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Is Hemoglobin Variant Analysis Helpful in the Diagnostic Work-up of Patients Revealing Microcytic Erythrocytosis on Complete Blood Count?

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INTRODUCTION

Microcytic erythrocytosis is an abnormal CBC (complete blood count) finding that is under-recognized, poorly understood, and consequently under-utilized in patient care. It is characterized by decreased MCV and increased RBC count. Its etiology is likely multifactorial and includes thalassemias and hemoglobinopathies. The focus of our study was to determine the relative prevalence of hemoglobin-associated disorders in patients revealing microcytic erythrocytosis on CBC and to demonstrate whether or not hemoglobin variant analysis should be included in the diagnostic work-up of such cases.

METHODS

Data from all CBCs within a 2 year period at Jefferson were reviewed, and patients meeting the inclusion criteria of microcytosis (MCV <80 fL) and erythrocytosis (RBC count ≥5.2x10^6 T/L (Female) and >6x10^6 T/L (Male)) were selected. The sample size was 137 patients with 87 females and 50 males; ages ranged from: 1-91 years with median age of 46 years. The racial distribution comprised of 49 Caucasians, 44 African Americans, 24 Asians and 20 unspecified. Hemoglobin values for the patients ranged from 7.2– 16.1 g/dL, MCVs ranged from 54.5-79 fL and RBC count ranged from 5.2-7.5x 10^6 T/L. 74 patients had mild anemia while 63 patients had hemoglobin levels within the gender-specified reference range. The results of hemoglobin variant analysis performed by high-performance liquid chromatography on these patients were reviewed.

RESULTS

Hemoglobin Variant Analysis Pattern Consistent With	Number of Patients	Percentage of Patients
Beta-thalassemia trait	70	51.1
Delta/beta-thalassemia trait	1	0.7
Hemoglobin E disease	4	2.9
Hereditary persistence of fetal hemoglobin (HPFH)	1	0.7
Possible HPFH	4	2.9
Beta-thalassemia with HPFH	2	1.5
Delta/beta-thalassemia with iron deficiency anemia	1	0.7
Hemoglobin C trait with beta-thalassemia	1	0.7
Hemoglobin C trait with possible alpha-thalassemia	2	1.5
Hemoglobin C with HPFH	1	0.7
Unidentified hemoglobinopathy with possible delta/beta-thalassemia	2	1.5
Hemoglobin S trait combined with beta and possible alpha-thalassemia	3	2.2
Hemoglobin S trait with beta-thalassemia	1	0.7
Normal pattern	44*	32.1
Total # of patients	137	100

Table 1: Relative prevalence of hemoglobin-associated conditions in patients revealing microcytic erythrocytosis on CBC.

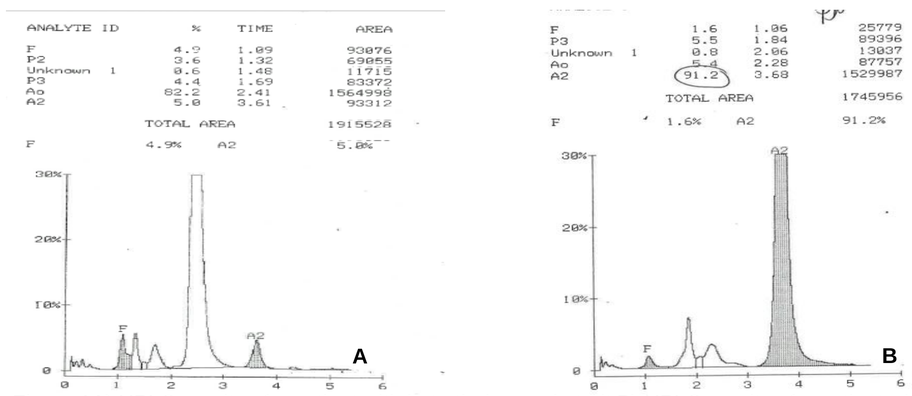

Figure 1A) HPLC results of a patient with beta thalassemia trait B) HPLC results of a patient with Hemoglobin E disease

DISCUSSION

- 93 of the 137 (67.9%) had a thalassemia trait and/or a hemoglobinopathy. Amongst these, beta-thalassemia trait topped the list, followed by hemoglobin E disease, possible HPFH,HPFH and delta-beta-thalassemia.
- The diagnosis of possible HPFH was entertained based on mild elevation of hemoglobin F (2.3% to 3.1%) by HPLC. Since HPFH is typically associated with normal MCV or RBC count, the microcytic erythrocytosis noted in these patients likely represent an associated undiscovered alpha-thalassemia trait.
- Majority, if not all, of the 44 cases with normal hemoglobin variance analysis pattern also represent patients with possible α-thalassemia trait, Microcytic erythrocytosis is uncommon in normal patients and alpha thalassemia is a diagnosis of exclusion (requires DNA analysis studies not performed here)
- Compound heterozygous conditions for either hemoglobinopathies and/or thalassemia(s) comprised 12 cases. Unspecified abnormal hemoglobins detected by the HPLC method remain unidentified as no additional analyses had been performed in both cases.
- The diagnosis of delta/beta-thalassemia and concomitant iron deficiency anemia made in 1 patient was supported by the laboratory findings of increased hemoglobin F, decreased hemoglobin A2 and decreased serum ferritin.
- With all these potential considerations, over 96% of the studied cases of microcytic erythrocytosis may be categorized as having a possible thalassemia trait and/or a hemoglobinopathy.

CONCLUSION

The answer to the question our study title proposed i.e. “Is Hemoglobin Variant Analysis Helpful in the Diagnostic Work-up of Patients Revealing Microcytic Erythrocytosis on Complete Blood Count?” is unequivocally “yes”. Based on the observed extremely high positive yield of hemoglobin variant analysis in determining the etiology of erythrocytosis, we recommend that the abnormality of microcytic erythrocytosis should automatically be flagged and such specimens should be reflexively processed for hemoglobin variant analysis for each previously undiagnosed patient.