Clinical Challenge | PATHOLOGY

Hoarseness and Stridor Following Stem Cell Transplant

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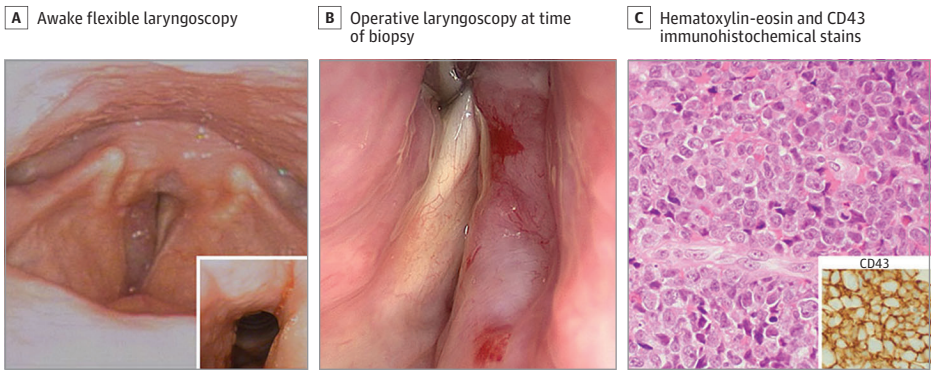

Figure. Evaluation of the larynx from awake flexible laryngoscopy (A) including posterior commissure (A, inset) and operative microlaryngoscopy (B) with biopsy (C; original magnification ×40).

A 59-year-old man presented with progressive hoarseness and dyspnea over a 2-month period. Fifteen months previously, he had undergone allogeneic stem cell transplant (allo-SCT) with a matched related donor for treatment of fms-like tyrosine kinase (*FLT3*) internal tandem duplication–mutated acute myeloid leukemia (AML). The patient had been diagnosed with chronic gastrointestinal graft-vs-host disease after a workup for diarrhea. Results of a restaging bone marrow biopsy 2 weeks prior to presentation showed no evidence of leukemia. Physical examination findings revealed no neck masses or abnormalities, but the patient was noted to be severely dysphonic and stridulous. Flexible laryngoscopy findings demonstrated a right vocal fold neoplasm crossing the posterior commissure with associated bilateral vocal fold motion impairment and obstruction of the glottic airway (**Figure**, A). Awake tracheostomy was performed for airway protection, and biopsy of the neoplasm was obtained via operative microlaryngoscopy (Figure, B). Histologic findings demonstrated diffuse infiltrate of large cells with irregular nuclear contours, vesicular chromatin, and prominent nucleoli (Figure, C). Immunohistochemical stains showed CD33, CD43, and CD117 positivity, with a subset positive for CD7 and myeloperoxidase. Stains were negative for CD3, CD20, and cytokeratin expression.

WHAT IS YOUR DIAGNOSIS?

- **A.** Squamous cell carcinoma of the larynx
- **B.** Graft-vs-host disease of the larynx
- **C.** Extramedullary myeloid sarcoma of the larynx
- **D.** Marginal zone lymphoma of the larynx

Quiz at jamacmelookup.com

Diagnosis

C. Extramedullary myeloid sarcoma of the larynx

Discussion

Diagnostic endoscopy results demonstrated a neoplasm of the larynx, excluding graft-vs-host disease, which most often manifests as mucositis in the upper aerodigestive tract. The lack of cytokeratin expression excluded malignant neoplasm of epithelial origin. Immunohistochemical staining for CD43 was positive, confirming that the neoplasm was of hematolymphoid origin. Negative staining for CD3 and CD20 excluded T-cell and B-cell lymphomas, while positive staining for CD7 is commonly seen with AML. A myeloid next-generation sequencing panel of the laryngeal tissue redemonstrated the known mutation in *FLT3* internal tandem duplication in the leukemia and laryngeal neoplasm. Subsequent bone marrow biopsy demonstrated no evidence of leukemia. Positron emission tomographic imaging only showed a hypermetabolic laryngeal mass. Thus, AML relapse manifesting as isolated myeloid sarcoma of the larynx was diagnosed.

Primary conformational radiation treatment was initiated with 24 Gy administered over 5 standard fractions. Follow-up positron emission tomographic imaging showed complete metabolic response of the laryngeal mass. Posttreatment laryngoscopy findings demonstrated complete tumor response with only residual motion impairment of the right vocal fold. His tracheostomy was decannulated, and he demonstrated no evidence of recurrent disease 9 months following treatment.

Myeloid sarcoma is a unique clinical presentation of AML that is defined as an extramedullary tumor composed of blasts from 1 or more myeloid lineages.[1-3] Myeloid sarcoma can be the de novo pre-

sentation of AML and may or may not be associated with peripheral blood or bone marrow involvement. It may present as a single lesion or involve multiple organ systems and may represent progression from an antecedent myeloid neoplasm.[2,3] Patients are considered to have isolated myeloid sarcoma if bone marrow aspiration and biopsy results reveal no evidence of hematologic disease.[3] Myeloid sarcoma can occur anywhere in the body but most commonly is found in soft tissues, bone, peritoneum, lymph nodes, and the gastrointestinal tract.[3] Involvement of the head and neck is less common, with a recent report implicating this region in 5.4% of cases of myeloid sarcoma.[4,5]

A high level of suspicion for myeloid sarcoma is needed upon the development of any persistent new mass in a patient with established leukemia. National guidelines recommend expedited laryngeal assessment for any patient experiencing dysphonia who is at risk of cancer.[6] Ultimately, laryngoscopy was the evaluation most essential to establishing the patient's diagnosis and allowing safe airway management throughout treatment. An analysis of patients who received an allo-SCT for AML showed a 5-year cumulative incidence of isolated extramedullary relapse of nearly 10%.[7] Risk factors for extramedullary relapse include younger age, high-risk disease cytogenetics such as the *FLT3* mutation, a myelomonocytic immunophenotype, and extramedullary disease prior to transplant.[3,7-9]

There are limited data to guide therapy for isolated myeloid sarcoma relapse after allo-SCT, and treatments are tailored to specific patient and disease characteristics. Options for treatment include tapering immunosuppression, systemic chemotherapy plus or minus donor lymphocyte infusion or second allo-SCT, local radiation therapy, and surgical resection.[3] In the present patient's circumstance, surgical excision was not possible without total laryngectomy, so radiation therapy was pursued to preserve laryngeal function along with systemic targeted therapy with gilteritinib.

The present case illustrates an unusual presentation of an isolated myeloid sarcoma involving the larynx manifesting with the primary complaint of dysphonia treated with radiation therapy. Acute myeloid leukemia can infiltrate almost any tissue, necessitating consideration of myeloid sarcoma upon the development of a new head and neck complaint in a patient with prior acute leukemia.

ARTICLE INFORMATION

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