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Respiratory syncytial virus infection is strongly correlated with decreased mean platelet volume

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SUMMARY

Background: To date, infections have usually been associated with elevations of the mean platelet volume. We correlated infection with respiratory syncytial virus (RSV) with changes in mean platelet volume (MPV).

Methods: A consecutive series of patients with positive and negative rapid RSV assays and viral cultures, as well as children under 10 years of age with bronchoscopy for pneumonia or airway obstruction, were compared.

Results: The MPV was significantly lower in patients with positive versus negative rapid RSV assays (9.7 ± 0.8 vs. 10.5 ± 0.9 fl, $p < 0.001$), as well as viral cultures (9.9 ± 1.0 vs. 10.5 ± 1.0 fl, $p < 0.001$). Children with RSV undergoing bronchoscopy ($n = 7$) also had significantly lower MPV than children without RSV ($n = 79$) (8.8 ± 1.0 vs. 10.2 ± 1.1 fl, $p < 0.004$). An MPV <8.9 fl had a sensitivity of 71% and specificity of 49% for RSV in children undergoing bronchoscopy.

Conclusions: We conclude that infection with RSV is associated with decreased MPV and this may be clinically useful in children undergoing bronchoscopy.

1. Introduction

The mean platelet volume (MPV) is a laboratory value that is defined as the mean volume of a large number of platelets as measured on automated hematology machines. MPV is associated with many factors including platelet age (younger platelets are larger), and is measured to help evaluate abnormalities in platelet function or number. MPV has also been associated with a wide variety of different medical and non-medical conditions. Elevations of the MPV have been described in smokers,[1] high elevation living,[2] diabetes,[3] obese patients,[4,5] and wine drinkers.[6] In addition, elevated MPVs are seen in patients who have thrombocytopenia,[7–9] hypothyroidism,[10] congestive heart failure,[11] right ventricular enlargement,[12] acute pulmonary embolism,[12] stroke,[13] acute myocardial infarction,[14] unstable angina,[15] and hypoxic chronic obstructive pulmonary disease.[16] Higher MPVs are associated with autoimmunity in general,[17] as well as psoriasis,[18] Raynaud's disease,[19] rheumatoid arthritis, and ankylosing spondylitis, and this correlates with the degree of activity as well as lack of treatment.[20,21]

In contrast, decreases in MPV have most commonly been associated with anemia[22] and chronic renal failure,[23] but have also been described in patients with vascular malformations,[24] as well as acute appendicitis,[25] acute pancreatitis,[26] ulcerative colitis, and Crohn's disease (which also correlates with the severity of the activity and is reversed with therapy).[27–30]

Only a few studies have examined the effects of infection on MPV. In a canine model, endotoxemia was associated with an increase in MPV,[31] and in humans, tuberculosis infection has been associated with a higher MPV which decreases with therapy.[32] Increased MPVs are also seen with lower platelet counts in patients with Crimean-Congo hemorrhagic fever.[33] Decreases in MPV have also been associated with some infections, including sepsis,[34] hookworm,[35] and Trichinella.[36] Recently, we noticed that some patients with infection with respiratory syncytial virus (RSV) had relatively low MPVs. To investigate this, we examined MPVs in a consecutive series of patients in a variety of settings.

2. Methods

This study was approved by the Institutional Review Board. A consecutive series of patients with positive and negative rapid RSV assays and viral cultures from respiratory specimens, as well as children under 10 years of age with bronchoscopy for pneumonia or airway obstruction, were compared. Searches began in January of 2012 and were conducted retrospectively until either 100 patients were obtained or no more cases were identified in the

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electronic record back to 2005. Patients with underlying hematologic diseases were excluded.

MPV was assessed on Sysmex 2100 hematology instrumentation. Reference ranges were 7.7–13.2 fl. The rapid RSV assay was performed using the BinaxNow RSV by Inverness Medical.

Specimens for viral culture were submitted fresh in sterile containers using viral transport medium VTM-M4 and inoculated onto shell vials of MRC5-CV1 (H&V), Super E-Mix, and R-Mix Too monolayer cultures. Cytopathic effect (CPE) confirmation for RSV and blind staining for RSV were performed at 48 h, 3 days, and 5 days of culture using an indirect fluorescent antibody respiratory stain (Quidel Corp., Santa Clara, CA, USA). Patients who were positive with the rapid test did not have cultures performed. Cultures were done on patients with either no rapid RSV test or in whom the rapid test was negative.

