

## CASE REPORT

# Lymph Node Metastasis from Papillary Thyroid Carcinoma or Tuberculous Lymphadenitis: A Diagnostic Dilemma

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## ABSTRACT

**Background:** Papillary thyroid carcinoma commonly presents with nodal metastases. The recommended treatment modality is total thyroidectomy with lateral neck dissection, i.e., a rather invasive surgical procedure with associated complications.

**Aim:** A rare case of coexistence of papillary thyroid carcinoma (PTC) and tuberculous cervical lymphadenitis in a patient that presented as a diagnostic and management dilemma intraoperatively is reported.

**Case report:** We hereby report a case of a Chinese female, who presented with a goiter and associated painful right lateral neck swellings. After preoperative investigations were done, the initial diagnosis was PTC with nodal metastases. However, the enlarged lymph nodes were eventually found out to be secondary to tuberculous infection through polymerase chain reaction (PCR) done on the surgical specimens.

**Conclusion:** In a small subset of patients with PTC, cervical lymphadenopathy is secondary to tuberculosis rather than nodal metastases. If preoperative and intraoperative investigations could be utilized to diagnose tuberculous lymphadenitis, lateral neck dissection could potentially be avoided.

**Clinical significance:** This clinical entity of coexistence of PTC and tuberculous cervical lymphadenopathy has only been minimally reported in the literature. In our patient, it was even more clinically significant as the enlarged lymph nodes were in close proximity to the innominate vessels, and thus required the potential need of a sternal split if the innominate vessels were injured in the process of surgery. In future, further studies would be recommended to determine the best approach for the management of concomitant PTC and tuberculous lymphadenitis, and future patients could benefit in terms of avoiding the complications associated with a potentially unnecessary invasive surgery.

**Keywords:** Metastasis, Papillary thyroid cancer, Tuberculosis.

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## BACKGROUND

Papillary thyroid carcinoma, the most common histological form of thyroid cancer, metastasizes most commonly via the lymphatic route.<sup>1-3</sup> Cervical lymph nodes that can be detected via palpation during physical examination when the patient first presents account for 23 to 56% of cases of PTC.<sup>3-5</sup> In such a patient, the recommended treatment modality is total thyroidectomy with lateral neck dissection.<sup>6</sup> However, lateral neck dissection brings along its own set of risks including nerve damage to the spinal accessory nerve and the vagus nerve. Moreover, in a small subset of patients with PTC, enlarged lymph nodes could be attributed to tuberculosis rather than metastasis, and this is especially so in regions in which tuberculosis infection is endemic.<sup>7,8</sup> We, hereby, report a rare case of a Chinese female patient with PTC and cervical lymphadenopathy as a result of tuberculous infection, which presented as an intraoperative dilemma.

## CASE REPORT

A 47-year-old Chinese Singaporean female had a neck swelling that was first noticed by her friends. On workup, the neck lump was confirmed via ultrasound to be a thyroid goiter. She was clinically and biochemically euthyroid, as supported by thyroid function tests.

One year after her initial presentation, she developed painful right lateral neck swellings that were associated with fever. Additionally, her goiter grew progressively larger. She also experienced hoarseness of voice, dysphagia, and dyspnea. She had significant loss of weight of 6 kg over 2 months, with normal appetite. She has had recent travel history to South Africa prior to experiencing the painful right lateral neck swellings. There was no known contact history. In addition, there was no known family history of thyroid cancer and no previous history of irradiation of the neck. Ultrasound of neck region revealed

