Aggressive cervical lymphoma presenting as airway obstruction

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Non-Hodgkin's lymphoma (NHL) is the second most common malignancy of the head and neck.[1] Patients with NHL typically have persistent, painless peripheral lymphadenopathy, often in the cervical region, although 12% have systemic symptoms of fever, night sweats, and weight loss.[1] More than half of head and neck lymphomas occur in Waldeyer's ring, and a third occur in extralymphatic sites, including the sinuses, nasal cavity, oral cavity, larynx, salivary glands, and thyroid gland. These cases present with symptoms based on the site of the lesion, including sore throat, nasal obstruction, nasopharyngeal mass, or pharyngeal foreign-body sensation. Approximately 20% of patients with NHL have mediastinal adenopathy and at presentation have persistent cough, chest discomfort, or superior vena cava syndrome.[1] Patients may have involvement in the retroperitoneal, pelvic, and mesenteric nodes, which is usually asymptomatic unless the tumor is massive or causing visceral obstruction.

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A painless cervical mass is the most common presenting symptom of lymphoma in the head and neck. However, we report a case of aggressive cervical NHL that presented with significant life-threatening airway obstruction. Patients with airway obstruction may pose a serious diagnostic and therapeutic challenge for the physician. Several of the dilemmas regarding treatment of these patients are highlighted by this case report.

CASE REPORT

A 48-year-old man was referred to the Houston Veterans Administration Medical Center Emergency Department for difficulty breathing. At the time of presentation, he reported a 4-month history of bilateral neck swelling and a 1-month history of hoarseness and mild dysphagia. During the 3 days before admission, he had noticed increasing shortness of breath, with complete inability to breathe when lying supine. He had no weight loss, fever, or night sweats. He had a 9 pack-year history of smoking and denied alcohol or illegal drug use. His only other significant medical problem was hypertension, which was treated with nifedipine. He had worked as a radar technician in the past but was currently unemployed.

On examination, the patient was found to be an obese man in mild respiratory distress. His blood pressure was 130/80 mm Hg, and his respiratory rate was 24 breaths/minute (sitting upright), with stridor on deep inspiration. He was found to have a dominant left neck mass (8 × 10 cm), a right neck mass (6 × 4 cm), and massive bilateral cervical lymphadenopathy (Fig. 1). His shirt neck size was 28 inches, but he had no significant facial swelling. Indirect laryngeal examination revealed pronounced extrinsic compression and anterior dis-

Fig 1. Patient at presentation was noted to have a markedly enlarged neck, with visible lymph node masses.

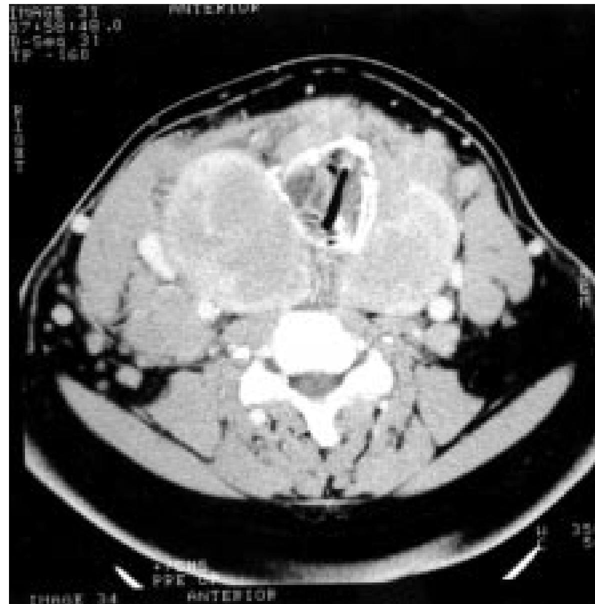

Fig 2. CT scan of the neck (axial section) demonstrates massive cervical and retrolaryngeal adenopathy, causing anterior and rightward displacement along with constriction of the endolarynx.

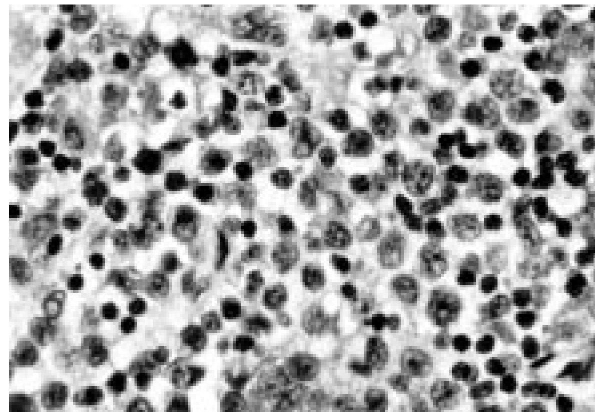

Fig 3. Lymph node biopsy reveals a diffuse population of predominantly large cells with vesicular nuclei, clumped chromatin, and occasional nucleoli consistent with large B-cell lymphoma. (Hematoxylin and eosin stain; original magnification ×400.)

