

Technetium-99m-MDP Uptake in Thyroid Cartilage in Invasive Squamous-Cell Laryngeal Carcinoma

Fabio Almeida, Chi-Kwan Yen, Robert J. Lull and Aileen D. Lim

Department of Nuclear Medicine, San Francisco General Hospital, Department of Laboratory Medicine, University of California San Francisco, San Francisco, California

A 36-yr-old male with a past history of invasive squamous-cell carcinoma of the larynx underwent ^{99m}Tc -MDP scintigraphy for the evaluation of lower back pain. The scan findings were unremarkable except for markedly and uniformly increased tracer uptake in the region of the thyroid cartilage, suggesting calcification and/or tumor invasion. Confirmation of significant pathology was obtained on tissue examination from a subsequent total laryngectomy demonstrating inflammatory infiltration and perichondrial invasion of the thyroid cartilage by carcinoma.

Key Words: technetium-99m-MDP; squamous-cell carcinoma; thyroid cartilage

J Nucl Med 1994; 35:1170–1173

Bone tracer uptake noted in the lower neck on anterior views of bone scans is usually mild and diffusely irregular (Fig. 1). This pattern of uptake is most commonly associated with osteoarthritis or metastatic disease of the cervical spine. Lordosis of the lower cervical spine and attenuation of photons from the upper cervical spine by the mandible and submandibular soft tissues also tend to emphasize the normal lower cervical spine uptake (1). Less commonly, calcification of the laryngeal cartilages and very rarely, free pertechnetate uptake by the thyroid gland, may be responsible for this appearance. However, more pronounced uptake in the neck may indicate specific pathology involving the anterior structures of the neck. We report a case of markedly and uniformly increased bone tracer accumulation in thyroid cartilage associated with perichondrial invasion by squamous-cell laryngeal carcinoma.

CASE REPORT

A 36-yr-old male who smoked a half pack of cigarettes a day, but was otherwise healthy, presented with a 5-mo history of hoarseness. The patient underwent direct laryngoscopy with biopsy which demonstrated pathologic findings consistent with

squamous-cell carcinoma of the larynx. Subsequent MRI of the neck revealed carcinoma extending from the epiglottis to the subglottic region, nearing the airway. The images demonstrated abnormal signal crossing the thyroid cartilage, suggesting invasion of tumor beyond the larynx. No abnormal nodes were reported (Fig. 2).

Shortly following the patient's initial presentation and workup, he began experiencing lower back pain and was referred for scintigraphic evaluation. A whole-body bone scan performed with 740 MBq (20 mCi) of ^{99m}Tc -MDP demonstrated markedly increased tracer uptake in the region of the thyroid cartilage (Fig. 3) and mildly increased uptake in the hyoid bone. The remainder of the bone scan was unremarkable.

Pathologic examination of tissue from a subsequent total laryngectomy performed 1 mo following the bone scan, demonstrated squamous-cell carcinoma invading the perichondrium of the thyroid cartilage with associated ossified cartilage and inflammatory infiltration.

DISCUSSION

Ossification of the laryngeal cartilages usually begins after the second or third decade of life, although direct correlation with age is poor (2–4). Ossification of the thyroid cartilage has been noted to follow a defined, symmetrical pattern which usually begins at the posterior border near the root of the inferior horn, spreading along the inferior border and reaching the midline where there is usually a separate center of ossification (2,3).

The thyroid cartilage uptake pattern seen on this patient's bone scan is homogeneous and more intense than can be explained by a normal degree of cartilaginous calcification expected for his age. The lateral image (Fig. 3B) demonstrates that uptake is clearly not in the cervical spine. Thyroid gland uptake of free pertechnetate is unlikely given the absence of uptake in the stomach and salivary glands as well as the excellent quality control results obtained on preparation of this patient's radiopharmaceutical dose. A tumor-mediated increase in osteoblastic activity is most likely responsible for this increased tracer accumulation, secondary to direct tumor invasion.

