Sir,

Pseudothrombocytopenia (Pstp) is an in vitro laboratory finding usually associated with the use of EDTA in blood collection tubes; it may cause unjustified alarm in the patient and physician, sometimes leading to the use of unwarranted diagnostic procedures or treatment. This rare phenomenon is related to in vitro platelet clumping caused by immunoglobulins (most often IgG) recognizing platelet antigens which are exposed on the membrane only in the presence of EDTA. Over the past 12 years we have collected about 200 cases of Pstp, almost always discovered during routine hematologic tests and sent to us for the treatment of vancomycin-resistant Enterococcus faecium (VREF) and methicillin-resistant Staphylococcus aureus infection. Can J Infect Dis 1995; 6(Suppl C), July 1995.

Transplacental transmission of EDTA-dependent pseudothrombocytopenia

Sir,

Pseudothrombocytopenia (Pstp) is an in vitro laboratory finding usually associated with the use of EDTA in blood collection tubes; it may cause unjustified alarm in the patient and physician, sometimes leading to the use of unwarranted diagnostic procedures or treatment. This rare phenomenon is related to in vitro platelet clumping caused by immunoglobulins (most often IgG) recognizing platelet antigens which are exposed on the membrane only in the presence of EDTA. Over the past 12 years we have collected about 200 cases of Pstp, almost always discovered during routine hematologic tests and sent to us for the treatment of vancomycin-resistant Enterococcus faecium (VREF) and methicillin-resistant Staphylococcus aureus infection. Can J Infect Dis 1995; 6(Suppl C), July 1995.

Key words
EDTA, pseudothrombocytopenia

Correspondence
Bruno Rotoli, M.D., Divisione di Ematologia, Università Federico II, via Pansini 5, 80131 Naples, Italy. Fax: international +39-081-7462165.

References

Acenocoumarol and 6-mercaptopurine: an important drug interaction

Sir,

Many drugs are known to interact with oral anticoagulants (OA), but the greater part of the reported interactions refer to warfarin. Acenocoumarol is the most widely used coumarinic derivative used in Spain as an OA. 6-MP is a metabolite of azathioprine, both used as immunosuppressant drugs in a variety of autoimmune disorders. 6-MP decreases warfarin activity, and severe bleeding was described in a patient on long-term warfarin treatment after discontinuing azathioprine.

Haematologica vol. 84(7) July 1999
In this paper, we report an increased acenocoumarol requirement in a patient receiving 6-MP. The patient was a 53-year old woman with an aortic prosthetic valve and aorto-coronary by-pass. She was on long-term OAT with acenocoumarol (mean dose 21 mg/week and mean INR=3.3) since January 1992 until August 1995. Her treatment included captopril, isosorbide trinitrate and furosemide. The level of hypocoagulability was measured every four weeks using bovine thromboplastin ISI=0.98 (Thrombotest from Nycomed, IMMUNO, Barcelona, Spain) with a mechanical coagulometer AMAX CS-90 (from Grifols-Movaco, Barcelona, Spain) assisted by a computer program (Sintromac from Grifols, Barcelona, Spain). Her dose of acenocoumarol was adjusted according to the results which were expressed as the INR as recommended by the Subcommittee of Standardization of the International Society on Thrombosis and Hemostasis. She had a mean INR = 3.37. In August 1995 she was diagnosed as having acute promyelocytic leukemia. Induction of specific treatment was excluded because of her age and cardiac disease. OAT was stopped and heparinization and all-transretinoic acid (ATRA) were started and continued until the end of September. From October 1995 she received 6-MP 100 mg daily p.o., methotrexate every two weeks i.v. and ATRA fifteen days every three months, for two years. During this time, liver damage was minimal (AST=60; ALT=70; total bilirubin = 1.2 mg/dL) and platelet count not less than 150×10^9/L. The level of hypocoagulability was, at that time, measured every two weeks. The dose of acenocoumarol was increased progressively from 21 mg/week when she started cytotoxic treatment to 70 mg/week in June 1996, with a mean INR=1.9. From June 1996 to November 1997, the patient maintained a mean INR=3.4 with a mean dose of 71 mg/week (see Table 1). When 6-MP was stopped, the patient continued receiving 70 mg/week for a week. At the end of this week, her INR had increased from 3 to 12. The acenocoumarol was stopped and reintroduced 24 hours later at her habitual dose (3 mg/day) without hemorrhagic complications. Although the interaction of azathioprine or 6-MP with acenocoumarol is not established, studies in rats indicate that 6-MP increases prothrombin synthesis or activation and decreases warfarin activity. An increase in warfarin requirements can be interpreted as a prothrombotic state in patients with disorders requiring immunomodulatory therapy. Our patient had a promyelocytic leukemia, known to cause a prothrombotic state. Our patient required a progressively increasing dose of acenocoumarol that she maintained during the remission period of the hematologic process; only when it finished, did she return to the normal requirements. In spite of the short life of acenocoumarol compared to warfarin, the increase of INR after stopping 6-MP was delayed, which suggests a metabolic interaction between 6-MP and OA, possibly induction of hepatic microenzymes activity, as seen with barbiturates. According to the behavior of our patient, OA dosage (acenocoumarol or warfarin) should be reviewed no later than a week after ending azathioprine or 6-MP and the OA dose reduced to the amount before 6-MP treatment.

Mª Angeles Fernández, Anabel Regadera, Justo Aznar
Unit of Anticoagulant Therapy. Department of Clinical Pathology, University Hospital “La Fe”, Valencia, Spain

Key words
Oral anticoagulants, 6-mercaptopurine, acenocoumarol

Correspondence
Mª Angeles Fernández, M. D., Unidad de Terapéutica Anticoagulante, Hospital Universitario “La Fe”, Avda Campaner, 21, 46009 Valencia, Spain. Phone: international +34-963868795 – Fax: international +34-963868730 – E-mail: muro@san.gva.es

References

Autologous peripheral blood stem cell transplantation in a patient with multiple sclerosis and concomitant Ph+ acute leukemia

Sir,  
Multiple sclerosis (MS) is a demyelinating disease of the central nervous system in which T-cell mediated immune destruction of myelin is thought to be pathogenetically relevant. Immunomodulating and immunosuppressive agents

Haematologica vol. 84(7): July 1999