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Evaluation of thrombocytopenia in the hematology clinic: a case series from a large tertiary care center

TO THE EDITOR: Thrombocytopenia is a common hematologic condition with multiple causes ranging from benign to potentially life-threatening disorders. Few evidence-based recommendations are available regarding a specific diagnostic approach to thrombocytopenia in the hematology clinic [1-3]. Although a limited test repertoire may be adequate in many cases, more extensive testing may be warranted in others. We sought to analyze the utilization and impact of different laboratory evaluation strategies in the initial workup of thrombocytopenia.

We included 68 patients seen at our outpatient hematology clinic between 2010 and 2015 for an initial workup of thrombocytopenia of unclear etiology (Table 1). The median age at thrombocytopenia diagnosis was 60 (range, 17-90) years, and the majority of patients (64.7%) were male. The median platelet count at diagnosis was 91 (range, 3-146)×10^9/L: 30 patients (44.1%) with a platelet count of 100-146×10^9/L, 26 (38.2%) with a platelet count of 50-100×10^9/L, and 12 (17.6%) with a platelet count of <50×10^9/L.

Although 37 patients (54.4%) and 27 patients (39.7%) underwent evaluation for autoimmune causes and infectious diseases, respectively, only the following few test results were positive: anti-glycoprotein platelet antibodies (N=2; although routine use of this testing is not recommended [4]), anti-nuclear antibodies (N=4), elevated rheumatoid factor level (N=1), and anti-IgM Epstein-Barr virus antibody (N=1). None had hepatitis B or C, or HIV despite routine use of these tests. Bone marrow biopsies performed on 16 patients (23.5%) revealed abnormalities in 2 patients (both with coexisting anemia and leukopenia at the time of the thrombocytopenia workup): one with hairy cell leukemia and one with myelodysplastic syndrome (refractory anemia with excess blasts-2).

Based on the results of these tests, 27 patients (39.7%) were diagnosed with primary immune thrombocytopenia, and 23 patients (33.8%) were diagnosed with thrombocytopenia due to possible multifactorial causes, 5 (7.4%) suspected to be due to drugs (tacrolimus, methotrexate, bosentan, amitriptyline, or adalimumab), 4 (5.9%) due to hypersplenism, 4 (5.9%) due to unclear etiology, and 2 (2.9%) due to hematologic malignancies; 1 patient (1.5%) each was diagnosed with thrombocytopenia secondary to lupus, liver cirrhosis secondary to non-alcoholic steatohepatitis associated with hypersplenism, and gestational thrombocytopenia.

Table 1. Evaluation of thrombocytopenia in the hematology clinic.

Type of workup	N (%) of patients (N=69)	Test results	
		Positive (%)	Negative (%)
Abdominal ultrasound	7 (10.3%)	3 (42.9%): chronic liver disease with hypersplenism in 2[a] and hypersplenism in 1	4 (57.1%)
Autoimmune workup	37 (54.4%)		
Anti-glycoprotein platelet antibody	33 (48.5%)	2 (6.1%)	31 (93.9%)
Antinuclear antibody	21 (31.0%)	4 (19.0%)	17 (81.0%)
Lupus anticoagulant	4 (5.9%)	0 (0%)	4 (100%)
Rheumatoid factor	13 (19.1%)	1 (7.7%)	12 (92.3%)
Bone marrow biopsy	16 (23.5%)	2 (12.5%): myelodysplastic syndrome and hairy cell leukemia	14 (87.5%)
Infectious disease evaluation	27 (39.7%)		
Cytomegalovirus	6 (8.8%)	0 (0%)	6 (100%)
Epstein-Barr virus	5 (7.4%)	1 (20%)	4 (80%)
Hepatitis A virus	2 (2.9%)	0 (0%)	2 (100%)
Hepatitis B virus	10 (14.7%)	0 (0%)	10 (100%)
Hepatitis C virus	22 (32.4%)	0 (0%)	22 (100%)
Human immunodeficiency virus	22 (32.4%)	0 (0%)	22 (100%)
Helicobacter pylori	4 (5.9%)	0 (0%)	4 (100%)
Peripheral blood smear	3 (63.2%)	4 (9.3%): large, elongated, well-granulated platelets (N=2); rouleaux formation; target cells; lymphocytes with circumferential hairy cytoplasmic projections	39 (90.7%)

[a]One of these patients with chronic liver disease also had other possible etiologies of the thrombocytopenia, including medications and possible Epstein-Barr virus reactivation, and hence was included as 1 among 23 cases with a multifactorial cause.