The increased susceptibility of ossified cartilage to cancerous invasion compared to nonossified cartilage has been well described (2,5–8). The pattern of laryngeal cartilage

Received Jan. 10, 1994; accepted Mar. 3, 1994.

For correspondence or reprints contact: Fabio Almeida, MD, Chief Resident, Department of Nuclear Medicine, SFGH, Building 100, Room 157, 1001 Potrero Avenue, San Francisco, CA 94110.

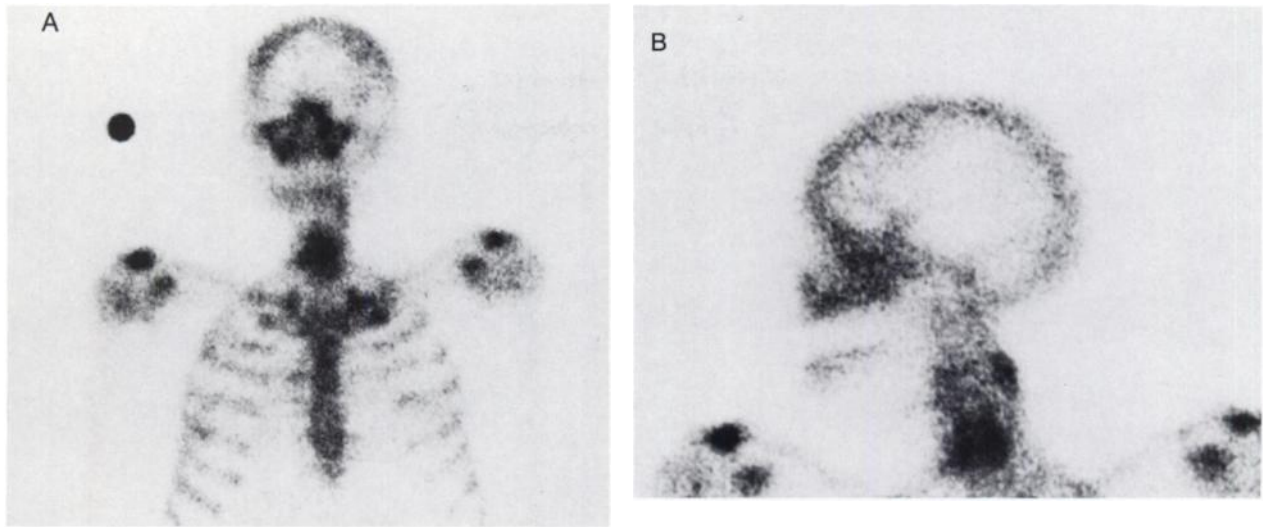


FIGURE 1. Technetium-99m-MDP planar images from a 65-yr-old female with known degenerative disease of the cervical spine demonstrating typical nonspecific anterior cervical bone uptake. (A) Anterior view and (B) left lateral view of the cervical spine.

invasion has been studied by Kirchner and others who found that invasion occurred almost invariably in the areas of ossification in the lower third of the thyroid cartilage and the upper edge of the cricoid ring in the early stages of tumor spread (2,7). The reason for this is not completely understood; however, the invasion of ossified cartilage has been attributed primarily to increased vascularization by which most carcinoma cells initially reach metaplastic bone (7). It has also been suggested that normal cartilaginous tissues may release a substance which inhibits tumor, or tumor substances that enhance invasion.

In a study by Bennett et al. (2,5), a prostaglandin-like substance was demonstrated to be produced by carcinoma of the head and neck. The cellular origin of this substance and other tumor-associated osteoclast-activating products, remains unclear; however, it is thought by some investiga-

tors that host cells, such as macrophages, may play a role in its production (2,5,8). The mechanisms of osteoblastic stimulation by this substance are obscure, although they seem to be linked to increased osteoclastic activity. A study by Gregor et al. (2) also demonstrated that framework invasion of the laryngeal cartilages was found to occur exclusively in ossified or calcified cartilage and was associated with osteoblastic activity which appeared to be at least partially mediated by tumor-produced alkaline phosphatase. Osteoclastic activity was noted to be linked to this process and, at this stage, tumor remained outside of the perichondrium. Other investigators have found that during the process of resorption, bone releases a factor that is strongly chemotactic for tumor cells (2).

