Bone Marrow Examination in Diagnosis of Immune Thrombocytopenia

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**Context**

Immune thrombocytopenia (ITP) is an autoimmune bleeding disorder. There are two categories of ITP: primary and secondary. In primary ITP, no other causes are identified, and in secondary ITP, clinical manifestation occurs as a result of another underlying condition. These underlying conditions can have immune or nonimmune origins. Clinical symptoms of ITP include a low platelet count, bleeding, and changes in skin appearance. For its diagnosis, a patient’s medical history, physical exam, and blood analysis are typically assessed to determine the presence of ITP.

**Research Question**

Is there a requirement for bone marrow examination in the diagnosis of ITP? Specifically, we were interested in whether evidence existed beyond what was included in the published 2011 American Society of Hematology guidelines.

**Conclusion**

The evidence supports Choosing Wisely Canada’s recommendation, “Do not perform a bone marrow aspirate and biopsy in patients less than 60 years of age with ITP in the absence of concerning features.”

In children and adolescents, bone marrow examination is not required in diagnosing ITP that presents with typical features. In adults, low-quality evidence from 3 observational studies shows bone marrow examination is not required in diagnosing ITP.

**Methodology**

Research questions are developed by Choosing Wisely Canada, in consultation with experts, end users, and/or applicants in the topic area. Evidence Development and Standards then produces one of two types of rapid reviews, or a special report to answer the research question. A rapid review of Systematic Reviews is conducted when a systematic literature search identifies relevant systematic reviews, health technology assessments, or meta-analyses that meet the inclusion criteria specified in the methods section. A rapid review of primary studies is conducted when none of the aforementioned study designs are available. On occasion, a special report may be provided that does not strictly follow the rapid review methodology set out by HQO. These reports are completed in a 2- to 8-week time frame. For more detail on rapid review methodology, please visit the Health Quality Ontario website at: [http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/rapid-reviews](http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/rapid-reviews)
Context

Choosing Wisely Canada is a national campaign that aims to help physicians and patients engage in informative conversations about tests, treatments, and procedures, and help physicians and patients make smart and effective choices to ensure high-quality care. It will support physicians as they work with patients to ensure they not only get the care they need, but avoid tests, treatments, and procedures that have no value and could cause them harm.

As part of this campaign, Health Quality Ontario (HQO) has developed rigorous, evidence-based reviews of tests, treatments, and/or procedures that may be overused. Choosing Wisely Canada has made recommendations based on the evidence provided by HQO. These recommendations are available on the Choosing Wisely Canada website.

Objective of Review

This analysis aimed to examine whether bone marrow examination is required in the diagnosis of immune thrombocytopenia (ITP).

Clinical Need and Target Population

Immune thrombocytopenia is an autoimmune bleeding disorder. There are two categories of ITP: primary and secondary. In primary ITP, no other causes are identified, and in secondary ITP, clinical manifestation results from another underlying condition. These underlying conditions can have immune or nonimmune origins. Clinical symptoms of ITP include a low platelet count, bleeding, and changes in skin appearance. (1) Diagnosis typically uses results from a patient’s medical history, physical exam, and blood analysis to determine the presence of ITP. (2)

Technology

Bone marrow examinations are performed to determine the health of the bone marrow and whether it is producing blood cells in the required amounts. The 2 types of bone marrow tests involve sampling bone marrow fluid in aspiration and its cells in biopsy. The harms of bone marrow examination are minimal but can include bleeding or infections. (3)

Existing Guidelines

In 2011 the American Society of Hematology (ASH) used an evidence-based approach to examine management of ITP. The ASH reviewed and formulated recommendations from published literature to 2009 on diagnosis of ITP in children and adults. (4)
Question, Methods, and Findings

Research Question
Is bone marrow examination required for diagnosis of ITP? Specifically, we were interested in whether evidence existed beyond what was included in the published 2011 ASH guidelines.

Methods

Literature Search Strategy
See Appendix 1 for a detailed description of the search strategy, including terms and results.

A literature search was performed on August 8, 2014, using Ovid MEDLINE, Ovid MEDLINE In-Process, and all EBM Databases for studies published from January 1, 2009, to August 8, 2014. (Appendix 1 provides details of the search strategies.) Abstracts were reviewed by a single reviewer and, for those studies meeting the eligibility criteria, full-text articles were obtained. Reference lists were also examined for any additional relevant studies not identified through the search.

