



TUBERCULOUS CERVICAL LYMPHADENITIS, THE “DANGEROUS MASQUERADER”: ANOTHER UNUSUAL PRESENTATION

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ABSTRACT

Tuberculous Cervical Lymphadenitis is the most common manifestation of extra-pulmonary tuberculosis. The disease has been known since antiquity and normally presents with neck masses. It has been referred to as “the great masquerader” as it is known to mimic several other pathologies, often constituting a diagnostic challenge. We report a patient who presented early but uncharacteristically with an acute febrile illness and initially without a neck mass. He proceeded to develop painful bilateral neck masses which assumed appreciable proportions in only a couple of weeks, thus mimicking an acute inflammatory neck mass. Tuberculosis was suspected early, but diagnosis could not be confirmed as the initial laboratory investigations (tuberculin skin test, staining for Acid Fast Bacilli and Fine Needle Aspiration Cytology) could not confirm the diagnosis. Since there was a high index of suspicion, however, the patient was eventually placed on a therapeutic trial of anti-tuberculosis medication. Diagnosis was later confirmed with a culture of *Mycobacterium tuberculosis* and treatment for extra-pulmonary tuberculosis was completed. The response was dramatic and the lesion resolved completely without need for further surgical intervention. This case emphasizes the need for openness to unusual modes of presentation, a sustained high index of suspicion, thorough evaluation and the need for a multidisciplinary approach in the diagnosis and management of tuberculous cervical lymphadenitis.

KEYWORDS: Tuberculosis, Cervical Lymphadenopathy, Tuberculous Lymphadenitis, Scrofula.

INTRODUCTION

Tuberculous Cervical Lymphadenitis is an inflammatory disease of the cervical lymph nodes associated with *Mycobacterium tuberculosis*, an obligate pathogenic species of the *Mycobacterium* genus of Actinobacteria^[1]. Certain other pathogens of the *Mycobacterium* genus can also cause cervical lymphadenitis. These non-tuberculous forms are caused by atypical mycobacteria such as *Mycobacterium scrofulaceum*, and other non-tuberculous mycobacteria (NTM)^[2,3,4]. Cases of cervical lymphadenitis have been reported since antiquity and two other names “Scrofula” and “King's evil”, stand out in history. “Scrofula”, a name still in use, is the Latin for “brood sow”, and the origin of the name is obscure. The name “King's evil”, used in the Middle Ages, derives its

origin from beliefs that the “royal touch” of the Kings of England or France, could cure the disease^[5].

Scrofula may be a manifestation of a systemic tuberculous disease or a unique clinical entity localized to the neck^[6]. It is the most common manifestation of extra-pulmonary tuberculosis (TB)^[3,6] and a frequent cause of peripheral lymphadenitis in the developing world where tuberculosis is endemic. Tuberculous lymphadenitis is seen in nearly 35 per cent of extra-pulmonary TB which constitutes about 15 to 20 per cent of all cases of TB^[6]. It was very common until the second half of the 20th century when the prevalence of tuberculosis significantly reduced^[2,3,5,6]. But in recent times with the resurgence of TB, the incidence has

increased in parallel with the increase in the incidence of mycobacterial infection worldwide^[6], particularly among the immunocompromised^[5,6]. Prior to this resurgence, scrofula was most prevalent among children, with only about 8% of the disease in this population being tuberculous^[7] as atypical mycobacteria such as *M. scrofulaceum* and other non-tuberculous mycobacteria (NTM) are usually responsible in immunocompetent children. Presently however, about 50% of cervical tuberculous lymphadenopathy occurs in adults^[7]. A vast majority of these (about 95%) is caused by *M. tuberculosis*, and is found most often in immunocompromised patients. In HIV-infected patients, extrapulmonary TB accounts for up to 53 to 62 percent of cases of TB^[8,9,10]. Cervical lymph nodes are the most common site of involvement and reported in 60% to 90% patients with or without involvement of other lymphoid tissue^[11].

