

The Management of Non-Tuberculous Mycobacteria Cervicofacial Lymphadenitis. A
Survey of U.K. paediatric tertiary hospitals

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Introduction

Non-tuberculous mycobacterial cervicofacial lymphadenitis (NTMCL) infection is a rare disease but a common cause of chronic cervical lymphadenopathy in the immunocompetent child. Presentation is classical with persistent cervical lymphadenopathy, usually unilateral, that doesn't respond to antibiotics. As the disease progresses the skin changes to characteristic cherry red and the lymph nodes liquefy resulting in a fluctuating swelling that will often form a sinus that will drain for a prolonged period with eventual resolution and scarring. Non-tuberculous mycobacteria (NTM) are ubiquitous in the environment, with over 125 Species having been identified¹. The incidence worldwide is quoted as between 0.8-3.1 cases per 100,000 with geographical variability^{2, 3} and is widely acknowledged to be on the increase. This has been demonstrated within the U.K.⁴ with a rise from 0.9 to 2.9 per

100,000 cases between 1995 – 2006. The most frequent causative sub species identified is *mycobacterium avium*^{1, 2, 3, 4, 5, 6, 7, 8, 9}. Management of this condition is controversial, with limited evidence base and certainly there is no universally agreed treatment. Proposed treatment options broadly include surgical, medical (often combined) or a watch-and-wait approach. We looked to survey U.K. paediatric tertiary centres to gain an understanding of the current practice in the management of these patients.

Materials and Methods

An 18-question online survey was sent to all 21 U.K. paediatric tertiary centres. The questions asked aimed to evaluate each unit's case load, involvement of cases, other specialty contributions, investigation and treatment choices as well as follow up decisions. The survey was sent to a nominated consultant within each paediatric ENT department. The questions were accompanied by multiple choice answers to be selected, with 11 of the questions incorporating additional free text to provide further information where deemed appropriate. The results were then received and analysed.

Results and analysis

We received 19 responses from the 21 centres surveyed. The majority (58%) see at least 4 cases a year, with 89% of centres receiving referrals from neighboring ENT departments for the management of this condition. Otolaryngology is almost always involved in the management of these patients (95%) often as the lead specialty (58%),

alongside multiple other specialties. These included Infectious Diseases (79%), General Paediatrics (47%) and Microbiology (32%).

The survey revealed that the most common method (89%) of diagnosis based on 'clinical suspicion alone, from history and examination.' Other investigations are variably used including, but not exhaustive of, 'microbiology / histopathology from excisional biopsy or fistulous?? drainage' (37%), 'AFB stains' (37%), 'lymphadenopathy serology screen' (37%), 'tuberculin skin testing, in a child without risk factors for M. tuberculosis and absence of previous BCG vaccination' (37%). 67% also selected that their investigation choice would be 'variable depending on presentation'. See figure 1.