Inclusion Criteria
- English-language articles published between January 1, 2009, and August 8, 2014
- studies that were observational or randomized controlled trials
- studies that included patients with suspected ITP
- studies that examined the diagnostic effect of a bone marrow examination

Exclusion Criteria
- case reports or case series
- animal or in vitro studies
- studies that included patients with diseases other than suspected ITP
- studies that examined the diagnostic effect of other technologies or blood parameters

Outcomes of Interest
- proportion of patients diagnosed with ITP
- proportion of secondary causes of ITP
- harms outcomes (e.g., bleeding, infection)

Findings
The database search yielded 69 citations published between January 1, 2009, and August 8, 2014 (duplicates removed). Articles were excluded on the basis of information in the title and abstract. The full texts of potentially relevant articles were obtained for further assessment.

No relevant studies were identified from the current systematic literature search.
2011 ASH Guidelines

Given the lack of current published evidence, the 2011 ASH guidelines were reviewed in detail. (4) The 2011 ASH guidelines used an evidence-based approach to examine management of ITP. A systematic literature search was conducted for the years 1996 to December 2009 and the evidence reviewed before formulating the recommendations. The guideline authors evaluated the strength of the recommendations using Grading of Recommendations Assessment, Development, and Evaluation (GRADE). For our purposes, the quality of these guidelines was evaluated using the Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool. (5) Overall, the 2011 ASH guidelines received an AMSTAR score of 7 (Appendix 2).

The 2011 ASH guidelines reviewed the use of bone marrow examination in the diagnosis of ITP separately for children and adults. Recommendations were as follows:

- In children, the 2011 ASH guidelines recommend that “bone marrow examination is not necessary in children and adolescents with the typical features of ITP” (Grade 1B).
- In adults, the 2011 ASH guidelines suggest “further investigations if there are abnormalities (other than thrombocytopenia and perhaps findings of iron deficiency) in the blood count or peripheral blood smear” (Grade 2C).
- In adults, the 2011 ASH guidelines suggest that “a bone marrow examination is not necessary irrespective of age in patients presenting with typical ITP” (Grade 2C).

Evidence Base

Notably, all of the above recommendations are based on observational studies (children: 1 study; adults: 3 studies). The study conducted in children was larger than the studies conducted in adults. Results showed no other important diagnosis (such as leukemia) in 332 children studied with typical features of ITP. Researchers calculated the risk of missing another important diagnosis, such as leukemia, as less than 1%, perhaps warranting the stronger recommendation given by ASH. Samples in the 3 studies of adults ranged from 66 to 86 patients. The ages also ranged from under 65 to 89 years of age. All 3 studies conducted in adult populations concluded that a bone marrow examination was unnecessary if the medical examination is thorough (e.g., clinical history, physical examination), and if blood work shows no abnormalities beyond thrombocytopenia. (4)
Conclusions

We conclude that the evidence from ASH and this special report supports Choosing Wisely Canada’s recommendation, “Do not perform a bone marrow aspirate and biopsy in patients less than 60 years of age with ITP in the absence of concerning features.”

Specifically, our conclusions are the following:

- In children and adolescents, bone marrow examination is not required in diagnosing ITP that presents with typical features.
- In adults, low-quality evidence from 3 observational studies shows a bone marrow examination is not required to diagnose ITP.
Acknowledgements

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Appendices

Appendix 1: Research Methods

Literature Search Strategy

Search date: August 08, 2014
Databases searched: Ovid MEDLINE, Ovid MEDLINE In-Process, Embase and All EBM Databases


Search Strategy:
1. Purpura, Thrombocytopenic, Idiopathic/ (4711)
2. (((immune or autoimmun* or idiopathic or purpura* or primary or secondary or acute or chronic) adj2 thrombocytopeni*) or ITP or werlhof* disease*).ti,ab. (16566)
3. or/1-2 (17228)
4. Bone Marrow Examination/ (6036)
5. (marrow adj2 (exam* or biops* or aspirat* or test*)).ti,ab. (12667)
6. or/4-5 (17535)
7. 3 and 6 (358)
8. limit 7 to (english language and yr="2009 -Current") [Limit not valid in CDSR,ACP Journal Club,DARE,CLCMR; records were retained] (75)
9. remove duplicates from 8 (69)
Appendix 1: Evidence Quality Assessment

Evaluation of Evidence

The Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool was used to assess the methodological quality of systematic reviews. (5)

Table A1: Detailed AMSTAR Scores of Systematic Reviews

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Abbreviations: AMSTAR, Assessment of Multiple Systematic Reviews; N/A, not applicable.

*Maximum possible score is 11. Each column represents a subscore: yes (1 point) or no (0 points). Details of AMSTAR score are described in Shea et al, 2007. (5)
References


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Conflict of Interest Statement
All authors in the Evidence Development and Standards branch at Health Quality Ontario are impartial. There are no competing interests or conflicts of interest to declare.

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