placement of the endolarynx. The posterior glottis was rotated to the right, and the airway was moderately constricted but patent. There were no mucosal lesions and no pooling of secretions. The vocal folds were mobile bilaterally but with restricted range of motion, particularly on the left. An attempt to place the patient in a supine position resulted in complete airway obstruction. The remainder of his examination was unremarkable. Purified protein derivative and HIV tests were negative; thyroid function tests were within normal limits. Chest roentgenogram demonstrated widening of the anterior mediastinum with hilar adenopathy.

On the evening of admission, the patient was placed in the intensive care unit for constant monitoring. He was given high-dose prednisone to decrease laryngeal edema, and by the next morning improvement of the patient's breathing was noted such that he could now lie flat on his back for about 5 to 10 minutes before tiring. He was transferred to a regular room on hospital day 2 and monitored with frequent nurse and on-call physician evaluations. A rapid, spiral CT scanner was used to image the patient's neck. This revealed massive cervical lymphadenopathy causing significant compression and displacement of the larynx (Fig. 2), with no distal tracheal obstruction.

Fine-needle aspiration (FNA) of the cervical mass revealed a population of large and small lymphocytes and scattered macrophages. The smears were thought to be most consistent with a reactive process and were interpreted as a benign lymphoid hyperplasia. The patient was then taken to the operating room for incisional biopsy while under local anesthesia and in a sitting position. The biopsy specimen revealed a diffuse population of large, irregular cells with clumped chromatin, irregular nuclear rims, and large irregular nucleoli (Fig. 3).

Atypical mitotic figures were present and numerous. Flow cytometry with immunohistochemical staining was performed, revealing a population of large B cells with monoclonal κ light chain restriction. This was confirmed as a B-cell population by immunohistochemical stains for B and T cells on the formalin-fixed paraffin sections. A diagnosis of large cell lymphoma, B-cell κ light chain type, was made.

Findings of staging CT scans of the chest, abdomen, and pelvis, as well as bone marrow biopsy were all negative with the exception of mediastinal adenopathy. The patient's lymphoma was classified as stage IIA. A treatment regimen of cyclophosphamide, doxorubicin (Adriamycin), vincristine, and prednisone was begun on hospital day 6. He had a dramatic response to treatment, and 24 hours later a slight decrease in the size of the patient's neck masses was visible. The patient received a total of six cycles of chemotherapy, after which he had no further symptoms of shortness of breath while lying flat. He continued to have a marked decrease in cervical adenopathy and currently has only one small palpable cervical lymph node remaining 1 year after treatment initiation. He has not had any further episodes of respiratory difficulty.

DISCUSSION

Lymphoma of the head and neck often presents as an asymptomatic enlarged cervical lymph node, causing patients to seek medical advice. In contrast, airway obstruction by lymphoma is quite rare. Most frequently, this occurs when the tumor is present in the mediastinum, leading to distal tracheal obstruction.[2] Life-threatening airway obstruction caused by mediastinal lymphoma has been seen with the induction of general anesthesia, when relaxation elicits a sudden collapse of an airway that had previously been stable.[3] Extranodal lymphoma involving the larynx, trachea, or thyroid occurs occasionally,[1,4,5] and primary lymphoma of the thyroid causing acute airway obstruction has been reported.[6]

This case of nodal NHL demonstrates a massive amount of disease that created critical airway obstruction within a short period of time. The differential diagnosis of massive cervical adenopathy includes infectious diseases (viral, HIV, fungal, mycobacterial, cat-scratch disease, parasitic), primary and metastatic malignant disease (Hodgkin's lymphoma, NHL, thyroid carcinoma, squamous cell carcinoma [SCC], rhabdomyosarcoma, neuroblastoma, salivary gland carcinoma, metastatic adenocarcinoma), and miscellaneous disease processes (benign massive lymphadenopathy, sinus histiocytosis, sarcoidosis, amyloidosis). The relatively rapid development of airway obstruction in conjunction with cervical adenopathy was more suggestive of a diagnosis of lymphoma, anaplastic thyroid carcinoma, or metastatic SCC.