Regardless of the mechanism, the finding of markedly increased bone tracer accumulation in cartilaginous tissue in patients with laryngeal carcinoma may be clinically significant since it implies invasion of the laryngeal framework by cancer. Laryngeal carcinomas, such as subglottic squamous-cell carcinoma, are known to quickly invade the perichondrium of the thyroid and cricoid cartilages and almost always extend to or through the cricothyroid membrane (9). Laryngeal carcinoma stage T3 and T4 are thus typically treated in most institutions with total laryngectomy. Some authors, however, advocate more conservative surgery and/or primary radiotherapy with total laryngectomy reserved only for recurrent disease. Radiotherapy is considered the preferred therapy for T1 and T2 glottic cancers in most centers since it offers a high cure rate in addition to the preservation of nearly normal voice quality (7,10). The response to radiotherapy may relate to many factors such as the patient's physical condition, sex, histology of the tumor, the site of origin and the extent of lesion (10). Determination of tumor infiltration into the cartilaginous structures is especially important because it rules out the possibility of conservative surgery and is a

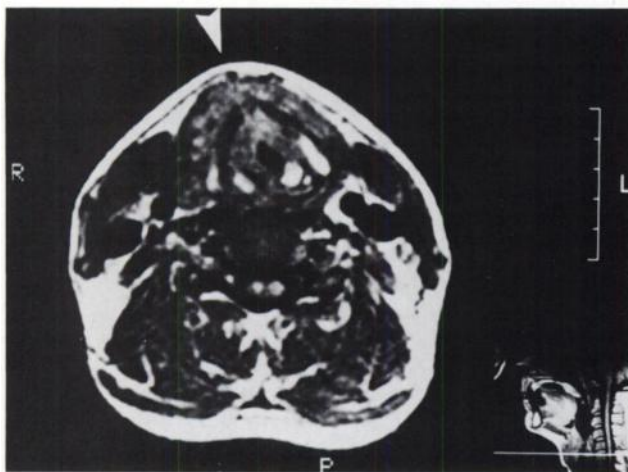


FIGURE 2. MRI of the neck in the transaxial plane demonstrating carcinoma involving the subglottic region with abnormal signal crossing the thyroid cartilage (arrow) which is suggestive of laryngeal cartilage invasion.



FIGURE 3. Thyroid cartilage invasion. Technetium-99m-MDP planar images demonstrate intense and uniform uptake in the thyroid cartilage (A) Anterior view and (B) left lateral view of the cervical spine.

relative contraindication to radiation therapy since it reduces the response to radiation and may then result in perichondritis, chondronecrosis and sequestration of cartilages (11). An increased risk of subsequent tumor recurrence has also been demonstrated in the presence of even small foci of invasion in thyroid cartilage (12). In addition, invasion of the laryngeal skeleton is considered an adverse prognostic feature associated with an increased incidence of nodal metastasis and decreased survival (7).

MRI and CT have therefore become important investigational procedures in the T-staging of laryngeal carcinoma (10,12-15). Both imaging modalities have been demonstrated to be effective in the detection of calcified cartilage invaded by cancer. MRI appears to have better sensitivity and specificity of 89% and 91%, respectively, compared with 46% and 88% for CT. The decreased sensitivity of CT may be due to the fact that laryngeal tumor invasion cannot be distinguished from normal irregular patterns of ossification in some patients (10,16,17). Additionally, noncalcified or poorly calcified cartilage may appear as erosion or destruction on CT scans. Both MR and CT fail to demonstrate microscopic disease and motion artifact due to disease related dyspnea, and cough may significantly interfere with image quality in many MR examinations (7,13).

