Coexistent cervical tuberculosis and metastatic squamous cell carcinoma in a single lymph node group: A diagnostic dilemma

Heitham Gheriani, FRCSI, FRCSEd; Maky Hafidh, FRCSI; David Smyth, FRCSI; Tigh O'Dwyer, FRCS, FRCSI

Abstract

Primary cervical tuberculosis is uncommon, although its incidence has risen somewhat over the past few years. In this article, we describe a rare case in which the patient developed a dual pathology—cervical tuberculosis and a malignant squamous cell carcinoma—in a group of lymph nodes on one side of the neck. Initially, tuberculosis was diagnosed on the basis of histology and culture. However, when the patient did not respond to antituberculous drug therapy, a repeat biopsy detected the second pathology: squamous cell carcinoma. To the best of our knowledge, no such presentation has been previously reported in the world literature. We conclude that repeat biopsy might be required in cases of tuberculous cervical lymphadenopathy that do not respond to conventional antituberculous therapy.

Case report

An 80-year-old man, a retired farmer, presented with a 2-month history of a progressively enlarging right-sided neck mass. He reported no associated constitutional symptoms. A few weeks earlier, before he had noticed the neck mass, he had undergone excision of a small lesion from the pinna of the right ear. Histology identified the mass as a squamous cell carcinoma with clear margins.

On physical examination, the mass appeared as a tender, 7 × 7-cm swelling in the right upper cervical area. The swelling encroached into the posterior triangle of the neck. Findings on examination of the upper airway and chest x-ray were normal. The patient was admitted for panendoscopic assessment of the upper airway and digestive tract; again, findings were negative. After the results of a fine-needle aspiration biopsy turned out to be inconclusive, an open deep biopsy was performed. The open biopsy yielded a purulent discharge that was sent for culture. Histology of the deep biopsy specimen identified features of granulomatous inflammation and palisading epithelioid cells, Langhans’ giant cells, lymphocytes, and a few neutrophils with small foci of caseous necrosis (figure 1). Culture of the discharge was positive for Mycobacterium tuberculosis and sensitive to ethambutol, isoniazid, pyrazinamide, and rifampin. A tuberculin skin test was positive. The presence of tuberculosis bacilli was confirmed by ligase chain reaction (LCR) assay. Based on the histology and culture reports, antituberculous chemotherapy was commenced.

An initial response to antituberculous medication manifested as a reduction in swelling. However, the area of
swelling subsequently increased, and ulceration and more purulent discharge appeared. A repeat incisional biopsy identified a squamous cell carcinoma within the lesion (figure 2). The patient was considered to be too ill to undergo any further surgical procedure, and palliative radiotherapy was administered until he died from the cancer.

Discussion
The differential diagnosis of cervical adenopathy includes bacterial and viral infections (including tuberculosis), congenital head and neck conditions, and malignancies. The case that we report herein featured an unfortunate coincidence of primary cervical tuberculosis and squamous cell carcinoma. The second biopsy, which was performed subsequent to the patient’s poor response to antituberculous therapy, identified the presence of the second pathology: squamous cell carcinoma. Our review of the world literature failed to find any similar presentation, although we did find a number of cases of squamous cell carcinoma that were initially believed to be tuberculosis.

Infection of the cervical lymph nodes with tuberculosis (scrofula) has increased in proportion with the current rise in the incidence of tuberculosis itself. Classic cervical tuberculosis is usually acquired by drinking milk contaminated with bovine M tuberculosis bacilli; the port of entry is usually the tonsils. The most common presenting sign is a mass or a draining fistula in the neck. Cervical tuberculosis is usually associated with constitutional symptoms such as fever, weight loss, and night sweats. Our patient had unilateral M tuberculosis in multiple lymph nodes that were matted together.

In a significant proportion of patients, head and neck cancer will involve the regional lymph nodes of the neck. It is accepted that a palpable lymphadenopathy in the neck in a patient with no obvious primary tumor who has previously undergone treatment of a primary tumor represents a metastasis. Confirmation by fine-needle aspiration cytology or biopsy guided by computed tomography (CT) is generally required prior to planning any radical treatment. Our patient had previously undergone successful treatment of a squamous cell carcinoma in the right pinna. The panendoscopic examination that we performed did not detect any pathology in the upper aerodigestive tract. Although analysis of the fine-needle aspiration of the node was inconclusive, the first incisional biopsy of the lymph node did not identify the presence of squamous cell carcinoma. Instead, it showed caseous necrosis, which was followed by a positive culture and a positive tuberculin test. As a result, the diagnosis of tuberculosis was made and the antituberculous therapy was started.