Scrofula presents with masses in the neck mass but the diagnosis is usually challenging as the condition is known to mimic many other pathologies^[12,13]. Even if cervical lymphadenopathy of inflammatory origin is suspected, the diagnosis of cervical tuberculous lymphadenitis is not easy especially if the host is immunocompetent. A sustained high index of suspicion is vital to making a diagnosis. If the patient does not have concomitant pulmonary tuberculosis, sputum may not be available for microscopic diagnosis. Secondly, tuberculin skin test results may be negative or inconclusive as the result (even if positive) is unreliable in making a diagnosis of active tuberculosis. Furthermore, Fine Needle Aspiration Cytology (FNAC) may not yield a positive result, histology may not be possible due to non-availability of tissue, and culture of *M. tuberculosis* takes several weeks. This is a report of yet another atypical presentation of tuberculous cervical lymphadenitis and the diagnostic challenges associated with it. The case emphasizes the need for openness to unusual modes of presentation, a sustained high index of suspicion, thorough evaluation, and the need for a multidisciplinary approach in the diagnosis and management of tuberculous cervical lymphadenitis.

CASE REPORT

The patient was a 28-year-old male who had a sudden onset illness with fever and malaise. The fever continued despite self-prescribed antimalarial medication. On the fourth day, he developed pain in the right side of the neck and discovered a tiny, firm and tender nodule less than the size of a pea at the site of the pain. He also had profuse night sweats but no noticeable weight loss. Despite taking Ciprofloxacin tablets that was also self-prescribed, fever persisted, and the nodule in the neck increase in size, became noticeable and more painful. By the end of the second week, a second painful mass had appeared on the left side of the neck.

He visited a hospital and after assessment, was found to have an elevated white blood cell count (WBC) of

10,900/mm³ (with normal differential percentages) and elevated erythrocyte sedimentation rate (ESR) of 54 mm/hr (Westergreen). Tuberculin skin test produced an induration of 3.00mm (which is considered normal in the environment) and the chest x-ray was normal. HIV test was also negative. Sputum examination was not done as he was not coughing. He was placed on oral Ampicillin-Cloxacillin (500mg qds) but the fever persisted, and the neck masses continued to increase in size. He was then referred to a teaching hospital where the WBC was noticed to have dropped to 7,900/mm³ but ESR had risen to 96mm/hr. Neck ultrasound at this stage showed bilateral supraclavicular lymph node enlargements but abdominal ultrasound was normal. Fine Needle Aspiration Cytology (FNAC) yielded a non-specific inflammatory smear and CT scan showed bilateral soft tissue neck mass without any other head and neck abnormality. He was subsequently scheduled for an Examination under Anaesthesia (EUA).

At this point, approximately ten weeks of the illness, the patient decided to seek another opinion in our centre. He still had continuous fever, bilateral neck masses and profuse night sweats. On examination, his temperature was 39°C and very loose clothing suggested weight loss. He had neck masses in both anterior triangles (14× 12cm on the right and 4 × 2cm on the left). Both masses were slightly tender with smooth shiny overlying skin. Physical examination was otherwise normal. We made a diagnosis of “Inflammatory neck mass (to rule out tuberculosis, other chronic granulomatous disease, and primary or metastatic cervical malignancy). We ordered repeat investigations (ESR, Neck and abdominopelvic USS, FNAC, HIV screening, X-ray of the postnasal space, pure tone audiometry and tympanometry and fasting blood sugar) and while awaiting results we placed him on oral Co-Amoxclav (1g b.d.) and Metronidazole (400mg t.d.s.).

At review one week later, ESR had risen to 102mm/hr. Fasting blood sugar was within normal limits, post-nasal space x-ray and audiometry were normal, and HIV screening test was negative. Abdominal scan was also normal but the neck ultrasound showed lobulated soft tissue neck masses bilaterally. FNAC reported a non-specific inflammatory smear. He still had fever, with his temperature ranging between 38.5°C and 39.5°C, neck pain was worse and was radiating to the chest. The masses had become fluctuant, so we did an ultrasound-guided aspiration which yielded 30ml of purulent material which we sent for cytology, microscopy, culture and Ziehl Neelsen (ZN) staining for acid fast bacilli (AFB). Unfortunately, these investigations did not yield any additional information.

