

Association between unilateral tonsillar enlargement and lymphoma in children: A systematic review and meta-analysis

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Abstract

Lymphoma is the most common head and neck malignancy in children, and palatine tonsils asymmetry is the most frequent clinical manifestation of tonsillar lymphoma. However, several studies with children with tonsillar asymmetry found no case of lymphoma, showing that the relationship of tonsillar asymmetry with lymphoma is unclear. In this review, we aimed to identify the association between tonsillar asymmetry and tonsillar lymphoma in children by conducting systematic reviews of the literature on children with palatine tonsil lymphoma and tonsillar asymmetry. Articles comprising the paediatric age group (up to 18 years) with information concerning clinical manifestations of tonsillar lymphoma or the diagnosis of the tonsillar asymmetry were included. The main cause of asymmetry of palatine tonsils was lymphoid hyperplasia, followed by lymphoma and nonspecific benign changes. The asymmetry of tonsils was present in 73.2% of cases of lymphoma. There was an association between asymmetric palatine tonsils and lymphoma, with a likelihood ratio of 43.5 for children with asymmetry of palatine tonsils and 8938.4 for children with asymmetry of tonsils and other signs of suspicion for malignancy. We also provide recommendations on the management of suspicious cases of palatine tonsil lymphoma.

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Keywords: Lymphoma; Children; Tonsil; Tonsil asymmetry; Unilateral tonsillar enlargement

Abbreviations: PT, palatine tonsils; LR, likelihood ratio; CI, confidence interval.

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1. Introduction

Lymphoma is the third most common malignancy of childhood, accounting for approximately 12% of all cancers in individuals under 15 years of age [1].

In the paediatric population, lymphomas are the most frequent malignant tumours of the head and neck, and non-Hodgkin lymphoma is the most common type [2]. The extranodal involvement is more common in non-Hodgkin lymphoma when compared with Hodgkin lymphoma, and the palatine tonsils (PT) are the most frequent site of extranodal involvement in non-Hodgkin lymphomas [3].

Knowledge of the most frequent clinical manifestations of PT lymphoma is critical for detection and early diagnosis [4], allowing treatment during the initial stages and increased disease-free survival and overall survival [5–7]. The size of tonsillar lymphoma also has a direct relationship with prognosis [8].

In a study with 47 children with tonsillar asymmetry and 43 children with symmetric tonsils undergoing tonsillectomy, no difference in the PT volumes between groups was observed, with the apparent asymmetry resulting from the difference in the depth of the tonsillar fossa [9]. In another study of 13 children with asymmetric PT, there were no cases of lymphoma in these children and no difference in the PT sizes when compared to children without asymmetry [10].

Other studies with patients with apparent asymmetry of PT found no difference between the PT sizes in 39–52% of cases, and in most of the patients, the PT considered bigger was smaller than the contralateral [11–13]. Clinical asymmetry in these cases was attributed to variations in depth of the tonsillar fossa or to anterior tonsillar pillar asymmetry.

The asymmetry of PT is the most common clinical manifestation in children with PT lymphoma and is present in 72.7% of patients, followed by alteration of the appearance of PT and cervical lymphadenopathy [4]. The correlation of the apparent asymmetry of PT with the asymmetry of PT sizes after tonsillectomy is unclear, and the asymmetry is a common finding in healthy children, present in 1.7% of children aged 4–17 years [14], and therefore, the relationship between tonsillar asymmetry and PT lymphoma is not clear.

The relationship of tonsillar asymmetry with PT lymphoma in children remains controversial and there are no reviews with a high level of evidence on the subject in the literature. To establish this relationship, this article intends to calculate the likelihood ratio (LR) of the presence of PT asymmetry with the presence of PT lymphoma.

In diagnostics, the likelihood ratio of a test provides a way to estimate the pre- and post-test probabilities of having a disease. The LR is the ratio of the sensitivity divided by 1 minus the specificity of a test. It determines how many times the likelihood of a given test result increases in the presence of a positive test compared with the likelihood of a negative test. In this case, it will determine how many times the presence of asymmetric PT increases the chance of the presence of

PT lymphoma in children; currently, this relationship has not been established.

This study aimed to perform a systematic review of the literature on the presence of PT asymmetry at the time of diagnosis of PT lymphoma in paediatric patients and a systematic review on the presence of PT asymmetry in children regardless of its cause. Furthermore, we evaluated the relationship of PT asymmetry with PT lymphoma and determined the likelihood ratio of this indication of lymphoma.

2. Methods

The systematic reviews and meta-analysis followed the criteria defined by the PRISMA statement [15] and the current recommendations of the Cochrane Collaboration.

2.1. Study selection and search strategy

The following databases were systematically used by two authors (ACG, GMC): PubMed/MEDLINE, LILACS, Cochrane, Scopus and SCIELO. Two searches were performed on these databases. To detect cases of PT lymphoma in children, the first systematic review searched the following MeSH terms and free text words “tonsillar lymphoma and children”. To identify cases of tonsillar asymmetry, the second search was made by the following MeSH terms and free text words “unilateral tonsillar enlargement or tonsillar asymmetry and children”. The search was restricted to articles in English, Spanish and Portuguese languages related to PT lymphoma in children up to 18 years old, from January 1996 to December 2013.

Two authors were responsible for selecting all articles; all abstracts were read and from the information contained therein, if there was the possibility of cases of PT lymphoma or tonsil asymmetry in children, the articles were completely read. From the articles read, those that covered the considered paediatric age range and contained information of the clinical manifestations of PT lymphoma at diagnosis or cases of tonsillar asymmetry were included. The inclusion of articles was reviewed by both authors. Review articles without clinical cases and those that did not allow the definition of the presence or absence of PT lymphoma for each patient were excluded. Only cases of PT lymphoma confirmed by histopathology were considered.

The following data were assessed from the articles: number of cases of PT lymphoma, gender, age, tonsillar asymmetry, classification used to determine the tonsillar asymmetry, aetiology in other cases of tonsillar asymmetry, authors and year of publication. Reported information in articles was considered and clinical information of the patients not reported was considered absent.

The children in the study were classified according to the presence or absence of PT asymmetry, presence of PT lymphoma and also according to the presence of other suspicion factors for PT lymphoma. The considered suspicion factors

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