Squamous cell carcinoma of the upper aerodigestive tract is associated with a higher rate of metastasis to the regional lymph nodes than is squamous cell carcinoma of the skin. The signs and symptoms of cervical lymphadenopathy caused by tuberculosis are similar to those caused by carcinoma. In both cases, patients may present with a painless swelling. Tuberculosis does result in more constitutional symptoms, but they are not specific. A history of pulmonary tuberculosis in a patient with a positive chest x-ray or a history of tuberculosis elsewhere in the body may be an important clue to the diagnosis.

The results of acid-fast staining can be reported within 24 hours or less, but this test lacks sensitivity and cannot distinguish among different species of Mycobacterium. Growth of M tuberculosis on culture is more sensitive than microscopy, but culture requires 1 to 8 weeks to yield results. Rapid detection of M tuberculosis can be facilitated by performing polymerase chain reaction (PCR) or LCR testing. With an LCR M tuberculosis assay, which we used in our patient, the nucleic acid amplification method detects the presence of M tuberculosis DNA in the clinical specimen directly. Results of the LCR M tuberculosis assay are available within 48 hours. This method has proved to be of value in the diagnosis of pulmonary, as well as extrapulmonary, tuberculosis. According to the American Thoracic Society, its sensitivity is 93% and its specific-
ity is 99%. However, this test should be combined with a properly taken lymph node biopsy for histopathologic assessment. Tuberculosis culture is associated with a false-positive rate of 3.5 to 5%, primarily because of cross-contamination. We investigated the possibility of laboratory contamination in our case, and we were satisfied that it did not occur. The microbiology laboratory at our hospital follows standard identification and susceptibility procedures. We also ruled out the possibility of wrongly labeled specimens.

Although our literature review did not turn up a similar case of dual pathology in the same group of lymph nodes, we did find a number of reports of the coexistence of tuberculosis and cancer in parts of the body other than the lymph nodes. For example, Watanabe et al found coexisting pulmonary tuberculosis in 16 of 758 patients with lung cancer (2.1%). In 6 of these cases, the two diseases were found at the same time during a clinical workup. In the remaining 10 cases, pulmonary tuberculosis had preceded lung cancer in 5 patients and lung cancer had preceded pulmonary tuberculosis in the other 5. In a study from the Tokyo National Chest Hospital, Tamura et al reported that the incidence of lung cancer among patients with active pulmonary tuberculosis was 0.7% and the incidence of active pulmonary tuberculosis in untreated lung cancer patients was 1.9%. They classified these patients into two groups: those with tuberculosis sequential to lung cancer and those whose tuberculosis and lung cancer were detected simultaneously; the tuberculosis in the sequential group was more extensive and more severe than it was in the other group. Mayall et al reported the case of a 53-year-old woman with esophageal squamous cell carcinoma whose CT demonstrated a left apical lung cavity; study of the bronchial washing revealed the presence of Mycobacterium shimoidei. Plaza Mayor et al reported 2 cases of synchronous tuberculosis and laryngeal carcinoma. Finally, Yerushalmi et al described the case of a patient whose lupus vulgaris was complicated by a metastatic squamous cell carcinoma in the neck.

Neoplasia resulting from chronic inflammation has attracted some attention. Proliferation in the setting of long-standing chronic inflammation appears to predispose affected patients to carcinoma in the lung, liver, large bowel, urinary bladder, and gastric mucosa. In a case-control study of the etiology of lung cancer in women in China, Dai et al found that one of the risk factors was pulmonary tuberculosis. Similarly, Chen et al studied 21 cases of urologic cancer and found that one of the risk factors was chronic tuberculous pyelonephritis. Honda et al suggested that the immunocompromised status of patients with a chronic inflammation such as tuberculosis may contribute to the development of cancer. Yanagisawa et al suggested that chronic inflammation is associated with an acceleration in epithelial cell turnover. Finally, Spechler showed that carcinoma can arise in foci of metaplasia, which is usually a consequence of chronic inflammation.

In conclusion, a repeat biopsy might be required in cases of tuberculous cervical lymphadenopathy that do not respond to conventional antituberculosis therapy. Close monitoring is required to assess the response to treatment.

References