As there was a strong suspicion of tuberculosis, no attempt was made to drain the abscess. Following a multidisciplinary team discussion, a repeat USS was done to search for isolated solid nodes that could be biopsied. None was found but an ultrasound-guided

aspiration was done and specimens sent for *M. tuberculosis* culture at the Regional Tuberculosis Reference Laboratory and for fungal studies. A therapeutic trial of DOT (Directly observed Treatment) anti-tuberculosis drugs (an initial two-month intensive phase of 4-FDC RHZE – fixed dose combination of Rifampicin, Isoniazid, Pyrazinamide and Ethambutol, total dose of 600mg + 300 mg + 1600mg + 1100mg daily, then 2-FDC RH – fixed dose combination of Rifampicin and Isoniazid, total dose of 600mg + 300 mg daily) was then commenced. The masses stopped increasing in size but fever persisted for several weeks, with the temperature remaining around 38°C. Four weeks into anti-tuberculosis medication, a sinus developed on the right side which closed spontaneously after two weeks. After six weeks of anti-TB medication, Mycobacterial culture result came back positive for *M. tuberculosis*. The fungal study was negative. By this time, the patient's temperature had normalized and the neck masses had reduced in size. By the fourth month of anti TB treatment, the masses were no longer noticeable, but the patient completed a 12-month course of anti-TB medication. At completion, a neck USS confirmed complete resolution of the neck pathology without any residual mass.



Figure 1: Neck – Week 10



Figure 2: Right side of Neck before ulceration of mass



Figure 2: Right side of Neck after ulceration of mass

DISCUSSION

Tuberculous cervical lymphadenitis has been called “the great masquerader” because it tends to mimic many other diseases^[6,12,13]. The list of differential diagnoses is long and includes infections (viral, bacterial, fungal), primary tumours of the neck (lymphoma or sarcoma), metastatic carcinoma, non-specific reactive hyperplasia, sarcoidosis, toxoplasmosis, cat-scratch fever, collagen vascular diseases and diseases of reticuloendothelial system^[6]. Scrofula has been known to be mistaken for many of these conditions^[12,13], so it is not surprising that this case eluded diagnosis for months after the onset of the disease despite early presentation. In this patient, several diagnoses were considered at various stages of his management. These included acute bacterial adenitis, metastatic carcinoma, lymphoma and fungal disease. As is usual with scrofula, there were several atypical features that confused the clinical picture.

Illness of sudden onset with constitutional symptoms of fever and malaise without an obvious neck mass is completely atypical of scrofula. Arguably, this mode of presentation may knock even the most astute clinician off-track. A diagnosis of tuberculous cervical lymphadenopathy is not likely to be considered if there is no neck mass. To the best of our knowledge, this is a previously unreported mode of presentation. We believe that this phase was noticed because of the early presentation. The lesson here is not new but one that cannot be overemphasized: any patient with fever should be assessed exhaustively and with an open mind. Assessment must include a good history, thorough physical examination and appropriate quality assured investigations. Every case is potentially complex and it must be recognized that it may take a further unfolding of the pathology before an accurate diagnosis can be made. An open mind, a high index of suspicion and thorough clinical evaluation are thus invaluable in the diagnostic approach.

As the pathology further unfolded in this case another unusual feature emerged – painful neck masses that appeared and assumed appreciable proportions in just a couple of weeks. This mode of presentation is typical of acute inflammation, and tuberculosis is again not likely to be on the list of differential diagnoses. While a patient with cervical tuberculous lymphadenitis could have some or all of the constitutional features that may accompany tuberculosis infection (fever, malaise and night sweats) in addition to the neck mass, the mass itself does not usually possess features of acute inflammation, a characteristic that earned it the name “cold abscess”. The mass usually presents as a slowly progressive, painless swelling of a node or group of lymph nodes^[9,10]. The duration of symptoms at the time of presentation is typically 1–2 months, varying from 3 weeks to 8 months^[14,15,16]. Patients do not generally report significant pain at presentation, and node tenderness during examination is noted in only 10%–35% of cases^[14,17,18].

