To the editor:

The American Society of Hematology: a success at age 50; blood banking and sodium citrate

I enjoyed the excellent article by Drs Jaffe and Kaushansky, “The American Society of Hematology: a success at age 50.”

There is some controversy concerning the introduction of sodium citrate for blood transfusion and the establishment of the first blood bank in the United States.

Dr Luis Agote used sodium citrate for transfusion of whole blood for a patient on November 9, 1914. Instead of publishing his work in a medical journal, he gave the story to “LaPresna,” the leading newspaper of Buenos Aires. Two months later in the “New York Medical Record” of January 23, 1915, Dr Richard Lewisohn of Mt Sinai Hospital in New York reported on 2 cases in which he used citrate of soda for transfusion. Agote was considerably displeased because Lewisohn did not mention Agote in this report. Actually, Albert Hustin, a Belgian surgeon, used sodium citrate and glucose as an anticoagulant for blood transfusion on March 17, 1914. He performed his transfusion at St Jens Hospital in Brussels.

The first blood bank was established by Dr John S. Lundy, Head, Section of Anesthesia, at Mayo Clinic in 1935. He had kept citrated blood in the “ice box” for as long as 14 days and found that it could be administered with the usual benefits to the patient and without reaction. The Cook County Hospital began such a service in 1936. Thirty-two percent of Mayo Clinic transfusions were administered to nonsurgical patients. Two years later, Lundy

References

investigated quick freezing as a method of prolonging the shelf life of banked blood.

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To the editor:

MPL and JAK2 exon 12 mutations in patients with the Budd-Chiari syndrome or extrahepatic portal vein obstruction

The Budd-Chiari syndrome (BCS) and extrahepatic portal vein obstruction (EHVO) are splanchnic vein thromboses (SVT) that may occur as presenting complications of undiagnosed chronic myeloproliferative disorders (CMPD). Diagnosis of the underlying CMPD may be difficult because hemodilution, occult blood loss, and/or hypersplenism often mask hematologic signs of myeloproliferation.

Recently, molecular mechanisms underlying Philadelphia-negative CMPD have been partially elucidated. The somatic JAK2V617F mutation is found in more than 90% of patients with polycythemia vera and in up to 60% of those with primary myelofibrosis or essential thrombocythemia (ET). Gain-of-function mutations causing the amino acid substitutions W515L and W515K in the thrombopoietin receptor gene (MPL) have been found in 5% to 10% of patients with primary myelofibrosis and 1% to 2% of those with ET. Finally, JAK2 exon 12 mutations have been identified as other genetic variants in patients with JAK2V617F-negative polycythemia vera.

The JAK2V617F mutation can be detected in 34% to 60% of patients with SVT. However, CMPD can be diagnosed on the basis of peripheral blood counts and bone marrow (BM) biopsy in some SVT patients who do not harbor the JAK2V617F mutation. We analyzed peripheral blood DNA samples from 93 patients with SVT for the presence of the aforementioned MPL and JAK2 exon 12 mutations. Approval for these studies was obtained from the Maggiore Hospital Foundation; Milan, Italy, institutional review board. Informed consent was provided in accordance with the Declaration of Helsinki. Prevalence of the JAK2V617F mutation in the same group of patients has been reported previously. Samples were screened for the MPL mutations by 2 allele-specific PCR reactions and subsequent agarose gel electrophoresis. Each reaction included a forward primer (5'-TGGGCGGAAGTCTGACTCTTT-3', 250.0 nmol/L), a reverse primer (5'-GAAGTGGCGAAGCCGTAGGTT-3', 1.0 nmol/L), and a second allele-specific, internal forward primer (5'-GGCCCTGCTGCTGCTGAGGCTGCTTT-3' and 5'-GGCCCTGCTGCTGCTGAGGCA-3' for the MPL515L and the MPL515K mutations, respectively, 1.0 nmol/L). Annealing temperature was 66°C. The wild-type PCR product is 218-base pairs (bp), but mutant samples show an additional 176-bp band. The method has a 5% to 10% sensitivity in terms of allele frequency. Samples with the mutations were confirmed by DNA sequencing.

Two EHVO patients who had been previously diagnosed as ET on the basis of peripheral blood counts and bone marrow biopsy had the MPL515K mutation. A third MPL515K-positive patient with EHVO was also JAK2V617F-positive, the allele frequency of both mutations being less than 50%; the only sign of possible CMPD in this subject was a platelet count at the upper normal limit (412 × 10^9/L). No patient had MPLW515L or JAK2 exon 12 mutations. Recently, a large study involving 241 patients with SVT could not detect MPL or JAK2 exon 12 mutations. The discrepancy with our findings may be due to the low prevalence of MPL mutations in this population of patients. In our series, 49 of 93 patients were diagnosed as CMPD; of these, 37 (75.5%) had JAK2 or MPL mutations. The sensitivity of BM biopsy in the detection of CMPD was 94.0%. Because interobserver variability may limit the usefulness of BM examination, this result further suggests that the search for JAK2 and MPL mutations associated with CMPD is warranted in patients with BCS and EHVO, because they can establish the clonal nature of the disease and may indicate the need for cytoreductive treatment, even in the absence of an overt myeloproliferative disease.

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References

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