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Review Article

Diagnosing nontuberculous mycobacterial cervicofacial lymphadenitis in children: A systematic review

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ABSTRACT

Objectives: Widespread controversy exists regarding correct diagnosing nontuberculous mycobacterial cervicofacial (NTM) lymphadenitis. This study intends to gather the available evidence with respect to diagnosing NTM cervicofacial lymphadenitis.

Methods: A review protocol was developed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)-statement (www.prisma-statement.org). A comprehensive search was performed in the bibliographic databases PubMed, Embase.com and Wiley/Cochrane Library. 10 Articles fulfilled the inclusion criteria and were included in the review. Assessing risk of bias of the articles was done using the revised Quality Assessment of Diagnostic Accuracy (QUADAS-2) tool.

Results: This systematic review shows that diagnostic studies of high methodological quality are scarce. Diagnostic accuracy of polymerase chain reaction (PCR), culture, skin testing, auramine staining, Ziehl-Neelsen staining, and immunodiagnostic assays was studied. Culture sensitivity proved to be 41,8%, while polymerase chain reaction has a sensitivity of 71,6%. Both methods showed a specificity of 100%. Sensitivity of Immunodiagnostic assays ranged between 87,5% and 100% and specificity between 81% and 100%. Overall sensitivity of skin tests containing purified protein derivative (PPD-S) was 70% (95% CI [62%–78%]) with an overall specificity of 94% (95% CI [88%–100%]).

Conclusions: In patients with a high clinical suspicion for NTM cervicofacial lymphadenitis, a positive PPD-S skin is indicative for the diagnosis of NTM cervicofacial lymphadenitis. Either PCR or culture is necessary to confirm the diagnosis. Interferon-γ release assays with purified protein derivative stimulation appear to provide good sensitivity and specificity as a non-invasive pre-operative test, but the evidence is weak. More studies of high methodological quality are needed to validate the results of this systematic review.

1. Introduction

Nontuberculous mycobacterial (NTM) cervicofacial lymphadenitis is a disease that most frequently occurs in young immunocompetent children. With a reported incidence ranging between 0,6 and 4,5 per 100.000 children, it is a rare disease [1-5]. The condition has a characteristic clinical course, which eventually leads to cutaneous fistula formation and spontaneous drainage [6]. Treatment strategies for NTM cervicofacial lymphadenitis were recently systematically reviewed [7]. A clinical example can be found in Fig. 1. Surgical excision of the affected lymph nodes appeared to be superior to antibiotic therapy. However, surgical treatment of advanced stages of disease is associated with the risk of facial nerve palsy and poor aesthetic outcomes [7-10]. Hence, it is important to establish the diagnosis at an early stage. Nevertheless, widespread controversy exists regarding correct diagnosing NTM cervicofacial lymphadenitis [11-16]. The aim of this study was to systematically review and critically appraise the existing literature on diagnostic methods of NTM cervicofacial lymphadenitis in immunocompetent children. Moreover, this study intends to provide recommendations for a structured approach with respect to diagnostic methods for nontuberculous mycobacterial cervicofacial lymphadenitis in children. To the best of our knowledge, this is the first study to systematically review this subject.

2. Materials and methods

2.1. Search strategy

- A review protocol was developed based on the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)-

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Fig. 1. Clinical example of NTM cervicofacial lymphadenitis.

statement (www.prisma-statement.org) [17].

- A comprehensive search was performed in the bibliographic databases PubMed, Embase.com and Wiley/Cochrane Library. PubMed was searched from inception up to 2 March 2017, Embase.com from inception up to 16 March 2017 and Wiley/Cochrane Library from inception up to 21 March 2017.
- The following terms were used (including synonyms and closely related words) as index terms or free-text words: "Mycobacterium Infections, Nontuberculous", "Lymphadenitis", "Child*".
- The full search strategies for all databases can be found in the Supplementary Information.

The search was performed without date, language or publication status restriction. Currently, no methodological filters are available to find primary diagnostic test accuracy reports [18].