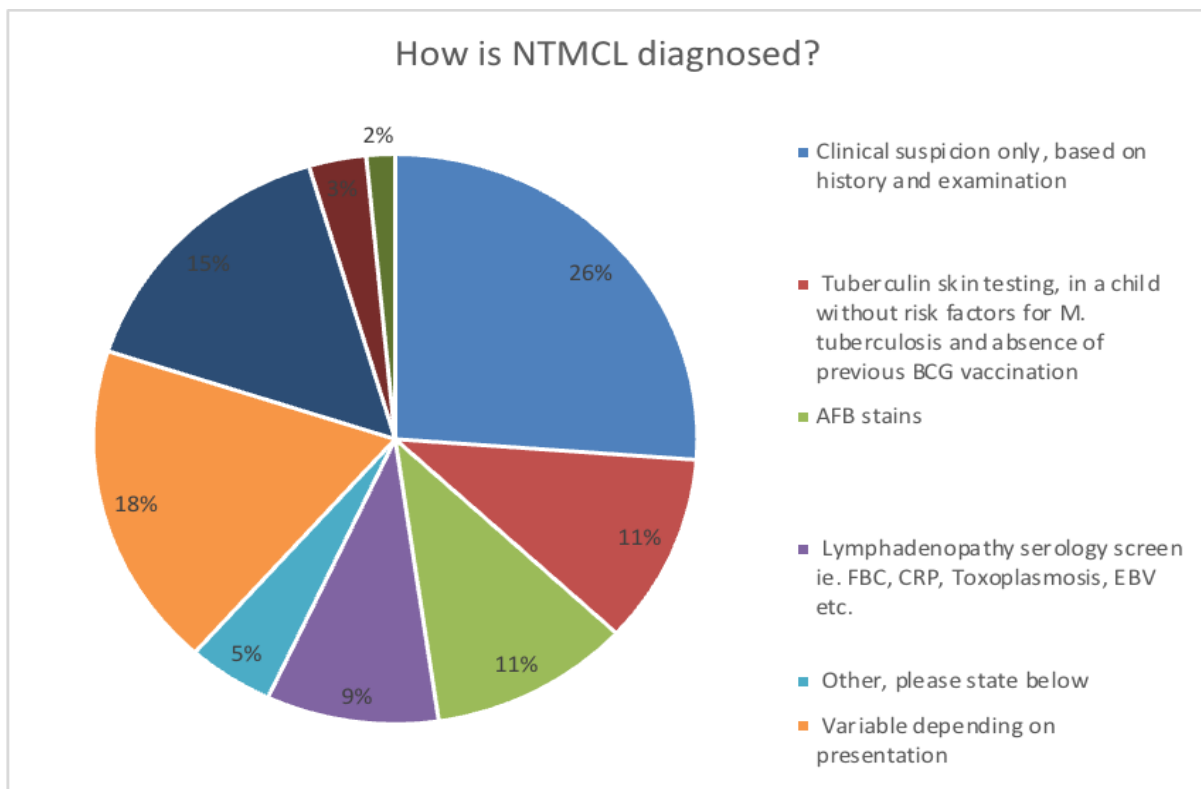


Fig. 1

Chart that demonstrates how U.K tertiary paediatric ENT centres choose to investigate and diagnose cases of suspected NTMCL

63% would routinely request an ultrasound and 11% would request a chest x-ray. 32% of responders would not request any routine imaging.

Management of NTMCL was assessed by presenting four common clinical scenarios, ranging from a milder presentation to a more extensive or problematic one, with our responders asked how they would manage each scenario. The scenarios and results are summarised in figure 2. A surgical procedure is the most common treatment choice on the whole, with a less extensive procedure subsequently opted for when more adverse features are present e.g. close proximity to facial nerve and / or skin involvement. Non-surgical treatment was also common, chosen as the preferred management option (16-47%) depending on the clinical presentation. Within these, observation was shown to be a common treatment choice with rates between the clinical scenarios ranging from 16% to 32%. Anti-mycobacterial monotherapy was selected between 0-21%. Where 'other' was selected commonly responders would use this space to comment that their treatment of choice may change related to variations and unique circumstances between individual cases.

