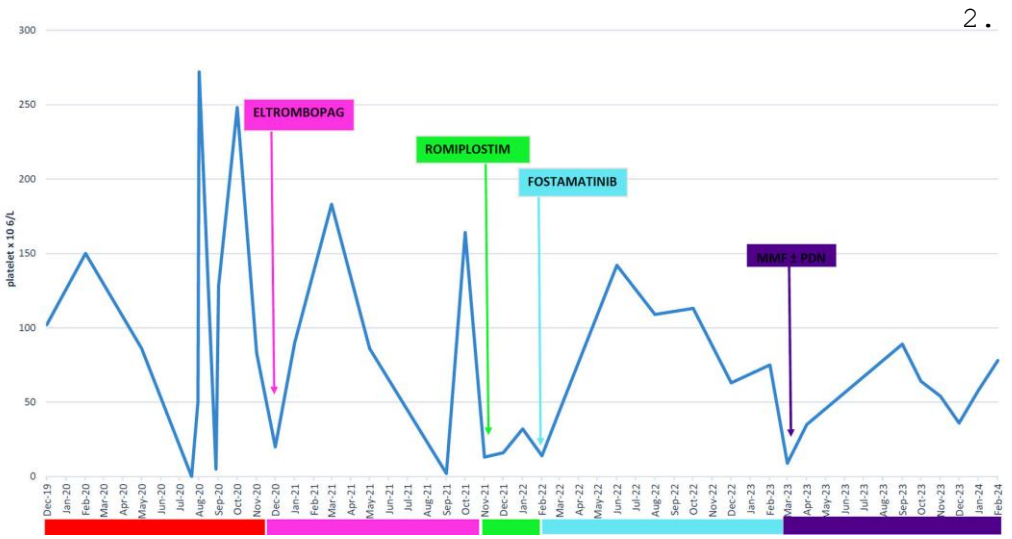

Fig. 1 Platelet variation from 2005 till July 2019. Dex: dexamethasone; IVIG: intravenous immunoglobulin; PDN: prednisone. Fig. 2 Platelet variation from July 2019 till February 2024. MMF: mycophenolate; PDN: prednisone.