Patients with thrombocytopenia are often recommended to undergo a variety of tests, much of which may not be indicated and/or diagnostically helpful. In this series, we found that although a large percentage of patients underwent multiple laboratory tests and pathologic evaluation, these tests often did not offer significant insight into the etiology of the thrombocytopenia. This is congruent with results from other studies specifically focusing on bone marrow biopsies in the workup of thrombocytopenia [1, 2] and further adds to the literature with regard to autoimmune and infectious workup. Additionally, nearly half of the patients in this series had a platelet count $>100\times10^9$/L, which may in some cases be considered a normal variant [3].

In summary, evaluation of thrombocytopenia should vary based on individual patient history and risk factors rather than a one-size-fits-all testing panel. Our study was based on a small cohort of patients but is likely representative of clinical practice at many large tertiary care centers. Large-scale prospective studies may be helpful to define the optimal workup for thrombocytopenia and formulate a protocol for cost-effective workup by stratification of clinical risk factors.

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Authors' Disclosures of Potential Conflicts of Interest

No potential conflicts of interest relevant to this article were reported.

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Microangiopathic hemolytic anemia as initial presentation of recurrent colon cancer

TO THE EDITOR: Microangiopathic hemolytic anemia (MAHA) refers to mechanical hemolytic anemia characterized by red blood cell fragmentation or schistocytes on peripheral blood (PB) smear [1]. MAHA is observed in various conditions such as thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), disseminated intravascular coagulation (DIC), systemic infection, and immune disorders [2-4]. MAHA can also occur rarely in malignant tumors as paraneoplastic syndrome. Gastric cancer is the most frequent malignancy associated with MAHA, followed by cancers of the breast, prostate, lung and cancer of unknown origin. Colon cancer presenting with MAHA is much rarer, and only a few cases have been reported [2, 3, 5]. In most cancer-related MAHA (CR-MAHA) cases, MAHA is detected at initial diagnosis of cancer. However, in about 20% of cases, it emerges at the time of cancer recurrence, particularly in gastric and breast cancers, and usually reflects late stage of disease [5]. When MAHA presents as the first sign of recurrent malignancy, the underlying cause may not be suspected initially, leading to inappropriate management. Herein, we describe a case of relapsed colon cancer which presented no sign of recurrence except MAHA as the initial manifestation.

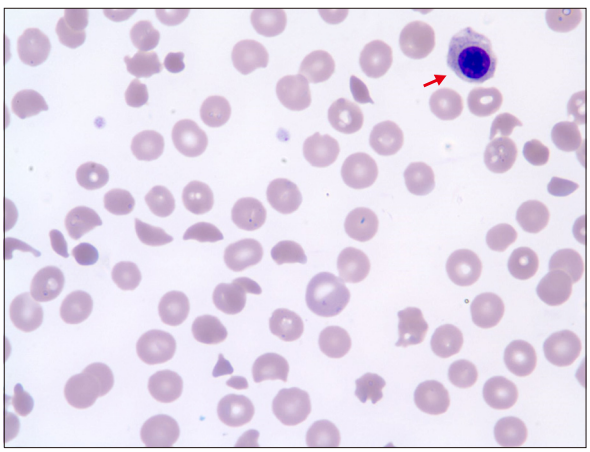

Fig. 1. Schistocytes, polychromasia and nucleated RBC (arrow) in peripheral blood (Wright stain, ×1,000).