Cervical tuberculous lymphadenitis: diagnosis and demographics, a five-year case series in the UK

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ABSTRACT

INTRODUCTION Cervical tuberculous lymphadenitis is a low-volume condition in the UK with a potential for delayed diagnosis. This study describes typical demographic and clinical features of patients diagnosed with cervical tuberculous lymphadenitis in a UK population. The utility of cytological, histological and microbiological investigations is reviewed with comparison between fine-needle aspiration and open biopsy. This information can facilitate recognition of new cases and guide initial management.

METHODS Patients diagnosed with cervical tuberculous lymphadenitis between January 2009 and December 2013 at two district general hospitals were identified from local infectious disease databases. Retrospective case-note review was undertaken to collect demographic and diagnostic data and associated complications.

RESULTS Full data were available for 51 patients aged 19–70 years (mean 32.4 years) with mean follow-up of 370 days; 49/51 patients were immigrants to the UK with a wide geographic spread in the countries of origin and time since arrival; 42/51 had no significant comorbidities, although two patients had coexistent HIV infection. The clinical presentation was most frequently without constitutional symptoms (39/51) and often with no history of tuberculosis contact. Posterior triangle neck nodes were most commonly involved (26/51).

CONCLUSION The 'typical' patient with cervical tuberculous lymphadenitis in our region is a young healthy individual who came to the UK from a high-risk country several years earlier. Diagnosis by fine-needle aspiration is as effective as open biopsy if fluid/pus is aspirated. Open biopsy is potentially associated with complications but does not appear to increase chronic wound discharge rates in our series.

KEYWORDS

Tuberculosis – Lymph node – United Kingdom

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Introduction

Tuberculosis (TB) infection caused by *Mycobacterium tuberculosis* is one of the top 10 causes of death worldwide and ranks as the leading cause of death from a single infective agent, above HIV.¹ Even though the incidence of TB in the UK is decreasing, it remains prevalent, with 6240 new cases in 2015. The UK has a low incidence of multidrug resistant TB (1.4%); however, this is expected to increase, making prompt diagnosis and treatment important.^{1,2}

While the majority of TB occurs as pulmonary infection, extrathoracic lymph node involvement occurs in 23.1% of UK cases with cervical nodes most frequently involved.³ The proportion of extrapulmonary TB was shown to be rising in the UK in 2009 (from 48% to 53%), despite the reduction in total TB cases.² This is thought to be due to the longer latency period of extrapulmonary TB in people who are non-UK born who entered the UK many years before developing clinically evident disease.^{2,4}

Diagnosis of cervical lymph node TB can be challenging, owing to the wide range of more common infective, neoplastic and systemic diagnoses, and as patients are often referred to a variety of specialties.⁴ Diagnosis is confirmed with fine-needle aspiration, core biopsy or open biopsy yielding material for microscopy, culture, cytology or histology.⁵ The ideal tissue sampling modality is a matter of debate with varying approaches described in the literature.^{6,7} It is frequently stated that open biopsy in TB predisposes to chronically discharging fistulae or sinuses,^{8–10} although there is a lack of conclusive evidence for this statement.

There are a number of recent case series of extrapulmonary TB from low-risk countries, although these are not directly applicable to the UK population.^{11–15} In 2006, Menon *et al.* published a series of 128 patients with head and neck TB in Bradford, which had a relatively high incidence of TB compared with the UK average.¹⁶ This series confirmed lymph node predominant disease but also demonstrated the diverse ways in which TB can present in the head and neck.

It highlighted the challenges in diagnosis, in part arising from the low proportion of surgical specimens sent for culture.

This study – a decade on from Menon *et al.* – characterises the typical features of patients with cervical tuberculosis lymphadenitis in a comparatively lower-risk UK region by reviewing demographics and clinical findings. The efficacy of diagnostic investigations in this series and complications of open biopsy are reviewed.

Materials and methods

Retrospective case-note analysis included all patients diagnosed with TB whose primary site of infection was the head and neck, between January 2009 and December 2013. Patients were identified from local infectious disease databases and covered a catchment area of 650,000 people, spread over two district general hospitals (Milton Keynes University Hospital and Northampton General Hospital).

Demographic data were collected including age, sex, country of origin and number of years residence in the UK. Clinical data included presenting history, examination findings, comorbidities, personal history of TB or contact with TB, investigations performed, referral pathways, diagnostic investigations and complications of investigation and/or treatment. Data analysis included a further one-year period until December 2014 to capture late complications. Total follow-up duration ranged from 35 days to 1580 days (mean 370 days) with 46/51 patients followed up for more than 6 months.

