Risk of systemic lupus erythematosus in patients with idiopathic thrombocytopenic purpura: population-based cohort study

We read with great interest the article by Zhu *et al.*¹ It was based on a national study regarding the association between idiopathic thrombocytopenic purpura (ITP) and the subsequent development of systemic lupus erythematosus (SLE), both representing clinically and genetically heterogeneous autoimmune diseases. According to the data presented in this study, the authors demonstrated that the patients with ITP had a 26 times higher risk of new-onset SLE in comparison with the control population.¹ Prevalence of ITP has been reported to be ranging between 7% and 30% in patients with SLE, while clinical characteristics of ITP in patients with SLE have been reported in several studies.² ITP is a haematological disorder characterised by thrombocytopenia, defined by low platelet counts, thus presenting with an increased bleeding risk due to an increased destruction of sensitised platelets by antibodies that react with glycoproteins expressed on platelets and megakaryocytes.³

Furthermore, this study by Zhu *et al.*¹ poses the intriguing question concerning the putative role of a shared genetic background as regards with the concurrence of ITP and SLE, an issue also discussed recently by Fanouriakis *et al.*⁴ Thus, although the main cause of ITP and SLE remains unidentified, various studies have pointed to certain polymorphisms in respective genes as potential factors for developing both ITP and SLE, thus suggesting a shared genetic predisposition in some cases. According to McGarvey *et al.*,⁵ 41 pathways are shared by ITP and SLE, and 27 genes are associated with both diseases. Moreover, a list of genetic polymorphisms leading to exacerbation of the disease in patients with ITP, such as *IL-10*-592C/A, *IL-4* VNTR, *IL-17F* rs763780, *IL-6*-174 G/C and interferon (*IFN*)-gamma 874 T/A, has been presented, with these factors also being associated with an increased risk of SLE.^{6,7} Notably, studies comparing molecular signatures of these two diseases do not seem to be promiscuous as regards the identification of a disease-specific signature, considering that a global expression profile of peripheral blood from patients with ITP identified an ITP-specific signature, which also included *IFN*-induced genes that have been observed in SLE as well.⁸

In conclusion, lessons learnt thus far from the genetic studies focusing on ITP and SLE suggest that the biological complexity of these diseases should not be underestimated, considering that identical gene variants have been previously associated with different clinical phenotypes, while, conversely, a significant clinical and molecular overlap has been identified between patients with mutations in different genes.⁹

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REFERENCES

- 1 Zhu F-X, Huang J-Y, Ye Z, *et al.* Risk of systemic lupus erythematosus in patients with idiopathic thrombocytopenic purpura: a population-based cohort study. *Ann Rheum Dis* 2020;annrheumdis-2020-217013.
- 2 Ziakas PDet *et al.* Lupus thrombocytopenia: clinical implications and prognostic significance. *Ann Rheum Dis* 2005;64:1366–9.
- 3 Iraqi M, Perdomo J, Yan F, *et al.* Immune thrombocytopenia: antiplatelet autoantibodies inhibit proplatelet formation by megakaryocytes and impair platelet production in vitro. *Haematologica* 2015;100:623–32.
- 4 Fanouriakis A, Bertsias G, Boumpas DT. Population-based studies in systemic lupus erythematosus: immune thrombocytopenic purpura or 'blood-dominant' lupus? *Ann Rheum Dis* 2020;annrheumdis-2020-217356.
- 5 McGarvey PB, Suzek BE, Baraniuk JN, *et al.* In silico analysis of autoimmune diseases and genetic relationships to vaccination against infectious diseases. *BMC Immunol* 2014;15:61.
- 6 Lee YH, Bae S-C. Association between interferon- γ +874 T/A polymorphism and susceptibility to autoimmune diseases: a meta-analysis. *Lupus* 2016;25:710–8.
- 7 Rischewski JR, Imbach P, Paulussen M, *et al.* Idiopathic thrombocytopenic purpura (ITP): is there a genetic predisposition? *Pediatr Blood Cancer* 2006;47:678–80.
- 8 Sood R, Wong W, Gotlib J, *et al.* Gene expression and pathway analysis of immune thrombocytopenic purpura. *Br J Haematol* 2014;140:99–103.
- 9 Demirkaya E, Sahin S, Romano M, *et al.* New horizons in the genetic etiology of systemic lupus erythematosus and lupus-like disease: monogenic lupus and beyond. *J Clin Med* 2020;9:712.