

## CASE REPORT

# Atypical mycobacterial cervical lymphadenopathy in a 2-year-old girl

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## ABSTRACT

Lymphadenopathy is a common clinical condition in the paediatric population. In 50% of cases it occurs in otherwise healthy children, and in 75% it presents as a localized form. Lymphadenopathy lasting more than 3 months is defined as chronic. Common conditions causing lymph node enlargement include infections, malignancies, and autoimmune disorders. Mycobacteria causing infectious lymphadenopathy are divided into tuberculous and non-tuberculous mycobacteria (NTM). Diagnosing mycobacterial disease is complicated, and definitive surgery is the best treatment option for NTM cervicofacial lymphadenitis. We present a case of a 2-year-old girl with chronic cervical lymphadenopathy, eventually diagnosed as NTM infection. The diagnostic and therapeutic process was complicated, demanding an interdisciplinary approach and several surgical procedures. The treatment was supported by negative pressure therapy.

## KEY WORDS:

**children, lymphadenopathy, mycobacteriosis, lymphadenitis, atypical mycobacteria.**

## INTRODUCTION

Lymphadenopathy, or enlarged lymph nodes, is one of the most common clinical manifestations that paediatricians encounter in their practice. It is localized in 75% of cases, and in 50% of cases it occurs in healthy children [1]. Enlarged lymph nodes are considered those exceeding 1 cm in the largest dimension or, in the case of supraclavicular, popliteal, supraclavicular, and iliac nodes, those exceeding 5 mm. Lymphadenopathy persisting for more than 3 months is considered as chronic. An adequate history and physical examination usually allow the identification of the cause without additional testing. The occurrence of red flag symptoms, such as weight loss, night sweats, and appetite loss, requires laboratory tests, imaging studies, and node biopsy [1, 2]. However, infection is the most common cause of limited lymphadenopathy. Cervical lymphadenitis is the most common clinical manifestation of non-tuberculous mycobacteria

(NTM) infection in children, and the predominant species are mycobacterium avium complex (MAC) [3, 4]. Lymphadenopathy due to mycobacteriosis most often affects children under 12 years of age, especially those aged 2–4 years [5, 6].

## CASE REPORT

A 2-year-old female patient with persistent cervical lymphadenopathy for 2 months was admitted to the Paediatric Surgery Department for a diagnostic biopsy. The child presented a history of a febrile infection 2 months earlier with bilateral cervical lymphadenopathy treated with amoxicillin. The fever and right-sided lymphadenopathy subsided, but left-sided cervical lymphadenopathy persisted without general symptoms. No appetite disorders were noted, the child was gaining weight properly. No history of chronic diseases was reported. The abdominal ultrasound examination showed no ab-

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**FIGURE 1.** Persistent left-sided lymphadenopathy with erythematous overlying skin and abscess-like formation after first surgical intervention



**FIGURE 2.** Complete wound dehiscence after second surgical intervention

normalities. Basic laboratory tests revealed no significant anomalies. In neck ultrasound, clusters (about 4–5) of enlarged round lymph nodes dimensions  $21.5 \times 14$  mm on the left side and 2–3 round lymph nodes with dimensions  $12 \times 12$  mm on the right side were visualized. A biopsy of the most superficially located cluster around the left mandibular angle was performed. During the dissection, purulent content was obtained for culture. The excised material was sent for histopathological, cytometric, and bacteriological examination. The suspicion of cat scratch disease was raised in the histopathological study, and a history of contact with a cat was confirmed. However, in immunological tests, the levels of antibodies against *Bartonella henselae* in IgM and IgG classes remained normal. One month later, the patient was readmitted because of persistent left-sided lymphadenopathy with erythematous overlying skin with abscess-like formation (Figure 1) and mediastinal widening on chest X-ray. The affected area was revised, and a large inflammatory tumour with a fistula in the central part was found. A smear was obtained again, and the inflammatory and necrotic tissues were excised along with several adjacent reactive lymph nodes. The material was again sent for histopathological examination. A negative pressure dressing (100 mm Hg) was applied to the wound. After oncology consultation, azithromycin was implemented in the treatment and a chest CT scan was done, which did not reveal significant pathology in the chest organs. Pending further test results, the child was discharged home on the third post-operative day. After a week, the child required readmission due to complete wound dehiscence (Figure 2). A surgical revision was performed again, necrotic tissue was

