Human granulocytic anaplasmosis (HGA) is an emerging tickborne infection caused by the bacterium Anaplasma phagocytophilum. Symptoms include fever, headache, and myalgias, and typical laboratory findings include leukopenia and thrombocytopenia. Polymerase chain reaction (PCR) is the preferred method for the diagnosis of acute infection, with a sensitivity and specificity nearing 100%. At our institution, Anaplasma PCR is over-utilized with only a 3-4% positivity rate. To improve this, a phase 1 retrospective analysis was performed to determine if common complete blood count (CBC) laboratory parameters could exclude Anaplasma infection. A screening algorithm was then created and prospectively evaluated during phase 2 of the study through a mock stewardship protocol.

Phase 1 Retrospective Analysis, Continued

In Phase 1, there were three PCR-positive patients whose counts were above the WBC threshold of 11,000 cells/µL and/or PLT threshold of 300,000 cells/µL.

- Patient 1 had a history of chronic lymphocytic leukemia (CLL) and an elevated WBC count of 33,430 cells/µL at the time of diagnosis (Figure 2). Closer analysis revealed the patient developed a relapse leukemia and thrombocytopenia during his Anaplasma infection, which resolved with treatment. These findings illustrate the organism’s effect on these cell lines and provide further support for the use of these laboratory parameters as potential markers of Anaplasma infection.

- Patient 2 had a history of type 1 diabetes mellitus and presented with refractory hyperglycemia and confusion. He required an ICU-level of care due to a vasopressor requirement and was found to have co-infection with Borrelia burgdorferi and Anaplasma phagocytophilum.

- Patient 3 had a history of autoimmune hemolytic anemia and had undergone splenectomy in the past. Both his WBC and PLT counts were slightly above the thresholds.

Phase 2 Prospective Mock Stewardship

Methods

Mock stewardship was performed over a six-month period. Daily reports of the WBC and PLT counts associated with each Anaplasma PCR test were reviewed by microbiology leadership. If a CBC was not obtained by the ordering clinician, an offline CBC was performed on the sample collected for Anaplasma PCR testing. PCR testing was “accepted” if the rejection criteria were not met. If the sample met laboratory criteria for “rejection,” a committee comprised of infectious diseases specialists, microbiologists, and pathologists reviewed to determine if approval should be granted based on clinical criteria. Approval was granted if the subject was critically ill requiring intensive care level of support or had one of the following conditions resulting in a high degree of immunosuppression: solid organ transplantation; stem cell or bone marrow transplantation; leukemia; lymphoma; aspergillosis; or the use of high dose immunosuppressive therapy.

Results

663 Anaplasma PCR tests were analyzed over the 6-month period. Of those, 155 (23%) met CBC rejection criteria and were reviewed by committee (Table 1). Of those, 110 (71%) tests were mock refused and 45 (29%) were mock accepted based on clinical criteria.

<table>
<thead>
<tr>
<th>Anaplasma PCR</th>
<th>Total</th>
<th>Negative</th>
<th>Positive</th>
<th>Negative tests cancelled (including clinical criteria)</th>
<th>Negative tests cancelled (excluding clinical criteria)</th>
<th>Positive tests accepted</th>
</tr>
</thead>
<tbody>
<tr>
<td>663</td>
<td>638 (96)</td>
<td>25 (4)</td>
<td>110 (17)</td>
<td>155 (23)</td>
<td>24 (36)</td>
<td></td>
</tr>
</tbody>
</table>

Table 1. Implementation of the laboratory stewardship algorithm in the Phase 2 study.

Conclusion and Next Steps

A CBC-based stewardship algorithm (WBC ≥ 21 K/µL and PLT ≥ 300 K/µL) can be used to improve Anaplasma PCR utilization by reducing unnecessary Anaplasma PCR testing by 23%. An upcoming Phase 3 study will implement the Anaplasma PCR stewardship algorithm using these criteria.

References