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ORIGINAL RESEARCH

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Acute myeloid leukemia: An unusual manifestation of the trachea

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Abstract

Objective(s): Hematologic malignancy involving the trachea is rare. It is even less common for tracheal involvement to be the initial manifestation of this disease. We present a case report highlighting an unusual diagnosis of acute myeloid leukemia (AML) that first presented with prominent tracheal manifestations. There have been only three other published case reports of extramedullary AML with involvement of the trachea.

Methods: We discuss direct laryngoscopy and bronchoscopy findings, including pinkish-white irregular lesions, which were similar to findings described in the available literature for tracheal AML.

Results: Laboratory findings from our case are reported, including peripheral smear demonstrating 57% blasts and bone marrow biopsy confirming the diagnosis of AML, and the relevance of these findings is discussed.

Conclusion: In patients with unusual airway lesions, laboratory testing and a comprehensive airway evaluation including biopsy are necessary to narrow the differential diagnosis.

Level of Evidence: 5.

KEYWORDS
cancer, chloroma, leukemia, myeloid sarcoma, trachea

1 | INTRODUCTION

It is uncommon for systemic diseases to present as tracheal lesions; the most common entities to do so include relapsing polychondritis, granulomatosis with polyangiitis, amyloidosis, and inflammatory bowel disease.[1] Tracheal involvement of malignancies with a primary source outside of the upper airway or directly adjacent organs, such as the thyroid, is even rarer. The relatively limited blood supply and lymphatic supply to the trachea acts as a barrier to involvement by distant metastatic disease, compared with other organs. It is important for physicians to consider uncommon etiologies of tracheal disease to avoid delayed diagnosis and disease progression. We describe a rare case of acute myeloid leukemia (AML) with an initial manifestation of tracheal lesions.

2 | CASE REPORT

A 50-year-old male with a history of HIV on highly active anti-retroviral therapy (HAART) (CD4 = 489), hypertension and hyperlipidemia

presented with shortness of breath, stridor, and dysphonia. The patient had been recently discharged after a 4-day admission with similar symptoms, during which he received steroids with subsequent improvement and was discharged home with methylprednisolone and budesonide.

Laboratory studies were negative for several rheumatologic markers including antineutrophilic cytoplasmic antibody (ANCA); however, immunoglobulin levels were elevated (IgG = 2045 g/L, IgA = 334 g/L). Studies were also notable for an ESR of 130 mm/h, CRP of 5.86 mg/L, and cytopenia involving multiple cell lines (platelets = 85,000/mcL, hemoglobin = 11.5 g/dL, absolute neutrophil count = 500 cells). CT neck revealed circumferential thickening with surrounding mediastinal fat stranding involving the entire trachea (Figure 1).

Bedside laryngoscopy was performed, revealing edema of the larynx and subglottis with about 30% of the lumen visible. The patient subsequently underwent direct laryngoscopy with biopsy (DLB) which revealed an infiltrative process involving the entire length of the trachea from subglottis to carina, as well as glottic edema (Figure 2). There was significant tracheomalacia without identifiable tracheal rings on endoscopic examination. The final pathology report demonstrated inflammatory infiltrate with few scattered inflammatory and atypical cells. Serum protein electrophoresis was performed without detection of monoclonal antibodies. A peripheral blood smear revealed 57% blasts, and bone marrow biopsy was subsequently performed with flow cytometry compatible with AML.

The patient self-extubated but did not develop respiratory distress and did not require reintubation. He began induction chemotherapy with idarubicin and cytarabine, which he tolerated well without issues. Restaging bone marrow biopsy performed 1 month later demonstrated minimal residual disease on flow cytometry (0.06% of all events). He then completed high-dose cytarabine for consolidation. Peripheral blood flow cytometry performed 8 months after initial surgery demonstrated no immunophenotypic evidence of increased blasts or a lymphoproliferative disorder. He is currently on azacitidine maintenance therapy and doing well with no further respiratory issues.