removed, and a negative pressure dressing was reapplied (100 mm Hg). *Methicillin-sensitive Staphylococcus aureus* was cultured from a second surgical intervention, and clindamycin was introduced in the treatment (cloxacillin was not available). The patient was again consulted by an oncologist, and additional laboratory tests were ordered, including QuantiFERON-TB Gold, which proved to be negative. The histopathological specimens obtained so far were forwarded for a consultative study in a tertiary centre. The results again suggested cat scratch disease, other zoonotic diseases including tularaemia, or mycobacterial infection. Despite vacuum therapy, there was no progression in healing, so the patient underwent another surgery. This time deep neck dissection was performed with complete and radical excision of lymphatic and necrotic tissues of the affected area, and the material was sent again for histopathological and bacteriological examination. Subsequent additional tests performed at the Tuberculosis Bacteriology Laboratory confirmed MAC infection. After pulmonological consultation rifampicin was implemented in the treatment. The patient was discharged home in good general condition. Ultimately the cure was achieved, but with scarring and discoloration (Figure 3).

## DISCUSSION

Conditions causing lymphadenopathy can be divided into a few groups: malignancies (*haematological malignancies: lymphoma, leukaemia; metastatic, others*), connective tissue disorders (*systemic lupus erythematosus, rheumatoid arthritis, dermatomyositis*), atypical lymphoproliferative disorders (*Castleman's disease, Wegener's*



**FIGURE 3.** After treatment. The plane, widened scar, and discoloration are visible

disease), granulomatous (*histoplasmosis, mycobacterial infections, Cryptococcus, Berylliosis, cat scratch disease, silicosis*); infections (*viral/EBV, CMV, HIV, bacterial, fungal, protozoal, rickettsial, helminths*), and others [1]. Mycobacteria causing infections are divided into tuberculous and non-tuberculous (NTM, atypical mycobacteria) [7]. Most NTM infections are due to MAC [8]. Atypical mycobacteria are microbes commonly existing in soil, fresh and salt water, food, and animals. The infection appears because of indirect contact with bacteria (inoculation), and through dirty items placed in the mouth or traumatic wounds; hence, the dominant group are children up to 5 years of age [9, 10]. Person-to-person spread is not observed [5]. The estimated incidence of NTM disease is 0.6–1.6 cases/100,000 children/year [4]. Of note, Tebruegge *et al.* showed a seasonal incidence cycle of around 12 months, with peaks in late winter/spring and troughs in autumn [4]. Among others, in clinical practice, it is necessary to distinguish between tuberculous and non-tuberculous mycobacterial infections due to different treatment modalities [8].

Mycobacterial cervical lymphadenopathy is caused by tuberculous mycobacteria in 64% and by atypical mycobacteria in 36% of cases [7]. If no contact with tuberculosis was established, the probability of tuberculous aetiology is low. Tuberculous lymphadenitis more often affects few posterior cervical as well as supraclavicular lymph nodes and is rather bilateral [7]. The young age of the patient and lack of constitutional symptoms (fever, weight loss, fatigue) suggest NTM infection [7]. Hence, in children the most common manifestation is lymphadenitis of the superficial lymph nodes of the head and neck [4], and in 95% of cases it is unilateral, subacute,

and progressive [5]. Without treatment, the lymph nodes become adherent to the skin, and in time they may fluctuate, with the overlying skin attaining a violaceous discoloration, and they may result in sinus formation [5, 11]. Nontuberculous lymphadenitis usually lasts several weeks or months, in contrast to acute course adenitis caused by *Staphylococcus aureus* or *Streptococcus pyogenes*. In contrast to suppurative lymphadenitis, where the overlying skin can also become erythematous, in NTM lymphadenitis the skin feels cool to the touch, and there is generally no or only mild tenderness [3]. Nevertheless, in the first stages the disease may be mistaken for a *Staphylococcal* or *Streptococcal* infection, leading to incision and drainage, which can cause cosmetic complications [5].