Results

A total of 65 patients were initially identified, of whom 14 were excluded: 5 had widespread systemic TB at diagnosis

(with head and neck involvement), 2 had subsequent alternative diagnoses (sarcoid and atypical mycobacterial infection), 7 had missing or incomplete clinical records preventing meaningful further analysis. The 51 included patients were treated for cervical tuberculous lymphadenitis. Most patients (38/51) had TB isolated on culture. The remaining patients were diagnosed on a combination of clinical features or microbiology/histology supportive of TB (acid–alcohol fast bacilli, AAFB, or caseating granulomas).

While most patients (32/51) were initially referred to ear, nose, and throat (ENT) services, six patients were referred to infectious diseases, five to oral and maxillofacial surgery, while general medicine, general surgery, urology (coexistent TB epididymitis), and haematology also received referrals. Three patients presented as acute admissions with abscess formation.

Demographics

There were 25 male and 26 female patients, with ages ranging from 19 to 70 years (mean 32.4 years) with 92% between 20 and 50 years old. Almost all our cases (49/51) occurred in patients who were born outside the UK and there was significant variation in time since arrival in the UK (Fig 1). The mean time of UK residence was 7.3 years. Three-quarters of patients had been in the UK for over two years at diagnosis while two patients had been in the UK for over 20 years. The most common countries of origin were on the Indian sub-continent and Africa (Fig 2). The two UK-born patients were of Indian ethnicity and travelled to India to visit family, where it is presumed they were exposed to TB.

Presenting features

Almost all cases (49/51) had cervical lymph node TB, with the remaining two cases having parotid and submandibular gland involvement. A majority of patients (38/51) reported

Figure 1 Time from entry to UK to time of diagnosis

having a neck lump for less than three months, although several (6/51) had been aware of a swelling for over one year. The predominant lymph node groups involved were the posterior triangle (level V) nodes (26/44).

Most patients (39/51) did not have constitutional symptoms at presentation; however, when these did occur they were most commonly sweats, fever and weight loss. Only two patients had respiratory symptoms of shortness of breath or cough. Most patients (42/51) were otherwise healthy and had no significant medical problems. Two

patients were HIV positive. Few patients had a previous personal history of TB or admitted contact with TB (Fig 3).

Investigation

All patients underwent diagnostic sampling with fine-needle aspiration or open excisional lymph node biopsy with material being sent either for microscopy, culture, cytology, histopathology or a combination. Owing to the wide range of specialties and different clinicians involved in the initial assessment of patients, diagnostic pathways were not

Figure 2 Map showing distribution of countries of origin of patients

Figure 3 Summary of presenting features and patient history. SOB = shortness of breath, ASA = American Society of Anesthesiologists (physical status)

standardised and this is reflected in the variable use of investigations.

Fine-needle aspirated samples were sent for microscopy and culture in 16 cases and for cytological analysis in 33 cases. AAFB were identified on smear in 56% (9/16) of samples and mycobacterium tuberculosis was isolated in 81% (13/16) samples. Cytology showed features suggestive of TB (granulomas) in 33% of cases (11/33), was non-diagnostic in 55% (18/33) of cases and was inadequate in 12% (4/33) of cases.

Lymph node excision biopsy samples were sent for microbiological analysis in 30 cases and for histological analysis in 33 cases. AAFB were identified in 42% (10/24) of samples analysed by microscopy (six microscopy reports could not be found) and mycobacterium tuberculosis was isolated in 77% (23/30) of samples cultured. Histology showed features suggestive of TB in 94% of cases (31/33), with 6% of samples non-diagnostic (2/33).

The rates of features supporting a diagnosis of TB on fine-needle aspiration and open biopsy were compared using the chi square test. There was no significant difference in the diagnostic yield between fine-needle aspiration and open biopsy for identification of AAFB on microscopy ($P = 0.37$) or of positive TB culture ($P = 0.72$). Open biopsy was significantly better than fine-needle aspiration at identifying histological features compatible with TB ($P < 0.0001$).

There were 41 open biopsy procedures in 39 patients, resulting in one haematoma and one temporary facial nerve palsy (partial parotidectomy performed). Our analysis shows no significant difference in the rate of chronic wound discharge or fistulae between patients undergoing open biopsy (7/39) compared with patients not having open biopsy (3/12) ($P = 0.58$, chi square test).

