Challenges faced by laboratories in differentiating between non-neoplastic, reactive lymphocytes and abnormal lymphocytes, neoplastic in a blood smear

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Introduction

Manual blood film reviews are performed after detecting abnormal counts, instrument flags or when the complete blood count (CBC) results fall outside of defined criteria. Automated analyzers are becoming more sophisticated adding new technology and improving laboratory workflow; however, hematological abnormalities such as the presence of abnormal leukocytes, abnormal red cell and platelet morphology is still dependent on the ability of a skilled technologist to identify abnormalities and subsequently refer to a hematologist, pathologist and/or laboratory physician.1,2

Differentiating between non-neoplastic, reactive lymphocytes and abnormal lymphocytes, neoplastic is dependent on the an individual’s experience as well as the available clinical information.3 Laboratories should have protocols for when a manual smear review is required, which should be based on clinical evidence or published criteria.4 The International Society for Laboratory Hematology (www.islh.org) has published consensus guidelines recommending slide review for a first time absolute lymphocytosis (adults >5.0 × 10^9/L, >7.0 × 10^9/L in children <12 years old), and atypical/ variant lymphocyte or blast flagging. The ability to differentiate between reactive (non-neoplastic) lymphocytes and neoplastic lymphocytes, during slide review can aid in a rapid diagnosis, and may be crucial for initiating prompt therapeutic interventions.

The Quality Management Program—Laboratory Services (QMP–LS) provides proficiency testing for peripheral blood morphology. A recent survey (November 2013) demonstrated some laboratories experienced difficulties distinguishing reactive lymphocytes from neoplastic lymphocytes. This poster illustrates a summary of the data obtained from the survey.

Methods

QMP–LS distributed a peripheral blood smear obtained from a patient sample diagnosed with infectious mononucleosis to assess laboratory performance on white blood cell (WBC) differential and descriptive morphology. Laboratories were provided with a typical clinical history of a young adult presenting with fever and sore throat. The laboratory data including the leukocyte count of 10.9 × 10^9/L was provided (Table 1). The monospot result (positive) was not provided.

Table 1. Laboratory Data

<table>
<thead>
<tr>
<th>Leukocyte count</th>
<th>Monospot result</th>
</tr>
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<tbody>
<tr>
<td>10.9 × 10^9/L</td>
<td>Positive</td>
</tr>
</tbody>
</table>

Results

A total of 162/173 (94%) of participating laboratories included reactive lymphocytes in their WBC differential count. Of these, 151 (87.2%) laboratories included only reactive lymphocytes in their differential, and were assessed as having provided a correct differential (Figure 1).

A total of 18 (10.5%) laboratories reported the presence of other abnormal WBC and were assessed as having provided an incorrect differential. Two (1.2%) laboratories reported reactive lymphocytes and blasts, and one (0.6%) laboratory reported both blasts and neoplastic lymphocytes. Five (2.9%) laboratories reported neoplastic lymphocytes, 9 (5.2%) reported both reactive and neoplastic lymphocytes, and 1 (0.6%) reported neither reactive lymphocytes nor neoplastic lymphocytes.

Additionally, four (2.3%) laboratories commented that reactive lymphocytes were present, but did not include them as a separate category in the differential count.

Out of 173 laboratories, 157/163 (91%) reported a diagnosis (Figure 2). Reporting the diagnosis from a peripheral blood film is voluntary and considered an educational component of the survey; laboratories are not assessed.

Assessment of Laboratories

Following the survey, responses are analyzed and participants are assessed based on assigned values that are determined by expert laboratory value through use of confirmatory testing and/or medical diagnosis of the testing material donor and consensus value from participants.

In this survey, 18 (10.4%) laboratories were assessed as having provided incorrect responses to identifying the contributing causes and to perform root-cause analysis (Table 2). Ten (5.7%) laboratories reported misidentification of blood cell morphology as a contributing cause of over-reporting of morphology.

Table 2. Summary of Discordant Findings Investigations – Contributing Causes

<table>
<thead>
<tr>
<th>No. of Labs</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>Misidentification of blood cell morphology</td>
</tr>
<tr>
<td>4</td>
<td>Over-reporting of morphology descriptive features</td>
</tr>
<tr>
<td>1</td>
<td>Results not correctly transcribed to analysis worksheet</td>
</tr>
<tr>
<td>1</td>
<td>Failed to remove the cells from Abnormal lymphocytes and include with reactive lymphocytes before reporting</td>
</tr>
<tr>
<td>2</td>
<td>Other</td>
</tr>
</tbody>
</table>

The blast cells in question were not brought to the pathologist’s attention for review prior to diagnosis. Additionally four laboratories commented that reactive lymphocytes were present, but did not include them as a separate category in the differential count.

Conclusions

The results of this proficiency testing survey highlight challenges for the morphologic identification of reactive lymphocytes (Figure 4–8) versus neoplastic lymphocytes (Figure 9) and reveals variation in laboratories’ reporting practice.

Counting reactive lymphocytes separately in the differential is a simple tool that can be implemented by laboratories to alert clinicians of their presence and aid in a diagnosis. In most cases, the clinical context and morphologic appearance should enable the experienced reviewer to reliably differentiate reactive lymphocytes from neoplastic, but it is approximated that in the real working world this may on occasion be difficult. In these situations, ancillary testing such as monospot and/or flow cytometry immunophenotyping may be helpful.

The review of a blood film can be the initial important tool for making the correct clinical diagnosis.1 Laboratories should have a process to ensure abnormalities found during review of a blood film get interpreted by appropriate laboratory professionals and are reported back to health-care providers.3,4

Further education in lymphocyte morphology and standardization of reactive lymphocyte reporting practice may be useful tools for laboratories to implement.

References