Diagnosing mycobacterial disease is complicated. It is based on thorough history, physical examination, laboratory and imaging tests, and node biopsy with further tissue testing. Inflammation markers (CRP, WBC, OB) remain normal or slightly elevated in most children with NTM infection. Additional tests include the tuberculin test (Mantoux), smears with Ziehl-Neelsen staining, cultures, histopathological examination, and IGRA and PCR tests. In Ziehl-Neelsen staining of the smears 10,000 cells are needed for smear positivity (30–57% sensitivity) [3, 7]. Several studies have emphasized the possibility of using the Mantoux tuberculin test in the diagnosis of mycobacteriosis, but the limitation of this test is its inability to distinguish between tuberculosis and atypical mycobacterial infections [7]. An alternative to the tuberculin test are IGRA tests assessing the level of interferon  $\gamma$ . Currently there are 2 commercial assays: the QuantiFERON-TB Gold and T-SPOT.TB; however, data on the effectiveness of IGRA tests in the diagnosis of NTM infections remain limited [3]. Currently, in children, fine-needle biopsy is not a recommended method [1], although according to some authors it may be useful, especially in combination with mycobacterial culture or the Mantoux tuberculin test [7]. In histopathological examination the presence of microabscesses, ill-defined granulomas, noncaseating granulomas, and a small number of giant cells is more prominent in nontuberculous adenitis [7]. Polymerase chain reaction testing is a fast and useful technique for the demonstration of mycobacterial DNA, and it allows confirmation of the infection even with the presence of 10 mycobacteria in the tested sample – according to Tebruegge *et al.*, it gave positive results in 91% of cases of NTM infection [4]. Culture of mycobacterium is diagnostic, but for atypical mycobacterial infection it may be negative in up to 50% of infected lymph nodes [7, 10]. Eight to 12 weeks are needed to obtain culture results, depending on the type of mycobacteria; therefore, the initial diagnosis depends greatly on the clinical course [10]. It should be noted that it is not feasible or practical to apply all of the diagnostic procedures in all patients [7].

The gold standard in treating lymphadenopathy caused by NTM infection is surgery because it is a di-

agnostic-therapeutic procedure. It allows a diagnosis by obtaining samples for further examination, and in most cases it results in a cure when performed radically [9, 10]. Although the surgical approach may vary from incision and drainage, through curettage, incomplete excision, to complete resection, current evidence suggests that radical excision is the best treatment option for NTM cervicofacial lymphadenitis [8]. Surgical approaches that do not involve the complete removal of diseased lymph nodes should be avoided because of high risk of recurrence, impaired healing, and sinus formation [6, 12]. The cure rate in patients treated primarily with radical excision ranges from 81% to 95% [9]. A multicentre randomized clinical trial conducted during the period 2001–2004 in a group of 100 children with confirmed NTM infection showed a significantly higher success rate of surgical treatment (96%) compared to antibiotic therapy (clarithromycin and rifabutin) (66%) [9]. Complete resection, however, has the highest risk of adverse events, including facial nerve damage [8]. Thus, pharmacological treatment (typically clarithromycin in combination with rifampicin, rifabutin, or ethambutol [8]) should be considered in patients with high risk of facial nerve injury and in extranodal infection [9]. It should be emphasized that iatrogenic facial nerve damage may occur not only during operation within the parotid gland, but also during resection of lesions located in the area of the mandible angle (most common location of NTM lymphadenopathy) because of its proximity to the marginal branch of the nerve. According to the literature, after excision temporary facial nerve palsy occurs in 3.3–21% of patients and permanent palsy in 2–3.7% of patients [11]. It should be noted that solely pharmacological treatment may lead to fibrosis and scarring of the skin as well as typical side effects [10].

It is worth adding that many genetic defects have been identified, resulting in mendelian susceptibility to mycobacterial disorders [13]; therefore, referral to an immunologist is recommended.

## CONCLUSIONS

The presented case report shows that the diagnostic and therapeutic process was long lasting and complicated. The course was significantly diversified; it initially suggested an infectious background, then an oncological and again infectious background, with great difficulties in making the correct diagnosis and final cure. Thus, a heightened awareness of these infections is essential to ensure appropriate early management [5].

## DISCLOSURE

The authors declare no conflict of interest.

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