Another unusual feature of this case was the absence of any evidence of immunosuppression in the patient. It is a well-known fact that there has been a resurgence of tuberculous cervical lymphadenitis since the appearance of HIV and a vast majority (about 95%) of patients are immunocompromised^[13]. This case underscores the fact that the absence of obvious immunosuppression does not rule out the condition. Chances are less definitely, but the possibility remains. This case therefore adds to the previously reported cases of scrofula in immunocompetent and otherwise healthy young adults. While noting this, we do pose a hypothesis that the atypical presentation in this patient might be a result of his immune competence.

Additionally, it should be noted that this patient presented early and that there was a suspicion of tuberculosis when he presented in the hospital. However, every investigation that could have confirmed the diagnosis early turned out negative. This further highlights how difficult it is to diagnose the condition and the need for care in the use and interpretation of the tuberculosis tests in the diagnosis of scrofula. A tuberculin skin test performed within the first few days of onset of symptoms yielded 3mm induration (considered negative for our environment), sputum was not available to stain for AFB and repeated FNACs from different pathologists, even though yielding inflammatory smears, did not give a diagnosis. Since standard head and neck oncological practice dictates that it must be ascertained that neck masses are not lymph node metastases prior to invasive procedures, there was a delay in taking a decision for a lymph node biopsy. By the time the decision was made, no solid node was available to biopsy and so the opportunity to make a diagnosis by histology was lost. Consequently, with no investigation to aid diagnosis it was only the clinical picture of a presumed inflammatory neck mass in a patient who did not deteriorate rapidly clinically in the presence of large bilateral inflammatory neck masses that sustained the suspicion of scrofula or other granulomatous neck disease.

We are however quick to observe that a diagnosis could have been made earlier. A biopsy of neck lymph nodes may have led to a diagnosis much earlier. Granted that it is a rule of thumb not to excise a neck node until the possibility of a squamous cell carcinoma has been ruled out, several features of the neck mass pointed away from malignancy. The sudden appearance of a neck mass of appreciable proportions within two weeks and the FNAC results which were consistently "inflammatory", persistent fever and night sweats strongly suggested an inflammatory cause. Fever could occur in malignancy but such malignancy is more likely to be a lymphoma. Access to other tuberculosis diagnosis tests modalities such as the Interferon-Gamma Release Assays (IGRAs) and molecular methods such as Nucleic Acid Amplification testing and Polymerase Chain Reaction where available could also have helped. In all likelihood,

these would have been positive, and while not to be relied on alone to diagnose an active infection^[19,20], put together with the other clinical features could have aided an earlier decision to biopsy. This helps make a case for promoting availability of these tests in developing countries. Also, prompt availability and review of investigations results could have shortened the time to the decision for biopsy and increased the chances of getting a solid lesion to biopsy.

We further reflect that getting a biopsy would have been the best line of management.

A biopsy is advantageous not just because it would aid earlier diagnosis, it is also capable of identifying other pathology that could present in the same manner. If culture had not yielded a growth of mycobacterium tuberculosis in this case, further management of this patient would have been challenging. Other pathologies that could have presented in the same way include other chronic granulomatous infections caused by fungi and protozoans. The utility of a biopsy therefore lies in the capability to identify a wider variety of pathology, and done early, would facilitate prompt appropriate treatment.

An additional point to note is the importance of radiology in the assessment of these cases. A neck CT scan was useful in the assessment of the neck and the upper aero-digestive tract for masses and neck ultrasound scans were useful in the assessment and follow up of the neck masses as well as in ultrasound guided aspirations and FNACs. Besides both CT scan and ultrasound could assist in making an earlier decision to biopsy, as both could pick up the early stages of suppuration, which may reinforce the diagnosis of an inflammatory mass.

In conclusion, our case report highlights several points. It brings to mind the masquerading nature of tuberculous cervical lymphadenitis with its myriad of presentation, mimicking several ailments, and it showcases yet another "masquerading" presentation. It also emphasizes the need for a sustained high index of suspicion, prompt and thorough assessment of suspected cases even as the pathology unfolds and careful use and interpretation of investigations. Finally, it demonstrates the need for a multidisciplinary approach and care for adequate management. Scrofula is indeed a "great masquerader" but careful attention to these details will aid in unmasking this most elusive of diagnoses.

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