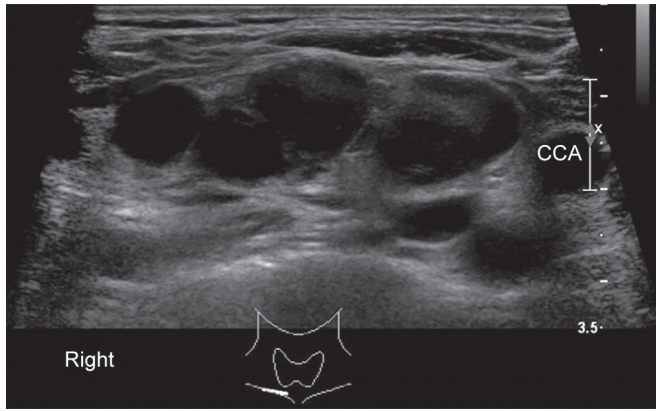
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**Fig. 1:** Ultrasound of patient's neck region revealing multiple enlarged lymph nodes seen predominantly along the right side of the neck

bilateral thyroid nodules with no suspicious features, and multiple enlarged lymph nodes were detected along the right side of the neck (Fig. 1). Ultrasound-guided fine needle aspiration cytology (FNAC) of the thyroid swelling revealed PTC on histology. The FNAC of right supraclavicular lymph node showed polymorphous lymphoid cells. Computed tomography (CT) scan of the head and neck region showed bilateral thyroid nodules; the largest nodule was located in the right thyroid lobe, measuring 8 × 6 mm (Fig. 2). Also, on CT scan, there are several enlarged right supraclavicular lymph nodes with central necrosis (Fig. 2). In view of the known right PTC, the enlarged right supraclavicular lymph nodes likely represented nodal metastases.

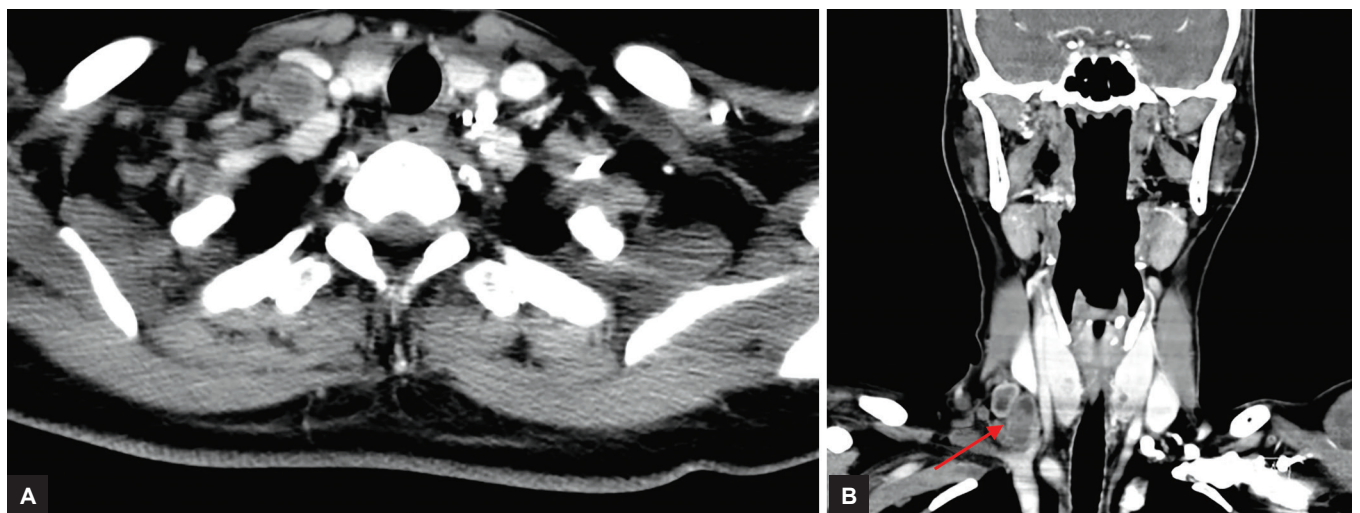
As some of the enlarged lymph nodes were near the innominate vessels of the patient, she was counseled preoperatively for a sternal split, if innominate vessels were inadvertently damaged during the surgery. Understanding this additional risk, the patient agreed to proceed with the surgery. Patient first underwent