2.2. Selection process

2.2.1. Duplicate articles were excluded

All titles were screened and appropriate abstracts reviewed by two reviewers (SW and LK). Discrepancies were resolved either by consensus or the use of a third reviewer (MO). The selection process was done using www.covidence.org. Two reviewers also performed full text review of the selected articles independently (SW and MO) and discrepancies were resolved either by consensus or consulting a third reviewer (LK). Articles were selected for full review according to the following a priori eligibility criteria: (1) studies reporting on NTM

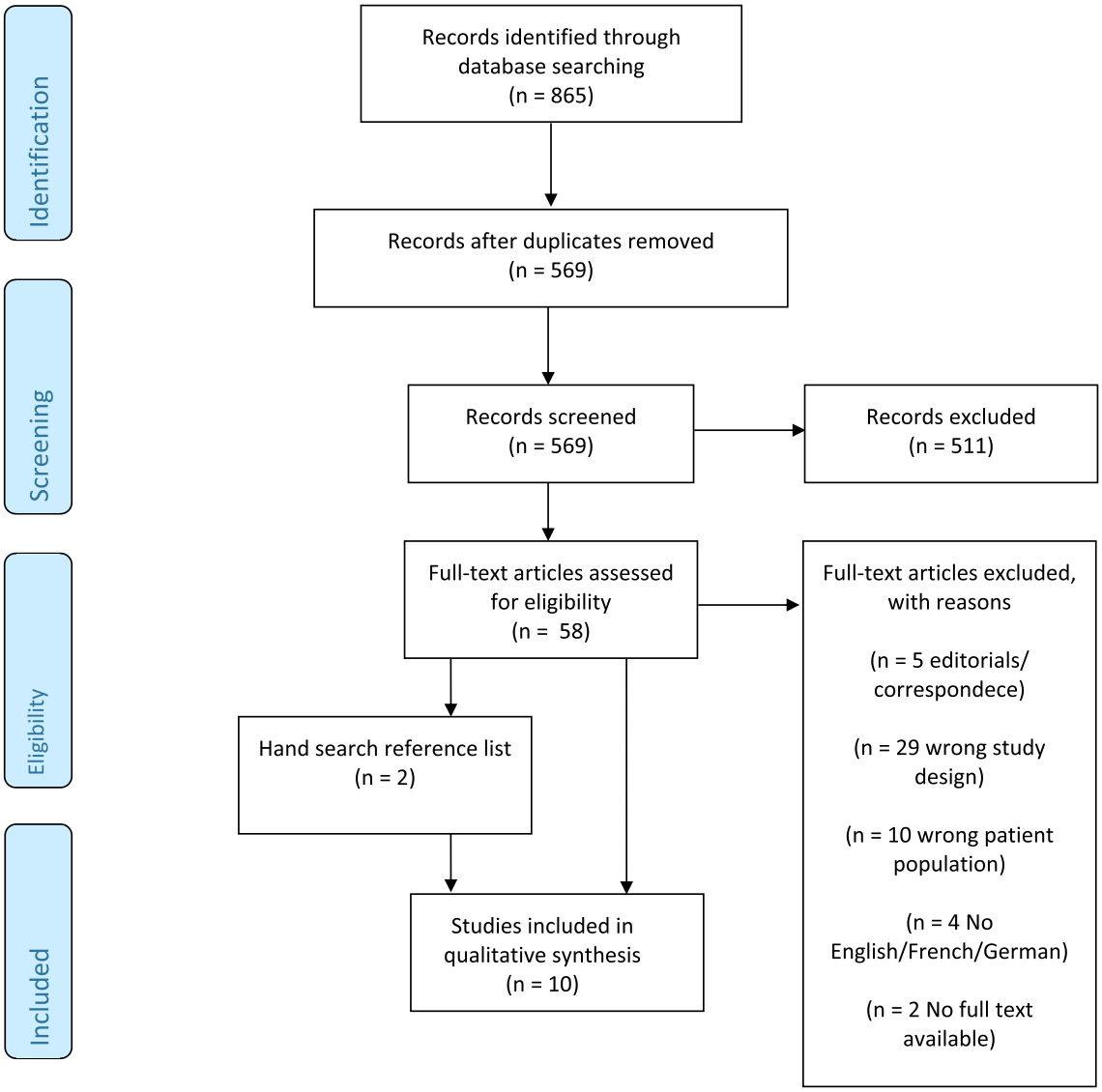

Fig. 2. PRISMA 2009 flow diagram.