PSEUDO-THROMBOTIC THROMBOCYTOPENIC PURPURA DUE TO VITAMIN B12: A SYSTEMATIC REVIEW

L. Panepinto, M. Merlo, S.A. Alhamed, S. Moruzzi, L. Delfino, S. Suardi, L. Marzano, E. Malloggi, G.L. Bonisoli, G. Malfer, F. Presa, F. Pizzolo, S. Friso, N. Martinelli

Department of Medicine, Unit of Internal Medicine B, University of Verona, Verona, Italy

Background and aims. Vitamin B12 deficiency is known as a "great imitator" of many blood disorders, including thrombotic thrombocytopenic purpura (TTP). This similarity may lead to unnecessary TTP-specific treatments, with inappropriate costs and risks. The clinical features of pseudo-TTP due to vitamin B12 deficiency have mainly been described in case reports and a comprehensive understanding of its overall characteristics remains limited so far. The aim of this study was to evaluate the clinical and laboratory characteristics of patients with pseudo-TTP due to vitamin B12 deficiency.

Methods. Prompted by a case of pseudo-TTP identified at our Institute, we conducted a systematic review of the medical literature following the PRISMA statement. Specifically, we searched PubMed and Scopus from 1977 to 2025, using various keywords related to vitamin B12 deficiency and pseudo-TTP combined with Boolean operators. Finally, 55 cases remained eligible for the analysis (Figure 1).

Results. The study cohort comprised 30 males and 25 females with a mean age of 54±18 years. The most common presenting symptoms were non-specific fatigue and/or dyspnoea (n=44). Neurological symptoms were reported by 12 individuals, including altered mental status, paraesthesia, and gait instability. Bleeding was reported by 11 individuals, predominantly cutaneous (n=7). All the patients had thrombocytopenia and anaemia with altered haemolytic biomarkers and schistocytosis. Thrombocytopenia was mild-to-moderate (mean platelet count: 66,300±30,060/mcL; only 6 patients <30,000/mcL), while anaemia was severe (mean haemoglobin: 5.30±1.54 g/dL) with an unexpected low absolute reticulocyte count (46,200±40,980/mcL; only 3 patients >100,000/mcL). White blood cell counts were slightly low (4,812±2,693/mcL). Mean corpuscular volume (MCV) was substantially elevated (mean MCV: 110±15 fL; only 3 patients <90 fL). The PLASMIC score, when calculable, tended to be high, thus not helping to differentiate pseudo-TTP from real TTP. Many patients awaiting ADAMTS13 activity results, which ultimately ruled out TTP diagnosis, were initially treated with therapies for acquired TTP: plasma exchange (n=24), high-dose corticosteroids (n=16), and caplacizumab (n=3).

Conclusions. Vitamin B12 deficiency should be included in the differential diagnosis of TTP. In suspected conditions of thrombotic microangiopathy where platelet count is not too low, anaemia is marked with macrocytosis, and reticulocytosis is poor or absent, clinicians should raise consideration for vitamin B12 deficiency.