The statistical analysis was performed using a two-tailed Student's *t*-test and a significance level of 0.05%.

3. Results

A consecutive series of 100 patients with ordered complete blood counts were used as a control group to verify our normal range. These patients had a mean MPV of 10.8 ± 0.9 fl.

MPV was compared in patients with rapid RSV tests (58 patients) and viral cultures (100 patients). These patients did not have an underlying hematologic disease and were both children and adults (mean age 38 years, range 16–91 years, 112 patients aged <18 years). They included 69 males and 89 females.

The MPV was significantly lower in patients with positive versus negative rapid RSV assays (9.7 ± 0.8 vs. 10.5 ± 0.9 fl, $p < 0.001$, $n = 100$ each), as well as viral cultures (9.9 ± 1.0 vs. 10.5 ± 1.0 fl, $p < 0.001$). Nevertheless, there was significant overlap between these two groups. Platelet counts were not significantly different between any of these four groups (342 ± 121 vs. $327 \pm 171 \times 10^9$/l, $p = 0.47$, and 350 ± 144 vs. $338 \pm 158 \times 10^9$/l, $p = 0.63$, respectively). Hemoglobin was not significantly different between these four groups (11.6 ± 1.4 vs. 11.9 ± 1.2 g/dl, $p = 0.11$, and 12.1 ± 1.8 vs. 11.7 ± 1.0 g/dl, $p = 0.07$).

Children with RSV undergoing bronchoscopy ($n = 7$) also had significantly lower MPV than children without RSV ($n = 79$) (8.8 ± 1.0 vs. 10.2 ± 1.1 fl, $p < 0.004$). An MPV <8.9 fl had a sensitivity of 71% and specificity of 49% for RSV in children undergoing bronchoscopy.

4. Discussion

We were motivated to do this study by an incidental finding of a very low MPV in a child with RSV. Our results support the idea that infection with RSV is associated with a decrease in MPV regardless of whether the infection is detected by rapid assay or culture. While significant, this difference is unlikely to be large enough to be useful in most clinical settings. However, in children who are undergoing bronchoscopy for presumptive pneumonia or airway obstruction, an MPV <8.9 fl was relatively sensitive and specific for infection with RSV. This change was not due to anemia, since there was no significant difference in hemoglobin between the RSV-positive and RSV-negative patients.

Measuring MPV can be problematic. MPV increases with prolonged storage in ethylenediaminetetraacetic acid (EDTA)[37] and there is variation in the measurement between analyzers, although there is substantial work to standardize this.[38] In this study, all measurements were made at the same hospital on the same analyzer, and specimens were received and processed in the usual fashion without substantial delays in measurement.

Changes in MPV are quite common in a variety of normal and pathologic conditions. Autoimmune and cardiac conditions and most infections measured to date tend to lead to an elevated MPV. This elevated MPV is often thought to be due to an increase in young platelets that are larger than more mature platelets. In contrast, vascular malformations and inflammatory conditions involving the bowel are often associated with a decrease in MPV. The mechanism of action of this change is not fully understood. Whether fragmentation of the platelets is involved is not known. Nevertheless, the most common cause of a decreased MPV is anemia, which is not known to cause platelet fragmentation. The specific mechanism of action of RSV on MPV is not known. As part of this study we examined the MPV of patients with other types of viral infections and could not demonstrate a consistent relationship between these other viral infections and changes in MPV. Thus we suspect that the effect of RSV on MPV is specific to this virus, at least among the commonly detected viruses in our hospital.

There are several limitations to this study. We chose to study MPV at the time of specimen collection for RSV. It is possible that the MPV changed over the course of the admission and the illness, and if so, we were not able to document this change. Similarly, our assessments of hemoglobin and platelet count were also performed at the time of specimen collection. It is possible that these variables also could have changed over the course of the illness. In addition, the timing of the specimen collection likely varied between the patients course of illness. We were not able to control for this variable. Finally, interventions by the medical staff to treat the illness were not controlled for in this study.

In conclusion, we have shown that infection with RSV as determined by both rapid testing and culture is associated with decreased MPV. This may be particularly useful clinically in children undergoing bronchoscopy.

Conflict of interest: No conflict of interest to declare.

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