3 | DISCUSSION

It is necessary to keep a broad differential when assessing airway obstruction. Etiologies of intrinsic tracheal disease include, but are not limited to infection, iatrogenic trauma, systemic illness, and benign or

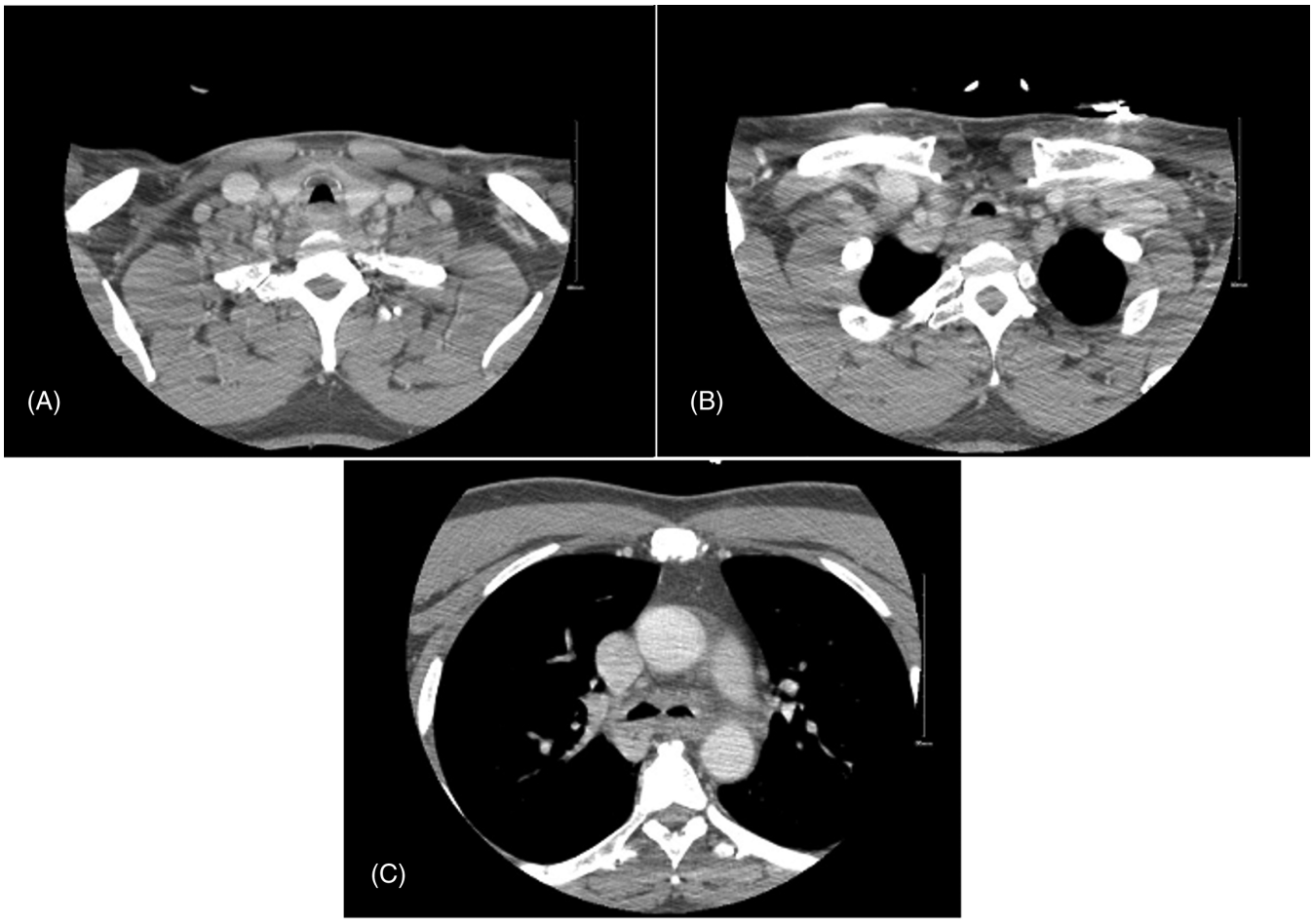

FIGURE 1 Axial CT neck. (A–C) In order from superior to inferior, from proximal trachea to carina, demonstrating circumferential thickening of the trachea down to the carina with mediastinal fat stranding.