FNA of neck masses is frequently able to establish a definitive diagnosis. Its reported sensitivity in diagnosing neck masses is 85%, and its specificity is 87%.[7] However, the majority of false-positive and false-negative FNAs of neck masses occur in the setting of lymphoma. In many instances, an open lymph node biopsy is necessary to visualize the histologic architecture and make a definitive diagnosis.[8] This is particularly important in NHL because the pathologic grading classification is used for disease staging, treatment planning, and prognosis assessing. This particular case highlights the problems that can be encountered in trying to diagnose lymphoma from a fine-needle aspirate. If malignant disease is suspected clinically, it is crucial to perform an incisional biopsy. In patients with airway obstruction that worsens in the supine position, an open biopsy with the patient in the sitting position under local anesthesia may be prudent.

Because of this patient's positional airway obstruction, obtaining a CT scan in this patient entailed a certain amount of risk. However, we believed it was necessary to delineate the extent and location of his disease. Besides the obvious laryngeal compression noted by physical examination, we were concerned about the possibility of lower airway obstruction, which would limit the effectiveness of a tracheotomy. Because the spiral CT scanner takes only 5 to 7 minutes to perform a neck scan, our patient was able to tolerate the procedure without difficulty. No distal tracheal compression was evident by CT scan, and so we felt confident that in the event of acute obstruction, a tracheotomy would allow ventilation of the patient.

Tracheotomy should always be considered in patients with significant upper airway obstruction; however, in patients with massive soft tissue proliferation that displaces the trachea and distorts the anatomy, performing a tracheotomy may be a difficult, even fatal undertaking. In some infectious diseases and tumors, avoiding a tracheotomy may prevent a host of serious complications, if a rapid response to nonsurgical therapy can be expected. Hessan et al.[1] found that only two of eight patients with extranodal NHL causing airway obstruction required tracheotomy. Hessan et al. stated that one of these tracheotomies could probably have been avoided had pathologic diagnosis been made earlier. They noted excellent responses and relief of airway symptoms within days of starting combined chemotherapy and radiotherapy. This was similar to the result achieved in our patient with nodal disease, although we did not give radiotherapy because of the risk of tumor swelling, which could lead to complete airway obstruction. In a patient with SCC or thyroid carcinoma, a tracheotomy would likely be required because of the slower response rate of these neoplastic processes to chemotherapy or radiation.

Therapy for lymphomas consists mainly of chemotherapy and external beam radiation.[9] Multiagent chemotherapy regimens have been found to be effective in treating NHL, with cure rates of 30% to 60%.[10] Lymphomas are highly radiosensitive, and radiation can also be useful in achieving local control. Mediastinal radiotherapy to relieve airway obstruction before mediastinal lymph node biopsy in suspected cases of

lymphoma has been suggested,[2] although this may alter the histologic picture of the disease and should not be encouraged. Steroids also have been noted to alter histology and should not be used before definitive diagnosis unless significant upper airway obstruction is present,[11] as in the case of this patient. Our patient had a clear improvement in ventilatory ability within 24 hours of starting steroid treatment. An additional response was also noted within 24 hours of chemotherapy initiation, with visible tumor shrinkage.

This case presentation is unusual because of the size, rapid growth, and extent of airway obstruction caused by the nodal disease from NHL. Airway obstruction caused by extrinsic compression at the level of the laryngeal framework is rare. Mediastinal disease commonly compresses the airway because of the containment by the surrounding chest wall, causing the force of the tumor mass to press inward. Extranodal laryngeal lymphoma similarly leads to airway obstruction because of containment by the thyroid cartilage. Cervical nodal lymphoma with no rigid anatomic structure to constrain tumor growth may grow quite large before becoming symptomatic. In this patient the lymphocytic proliferation grew to massive proportions, leading to airway compromise only after the entire larynx was surrounded by tumor. This caused the force of further tumor growth to be directed inward onto the airway. Airway symptoms were exacerbated by concomitant local lymphatic and venous obstruction.

In conclusion, this report highlights the importance of having a high index of suspicion for lymphoma in patients with neck masses and airway obstruction. In these situations it is necessary to obtain a tissue diagnosis as quickly as possible. If the patient is not in acute distress, an FNA should be performed. If the FNA is diagnostic, management can be initiated accordingly. If the FNA is not diagnostic, an open biopsy should be considered and performed as soon as possible. This case illustrates the rationale for proceeding with an incisional biopsy of suspicious lesions after negative fine-needle aspirate results, particularly when the possibility of lymphoma is entertained. If one proceeds expeditiously, it is often possible to avoid a tracheotomy, sparing the patient an operation done under the difficult conditions created by a large tumor bulk in the anterior neck. A CT scan of the neck is also useful to rule out distal airway obstruction and for preoperative planning in the event a tracheotomy is required. We advocate reserving tracheotomy for the patient in acute airway distress or with slow-responding tumors, when airway obstruction is likely to worsen before it improves.

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