SLRL Study Detects Monoclonal B Cells in Blood Donors

Blood donor screening by flow cytometry has been performed in Saint Luke’s Hospital laboratory since 1995. The laboratory routinely utilizes unidentified samples from blood donors for quality control and reference range procedures. During the period of January 1995 through December 1998, a total of 656 samples from randomly selected donors were analyzed. Three of these samples (0.5%) unexpectedly demonstrated abnormal monoclonal B cells. Based on these findings, a larger research study was undertaken to establish the prevalence of monoclonal B-cell lymphocytosis (MBL) in blood donors.

Monoclonal B-cell lymphocytosis (MBL) describes a clonal expansion of B-lymphocytes in the absence of clinical and diagnostic features of chronic lymphocytic leukemia (CLL) or other B-lymphoproliferative disorders. Diagnostic criteria for MBL were proposed in 2005 by a subcommittee of the International Familial CLL consortium. The distinguishing feature is the stable presence of a monoclonal B-cell population expressing a disease-specific phenotype, with an overall kappa:lambda ratio >3.0 or <0.3. The most specific hematological exclusion criterion is an absolute B-lymphocyte count >5 x 10^9/l, which is the diagnostic threshold for CLL.

Blood samples were obtained from 5,141 randomly selected donors during the period of June 2000 through July 2002. Seven donors were found to have MBL, giving an overall prevalence of 0.14%. Consistent with MBL/CLL demographic patterns, most were male and over 65 years of age. Interestingly, the two youngest donors with MBL were the only females. On the basis of hematologic and immunophenotypic findings, one donor was classified as CLL due to the presence of B-cell lymphocytosis. The remaining six donors appeared to meet criteria for MBL.

This is the first report of the prevalence of MBL/CLL in blood donors. The clinical importance of these findings with regard to blood transfusion has not been established. Approximately 15 million allogeneic blood donations are collected annually in the United States. Based on our study prevalence of 0.14 %, which is likely a low estimate, 21,000 donations annually may contain MBL. Our initially observed prevalence of 0.5% would represent 75,000 annual donations. Recent evidence suggests that MBL patients have a low but distinct probability of progression to CLL, so blood donors with MBL may remain healthy enough to donate repeatedly. It is worth mentioning that recipients of blood transfusions are not healthy individuals, and many are immunocompromised. The use of leukocyte reduction techniques may effectively reduce the theoretical risk of transfusing MBL. However, the ability of MBL or CLL clones to persist or proliferate in transfused recipients is unknown.

This study was funded in part by a grant from the Saint Luke’s Hospital Foundation and has been accepted for publication in the British Journal of Haematology.

Lessons Learned from Community Based Thyroid Screening

A retrospective analysis of the computerized database of a large health medical organization in Tel Aviv, Israel that included 2800 primary care physicians and 2.3 million insured persons, recently revealed some very interesting findings about routine thyroid screening (Arch Intern Med 2007;167(14):1533-38). A total of 422,242 persons aged 21 years and older with no known thyroid disease or previous treatment with thyroid medications, who had at least one TSH measurement during 2002 and were available for follow-up through 2006, were included in the study. The TSH reference range used for this study was 0.35-5.5 mIU/L.

Ninety five percent of the initial TSH concentrations were within normal limits, whereas 3.7% were elevated and 1.2% were decreased. Thirty seven percent of patients with abnormal initial TSH levels
were treated with medication and excluded from further analysis. The remaining patients had an average of 3.7 additional TSH measurements during the 5 year follow-up.

- Of the patients with initially normal TSH results, 98% remained normal at the end of 5 years.
- Of the patients with initially elevated TSH results, 38% remained elevated and 62% returned to normal.
- Of the patients with initially decreased TSH results, 47% remained decreased and 52% reverted to normal.

Two important conclusions can be drawn from this study. When TSH concentration is normal and there are no new clinical indications of a thyroid disorder, the likelihood of a subsequent abnormal TSH level within 5 years is only 2%. This finding supports recent evidence based recommendations against population based TSH screening.

Secondly, more than 50% of patients with abnormal TSH results revert to normal without medical intervention, suggesting that at least two TSH measurements should be obtained before considering treatment.

**Leukocytosis is a Major Risk Factor for Thrombosis in Patients With Chronic Myeloproliferative Disorders**

White blood cell count has previously been linked to the incidence of thrombosis in the general population. Polycythemia vera (PV) and essential thrombocythemia (ET) are chronic myeloproliferative disorders which are considered hypercoagulable states, due to the high incidence of thrombotic complications, associated with high morbidity and mortality. Ten percent to 30% of patients with these disorders present with major thrombotic complications, and a similar proportion develop a thrombotic complication during their disease course. Arterial thromboses, especially affecting the cerebral or coronary arteries, are more common than venous thromboses. Recent studies on the pathogenesis of thrombosis in myeloproliferative disorders have suggested a role for leukocyte activation, and leukocyte interaction with platelets and endothelial cells. Two recent studies investigated a possible association between leukocyte count and thrombosis in PV and ET.

In PV, major known risk factors for thrombosis include age over 65 years and previous thrombotic history. A recent study (Blood. 2007;109:2446-2452) analyzed the role of other potential risk factors, including white blood cell count and classic cardiovascular risk factors, in a large database of 1638 patients with PV. Patients with a white blood cell count >15,000/uL had a significant increase in the risk of thrombosis compared with those with a white blood cell count below 10,000/uL, mainly due to an increased risk of myocardial infarction (hazard ratio 2.84). Smoking was also associated with an increased risk of arterial thrombotic events.

In ET, age over 60 years and prior thrombotic events are known independent predictors of vascular complications. These two factors are widely used to stratify thrombotic risk in these patients for cytoreductive drug treatment decisions. A recent study (Blood. 2007;109:2310-2313) of 439 patient with ET investigated whether an increased white blood cell count was associated with thrombosis, and whether this effect could be modulated by cytoreductive therapy. The authors reported that a white blood cell count greater than the median value (8,700/uL) at diagnosis was associated with an increased risk of thrombosis during follow-up (hazard ratio 2.3), and that hydroxyurea-induced lowering of the white blood cell count was associated with a reduction of this thrombogenic risk. The presence of JAK2 mutation was not identified as a risk factor for thrombosis in this study, despite a significant association between the mutation and leukocytosis.

Interestingly, neither hematocrit nor platelet count elevations influenced thrombotic risk in either PV or ET. In summary, leukocytosis is a significant risk factor for thrombosis in PV and ET. The authors of these studies suggest that leukocyte count should be considered in defining vascular risk in patients with myeloproliferative disorders, and should be taken into account as an additional factor in cytoreductive treatment decisions. Validation of these findings in prospective studies is indicated.

**Alkaline Phosphatase Reference Range Change**

The lower end of the reference range for alkaline phosphatase has been changed from 53 to 42. The new reference range is 42 – 128 IU/L.