CONCLUSION

Bone scintigraphy may have a role to play in the detection of local extension of this tumor due to its high sensitivity for osteoblastic bone and cartilaginous lesions. Intense and uniform thyroid cartilage uptake clearly differentiated from nonspecific low-grade uptake, strongly suggests tumor invasion in these patients. Since laryngeal carcinoma only rarely metastasizes to bone or bone marrow, bone scintigraphy has not been routinely performed in the evaluation of this disease (12). This may explain why

increased bone tracer uptake in thyroid cartilage invaded by laryngeal carcinoma has not been previously well described. Further study may be warranted to evaluate the sensitivity and specificity of bone scintigraphy in the detection of vascular changes and microscopic disease associated with invasion of the laryngeal cartilages by carcinoma, and its potential role as an adjunct to MRI in the T-staging of invasive laryngeal carcinoma.

REFERENCES

1. Oppenheim BE, Cantez S. What causes lower neck uptake in bone scans? *Radiology* 1977;124:749-752.
2. Gregor TR, Hammond K. Framework invasion by laryngeal carcinoma. *Am J Surg* 1987;154:452-457.
3. Harrison DFN, Denny S. Ossification within the primate larynx. *Acta Otolaryngol (Stockh)* 1983;95:440-446.
4. Keen JA, Wainwright J. Ossification of the thyroid, cricoid and arytenoid cartilages. *S Afr J Lab Clin Med* 1958;4:83-108.
5. Bennett A, Carter RL, Stamford IF, Tanner NSB. Prostaglandin-like material extracted from squamous carcinomas of the head and neck. *Br J Cancer* 1980;41:204-208.
6. Carter RL, Tanner NSB. Local invasion by laryngeal carcinoma: importance of focal ossification within laryngeal cartilage. *Clin Otolaryngol* 1979;4:283-290.
7. Gallo A, Mocetti P, De Vincentiis M, et al. Neoplastic infiltration of laryngeal cartilages: histochemical study. *Laryngoscope* 1992;102:891-895.
8. Kirchner JA. Invasion of the framework by laryngeal cancer. *Acta Otolaryngol (Stockh)* 1984;97:392-397.
9. Freemont CAJ, Tun T. An unusual case of laryngeal carcinoma. *J Laryngol Otol* 1986;100:477-482.
10. Gerritsen GJ, Valk J, van Velzen DJ, Snow GB. Computed tomography: a mandatory investigational procedure for the T-staging of advanced laryngeal cancer. *Clin Otolaryngol* 1986;11:307-316.
11. Curtin HD. Imaging of the larynx: current concepts. *Radiology* 1989;173:1-12.
12. Toner GC, Thomas RL, Schwarz MA. Metastatic bone marrow involvement from supraglottic squamous cell carcinoma. *J Laryngology and Otolology* 1989;103:225-226.
13. Castellijns JA, Gerritsen GJ, Kaiser MC, et al. Invasion of laryngeal cartilage by cancer: comparison of CT and MR imaging. *Radiology* 1988;167:199-206.
14. Garcia Fernandez E, Munoz A, Gil M, Cavallieri I. Diagnosis of tumor

- invasion of the cartilages in neoplasm of the larynx using computed tomography [Abstract]. *Acta Otorrinolaringologica Espanola* 1989;40:409-412.
15. Steinkamp HJ, Heim T, Zwicker C, Mathe F, Schorner W, Felix R. The value of nuclear magnetic resonance tomography in tumor staging of laryngeal/hypopharyngeal cancer [Abstract]. *HNO* 1992;40:339-345.
 16. Casteljjins JA, Valk J, van Schaik C, Golding RG, Gorden SB. MR findings of cartilage invasion by laryngeal cancer: value in predicting outcome of radiation therapy. *Radiology* 1990;174:669-673.
 17. Yeager VL, Lawson C, Archer CR. Ossification of the laryngeal cartilages as it relates to computed tomography. *Invest Radiol* 1982;17:11-19.