total thyroidectomy. Intraoperative frozen section of thyroid gland was consistent with initial diagnosis. Upon patient's prior request, intraoperative frozen sections of the level IV lymph nodes were done. The first node sent revealed necrotizing granulomatous inflammation. Several more lymph nodes were taken from level IV, with the aim of confirming nodal metastasis. However, all the lymph nodes examined were negative for malignancy, and instead revealed necrotizing granulomatous inflammation. Despite the infective preliminary results, in view of PTC and the necrotic lymph nodes' appearance on CT scan, the attending surgeons proceeded with lateral neck dissection to clear all the lymph nodes in the neck to ensure that no residual disease was left behind. Fortunately, there was no need for sternal split and the patient recovered with no complications.

Final histopathological results confirmed PTC, but all the lymph nodes were negative for metastasis and most showed extensive necrotizing granulomatous inflammation. Ziehl–Neelsen stain was negative for acid-fast bacilli. However, lymph node tissues were then sent for tuberculosis PCR, which then confirmed that deoxyribonucleic acid of *Mycobacterium tuberculosis complex* was present. Patient was referred to an infectious disease specialist for treatment of tuberculosis upon confirmation of results. Thus, the final diagnosis was PTC with concomitant cervical tuberculous lymphadenitis.

**DISCUSSION**

It is hard to differentiate tuberculous lymphadenitis from lymphatic metastasis in a patient with PTC and enlarged lymph nodes. Lymph node enlargements in the supraclavicular area or the posterior triangle of the neck are common to both tuberculosis lymphadenitis and metastasis from PTC.<sup>9</sup> Our case example revealed



**Figs 2A and B:** Axial and coronal views of patient's CT scans of the head and neck. The arrow reveals the enlarged lymph nodes in close proximity to the innominate vessels, thus posing a surgical challenge

lymph nodes' enlargement in the supraclavicular region, common to both infective and metastatic disease. Likewise, as seen in our patient's case, the lymph nodes could not be easily differentiated radiologically. The diagnostic dilemma is particularly troublesome for our patient's case because the supraclavicular lymph nodes were near the innominate vessels. If the innominate vessels were injured, a more complex surgery involving a sternal split might be required.

Cervical tuberculous lymphadenitis may be the only presenting symptom without other pulmonary or systemic manifestations evident.<sup>3,10</sup> In a country where tuberculosis is prevalent, one should consider the possibility of cervical lymphadenopathy secondary to tuberculosis. A simple chest X-ray could support the diagnosis of tuberculous infection if it is positive for pulmonary tuberculosis. In the absence of pulmonary tuberculosis, cervical tuberculous lymphadenopathy could still be possible, as in this case, where a retrospective chest X-ray was done for our patient, and it did not show any lesions suspicious of tuberculosis. Likewise, Kim et al<sup>2</sup> showed that only a minority of a small group of patients with PTC and cervical lymphadenopathy had features in their history or investigative findings suggestive of tuberculosis.

A number of preoperative investigations are often done prior to surgery and their efficacies are varied, especially in terms of differentiating tuberculous cervical lymphadenitis from metastatic lymph nodes from PTC.

In terms of radiological investigations, ultrasonography (US) and CT findings in tuberculous cervical lymphadenitis resemble that of metastatic lymph nodes from PTC.<sup>10-13</sup> Cystic necrosis, calcification and hypo-echoic, round-shaped masses usually located in the supraclavicular region or the posterior triangle of the neck are characteristic US features of both tuberculous lymphadenitis and nodal metastasis of PTC.<sup>8</sup> The CT scan in both cases will often reveal peripheral irregular contrast and central low density.<sup>3</sup> Despite the fact that US is the most useful radiological tool in differentiating benign from metastatic cervical lymph nodes,<sup>14</sup> even superseding magnetic resonance imaging (MRI), it is still difficult to differentiate tuberculous cervical lymphadenitis from metastatic lymph nodes from PTC via US. In the case of our patient, both radiological tools of US and CT were unhelpful in the diagnostic dilemma. The MRI was not done.