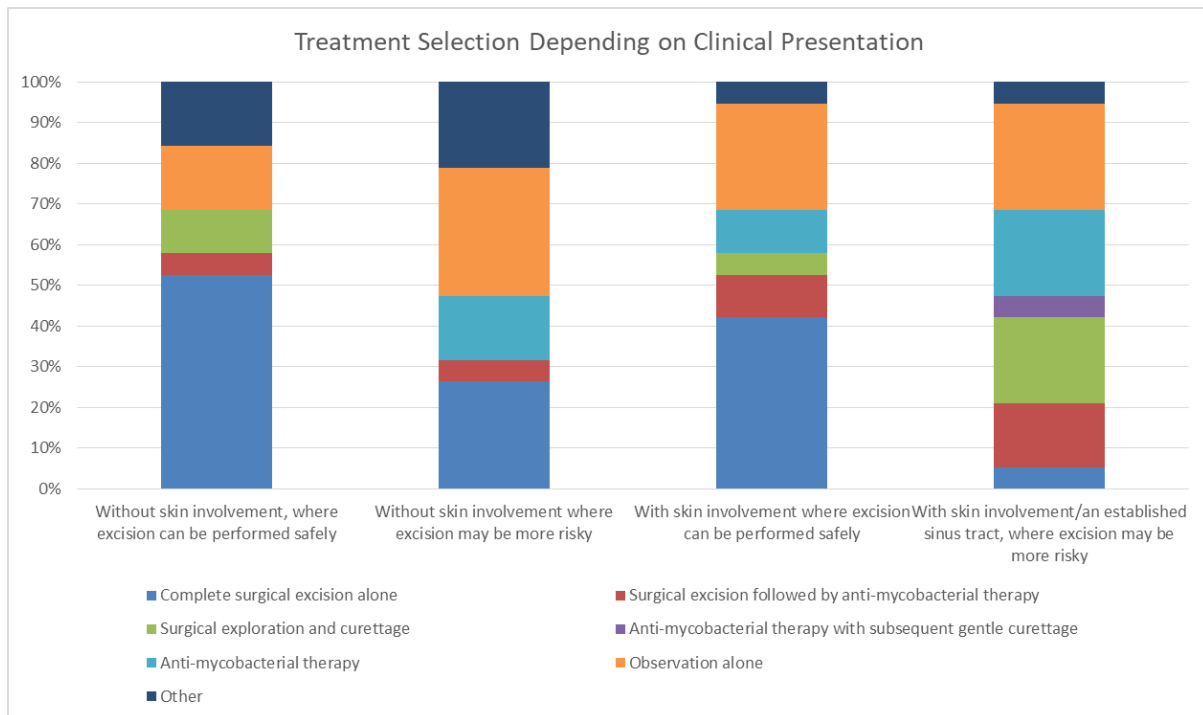


Fig. 2

Bar Chart demonstrating how U.K tertiary paediatric ENT centres prefer to treat NTMCL dependent on different clinical presentations

Where medical treatment is used, the majority (56%) were unsure of the anti-mycobacterial regimen used in their respective hospitals as this decision was made by other specialities. Where known, the commonest choice (17%) was of dual therapy with rifampicin and clarithromycin. The duration of anti-tuberculous treatment was also varied. Where known, most centres typically give 3 months of treatment (39%). Others provided 6 months of treatment (17%) or until clinical resolution (17%).

Follow up protocols were also identified. If observation alone was chosen, most commonly monthly follow up was undertaken (58%), followed by 3 monthly (21%) and 6 monthly (5%) follow up respectively. Some advocated for patient initiated follow up. If surgery was undertaken, regular follow up until the wound had healed was the most common choice (58%), with some only scheduling one follow up to check the wound. Where anti-tuberculous therapy has been completed, most (42%) would still arrange regular interval follow up until the wound has healed. 26% state with this management avenue follow up would be undertaken by a different specialty.

68% of the responders said they incorporate the views of the patient's parents when deciding on treatment. 26% responded that their management of this condition has been altered by adverse outcomes or complications in their own practice or within their department. Where comments were shared, universally a change from a surgical approach to considering and utilising more conservative surgery or non-surgical choices appeared to be the norm.

Only 21% of the units that responded have local management guidelines and 79% of them have the opinion that management of this condition would be improved by written national guidelines.

Discussion

The objective of this survey was to gain an up to date understanding of the way in which NTMCL is currently managed in the United Kingdom. The management of NTMCL is controversial and its optimum management is often debated both locally and internationally. There is a lack of high-level evidence, which likely contributes to this difference in opinion. The lack of evidence can be partly explained by the challenge in achieving such evidence. There is a wide variation of heterogeneity of patients, variable anatomical locations and the extent of disease can vary. Thus, potential subsequent differences in risk profile associated with the investigation and management of the condition for each individual based on these mentioned factors. There are only 3 randomised control trials^{10,11,12} on the treatment of this condition, each with their own limitations. In addition, there is one systematic review and analysis¹³ from 2015 by Zimmerman et al. This paper provided data from nearly 2000 patients and is the largest and most robust evidence in the management of NTMCL. A demonstration of the lack of evidence to inform a definitive management plan was highlighted when the International Pediatric Otolaryngology Group (IPOG)¹⁴ published their recommendations in 2023. Though guidance was provided, they did not achieve complete consensus. Of importance, this guidance does recognise the role of other medical specialities namely from Infectious diseases and paediatrics, encouraging a multidisciplinary approach to management. This approach is demonstrated in our survey results. Most recently, further guidance has been provided by the British Association of Paediatric Otolaryngology (BAPO)¹⁵ for the management of this condition.