Discussion

While cases of cervical tuberculous lymphadenitis are not rare, they are relatively uncommon, particularly in lower-risk areas of the UK (Northampton and Milton Keynes had fewer new cases of TB in 2015 than the national average of 10.5/100,000 population).⁵ An awareness of the range of presentations is essential if the diagnosis is to be considered and for the appropriate tests to be requested. The variable rates of samples sent for microbiology, cytology and histology suggests that this remains a challenge.

This study shows some similarities to previous works in relation to presenting features but also important differences, particularly in demographical findings. The largest UK series of head and neck TB by Menon *et al.* in 2006 found that the average duration of symptoms was four months, that 26% of patients had constitutional symptoms and only a small minority of patients were immunocompromised, which is in keeping with our data.¹⁶ Posterior triangle involvement was reported less frequently in that series (21%) than in our study (59%); however, posterior triangle preponderance has also been reported by others.¹⁰

Menon *et al.* described 75% of their patients as being of Pakistani origin, while in Thompson's series of 67 patients with peripheral tuberculous lymphadenopathy in Leicester,

80% of patients were from the Indian subcontinent, which contrasts with a more varied population in our series.¹⁷ Nohrstrom's Finnish study of a low-risk population showed that over half of their 63 TB patients in a ten-year period were native Finns. This demonstrates the importance of understanding the demographics of the local population at risk of TB as this will vary on a regional and national level.^{2,5}

Several studies reporting on the diagnostic efficacy of fine-needle aspiration and open biopsy have been undertaken worldwide.^{8,18–22} Fine-needle aspiration has been shown to yield features suggestive of TB in 32–79% of cases, with AAFB seen in 8–35% of cases and culture positivity in the range 10–67%.¹⁸ Lymph node biopsy is more likely to show features of TB (59–88%) and to yield positive culture results (18–93%).¹⁸ The high culture positive rate for fine-needle aspiration in our study may represent sample bias as we suspect purulent aspirates were more likely to have been sent for TB culture than cellular fine-needle aspirates – this could not be confirmed from the information available on retrospective review.

The challenge in diagnosing TB on fine-needle aspiration alone is that culture results may take up to eight weeks to become positive, which represents an unacceptable delay in cases where there is diagnostic uncertainty and malignant processes need to be excluded. In 2015, Meghji *et al.* suggested a potential pathway for diagnosing suspected TB by initially performing fine-needle aspiration on all lymph nodes and deferring open biopsy if purulent aspirate is obtained or AAFB are seen on microscopy as in these cases a positive culture result is likely – this approach would be supported by the findings in our study.¹⁹

Recent technological developments have increased the role of ancillary tests in the diagnosis and characterisation of TB infection. Traditionally, tuberculin skin tests (e.g. Mantoux test) have been used to identify patients exposed to TB; however, newer interferon gamma release assays (e.g. QuantiFERON® test) are more accurate and may be used in selected cases.²³ Direct molecular testing for fragments of the TB genome based on targeted amplification of genetic material (polymerase chain reaction) is increasingly being used in the initial diagnosis of TB and can also identify drug-resistant strains.²⁴

While there is compelling evidence to suggest that incisional lymph node biopsy increases chronic wound discharge rates as compared with excisional lymph node biopsy,²⁵ we could find no evidence in the literature or in this study to suggest that excisional biopsy increases wound discharge rates.

Conclusion

This study shows that, in our population, cervical tuberculous lymphadenitis is a condition almost exclusively affecting foreign-born UK residents originating from high-risk countries. Patients are mostly aged between 20 and 50 years, are usually in good health and have often resided in the UK for several years prior to presentation. Our data suggest that posterior triangle lymph node involvement predominates

and that constitutional symptoms occur in a minority of patients.

There is a clear role for fine-needle aspiration as the first line diagnostic test and in cases where a purulent aspirate is obtained or AAFB are seen, this may be used in isolation. However, open biopsy is more likely to lead to a definitive diagnosis, is often required in cases of diagnostic uncertainty and may be required to guide microbiological sensitivities. It is crucial that material is sent for both for microbiology and cytology/histopathology in all cases where TB is considered in the differential diagnosis.

We did not find any evidence to suggest that open excisional lymph node biopsy increased the risk of a chronically discharging fistula or sinus and we feel that this should not necessarily be considered a reason to avoid this intervention.

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