In detecting tuberculosis lymphadenopathy, one study reported that preoperative FNAC has 88% sensitivity and 96% specificity.<sup>3</sup> A few other studies reported that sensitivity of FNAC was 46 to 90%, depending on the institution,<sup>11,12,15,16</sup> highlighting that results vary widely. Moreover, one could not base the diagnosis on merely

seeing granulomas on FNAC.<sup>3</sup> Further tests are indicated to confirm the diagnosis of tuberculosis, and they include *M. tuberculosis* culture, acid-fast bacilli smear, and PCR.<sup>3</sup> Culture is time-consuming, while smear test is less accurate.<sup>17,18</sup> By contrast, PCR gives precise and rapid results. As such, Choi et al<sup>16</sup> state that PCR for *M. tuberculosis* from aspirated materials from FNAC of enlarged lymph nodes should be done to rule out tuberculous cervical lymphadenitis. In our patient, preoperative PCR for *M. tuberculosis* within aspirated materials from FNAC of enlarged lymph nodes was not done as coexistence of cervical tuberculous lymphadenitis and PTC was neither part of routine investigations nor part of clinical suspicion. In retrospect, PCR as a preoperative diagnostic modality in distinguishing cervical tuberculous lymphadenitis from nodal metastasis from PTC can be considered.

Intraoperative sampling and frozen sections of lymph nodes suspicious of metastasis have shown to be helpful.<sup>2</sup> This is also reflected in our case whereby intraoperative frozen sections of lymph nodes actually raise suspicion of tuberculous lymphadenitis, rather than malignancy.

As mentioned in the introduction, lateral neck dissection is a rather invasive procedure with risks involved. By contrast, cervical tuberculous lymphadenitis is treated noninvasively via antituberculous drugs with surgery having a minimal role.<sup>1</sup> Hence, there is a role of preoperative FNAC with PCR for detecting *M. tuberculosis* to aid in the diagnostic dilemma,<sup>16</sup> especially in endemic regions. In patients who tested positive for *M. tuberculosis*, lateral neck dissection may not be needed.<sup>8</sup> Surgeons would then be able to minimize various complications associated with lateral neck dissection in this subset of patients.

While acknowledging that some surgeons may still have reservations leaving residual metastatic disease behind even if the patient is positive for tuberculous lymphadenitis, there is an option of treating the tuberculous lymphadenitis with antituberculosis drugs and waiting and watching to see if the enlarged lymph nodes respond to treatment and subside before determining the surgical plan. If the enlarged lymph nodes decrease in size and subside, there might not be a need for further lateral neck dissection.

Nevertheless, there is potential for further large-scale studies to be conducted so that further conclusions can be made as to which is the best approach in the diagnostic dilemma.

## CONCLUSION

In conclusion, in a small group of patients with PTC, enlarged lymph nodes could be attributed to tuberculosis rather than metastasis, and this is especially so in regions where tuberculosis infection is endemic. Hence, if preoperative and intraoperative investigations could be

utilized to diagnose tuberculous lymphadenitis, invasive lateral neck dissection and its associated complications could potentially be avoided.

## CLINICAL SIGNIFICANCE

This clinical entity of coexistence of PTC and tuberculous cervical lymphadenopathy has only been minimally reported in the literature. In our patient, it was even more clinically significant as the enlarged lymph nodes were in close proximity to the innominate vessels, and thus required the potential need of a sternal split if the innominate vessels were injured in the process of surgery. In future, further studies would be recommended to determine the best approach for the management of concomitant PTC and tuberculous lymphadenitis, and future patients could benefit in terms of avoiding the complications associated with a potentially unnecessary invasive surgery.

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