For a definitive diagnosis of NTMCL a positive mycobacterial culture or PCR is required. This is desirable but there is a classical presentation where a probable diagnosis can be made. This is of an immunocompetent, systemically well young child with a chronic unilateral, single, above the hyoid neck lesion^{1,16} with a red or purple discolouration. Our survey shows that our clinicians are happy to make the diagnosis based of this classical presentation. However, other microbiology and virology tests are considered and used within the U.K. These investigations have often been performed by primary or secondary care providers, prior to presentation to tertiary centres, in the effort to confirm diagnosis as well as to rule out other differential diagnosis. There is a common concern that diagnostic fine needle aspiration may be a risk for fistula formation, with limited evidence¹³ to support this complication. However, this, along with other invasive investigatory and therapeutic choices (e.g. incision and drainage, lymph node excision) is difficult to ultimately prove owing to the natural progression of disease that can demonstrate development of a fistula in the absence of any of the above.

Ultrasound is commonly routinely used to aid diagnosis. This is not surprising given its favourable attributes of being easily accessible, non-invasive and its ability to demonstrate characteristic findings to support a diagnosis of NTMCL. The use of other imaging modalities is not favoured routinely, this matches the available literature, with an additional MRI scan often reserved for surgical planning in more extensive cases or where there is concern of deeper involvement.

Definitive management of this condition generally falls into 3 categories; surgical excision, medical management with anti-mycobacterial therapy or observation. Within the U.K. the most common practice appears to be surgical excision, historically the preferred treatment choice in the literature. However, a more limited procedure is often preferred in the setting involving more risk, such as skin break down or proximity to a branch of the facial nerve. Our survey shows that alternatives to surgery are certainly commonplace within current U.K. practice. In fact, observation alone is commonly used in a variety of clinical presentations seen by NTMCL and is shown to be the treatment of choice when there is concern about the risk of damage to the facial nerve with surgery. The literature shows¹³ there is a temporary facial nerve palsy rate of 10% with a permanent palsy rate of 2%. This perhaps demonstrates a change in practice, certainly from literature which has historically demonstrated that surgery to be the mainstay of treatment. This suggestion is further supported by our survey results when evaluating changes of practice over one's career. According to our survey, where practice has changed it has transitioned from a pro-surgical to a more conservative approach in the management of this condition. This appears to be based on previous adverse outcomes as a consequence of a surgical approach.

Where anti-mycobacterial therapy is utilized, the regime of choice is varied. This once again may be a reflection on the lack of published evidence on any recommended regimen and duration of anti-mycobacterial agents, aside from the consensus that at least dual therapy for an extended period is advocated owing to the known resistance profile of the organisms. This is a significant undertaking for the patient. In addition,

side effects to recommended anti-mycobacterial agents are experienced commonly¹⁰,¹¹ such as teeth discolouration, fatigue, fever and abdominal pain. The economic cost for long term antibiotics should also be considered. Some will argue that the benefits thought attributable to long term anti-mycobacterial agents are more a reflection of the natural course of the pathology, therefore preferring observation alone. This theory is supported in some evidence¹³ where there was demonstrated to be no improved cure rate between anti-mycobacterial therapy when compared to observation.

With the great variability of choice and duration of anti-mycobacterial therapies used in the limited available literature, this is area of potential research.

Another area of potential research would be into qualitative research to evaluate the patient and parents experience of their clinical journey. As far as the authors are aware there is no publication on this. Our survey demonstrated that the views of parents influenced management choice in 68%.

Conclusion

Our survey shows that local guidelines are infrequent despite the fact that there is a demonstrated appetite for national guidance. Respondents felt that National guidelines would improve the care of this patient group.

The results of our survey, with data collected prior to the publishing of the IPOG paper¹⁴, appears to demonstrate that the management of NTMCL within the U.K. is comparable to the current international consensus. The paper makes recommendations of establishing a 'probable NTM lymphadenitis' diagnosis based solely classical clinical presentation, an approach heavily favoured in U.K. as established above. Perhaps where current U.K. management mirrors the international consensus the most is centred around treatment choice. Though the paper states 'clinical resolution was best achieved with complete surgical excision... some institutions strongly favour non-operative management.' Further with regards to treatment, the paper acknowledges when medical management is pursued 'there is high variability amongst institutions both in antibiotics regimen and duration.'

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Summary statement

- There is no universally agreed management of paediatric NTMCL, with limited high-level evidence which likely contributes to the different approaches in the management
- Paediatric NTMCL is broadly managed surgically, medically often with prolonged multi agent antimicrobials or through observation
- The available literature suggests that surgery was the mainstay of treatment historically
- Non – surgical management of paediatric NTMCL is now commonly used within the U.K.
- The management of paediatric NTMCL within the U.K. is in keeping with current international consensus