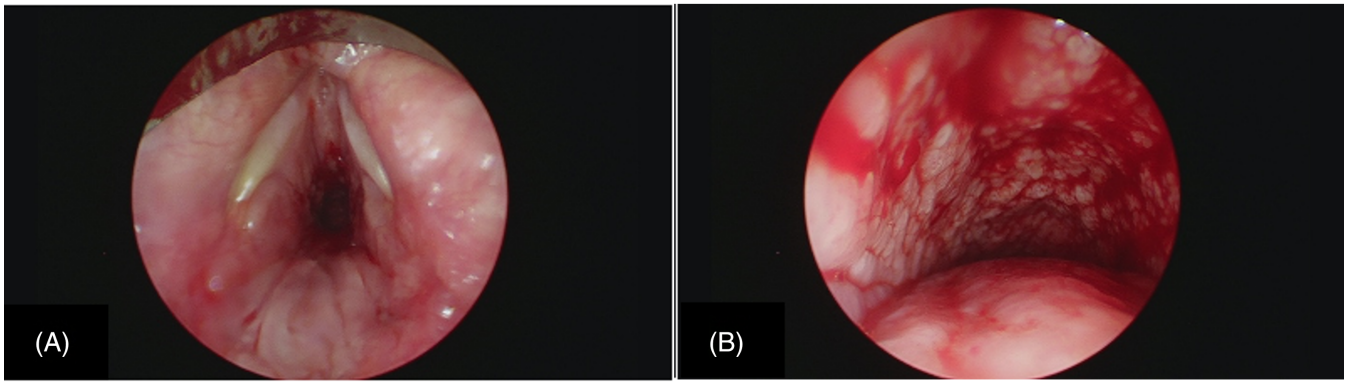

FIGURE 2 (A) Direct laryngoscopy revealing glottic edema and subglottic thickening. (B) Bronchoscopy demonstrating tracheal lesions and no obvious tracheal rings.

malignant neoplasms. Radiographic imaging revealing suspicious lesions should be followed up with a thorough airway evaluation with biopsy, as available imaging modalities are not sensitive enough to evaluate for pathologic mucosal changes.[2] Neoplastic lesions causing acute airway obstruction are rare but should be considered, especially when suspicious symptoms are present. These symptoms can include hoarseness, dysphagia, odynophagia, throat tightness, and referred otalgia; shortness of breath or wheezing that is unresponsive to bronchodilators should also raise suspicion for a tumor of the trachea.[3]

The two most common tracheal malignancies are squamous cell carcinoma and adenoid cystic carcinoma, with others including carcinoid tumors, non-squamous carcinoma, and mucoepidermoid carcinoma. Hematologic malignancy arising in the trachea is a rare event but has been reported. A few examples, in addition to AML, include chronic lymphocytic leukemia, lymphoma, and plasmacytoma.[4,5] Despite the limited supply of blood and lymphatics to the trachea, cancerous lesions affecting the trachea are most commonly due to metastatic spread, exceeding primary malignancies by a factor of 1000.[6] Thus, when tracheal lesions are confirmed to be cancerous in nature, metastatic malignancy should be suspected until proven otherwise.

AML can present with a variety of symptoms. Patients may be asymptomatic, with suspicion for disease raised only after laboratory studies reveal abnormalities, while others may present symptomatically with infection, bleeding, disseminated intravascular coagulation, and more.[7] Diagnosis of AML requires the presence of ≥20% blasts in the peripheral blood or bone marrow, and subsequent bone marrow evaluation should be performed for morphologic assessment.[8] Our patient presented with complaints related to airway obstruction rather than more classic AML-related symptoms. Due to our unusual operative findings, a broad workup was initiated and laboratory studies revealing 57% blasts and cytopenia were crucial in guiding the diagnosis. Blood tests also revealed hypergammaglobulinemia (IgG = 2045 g/L, IgA = 334 g/L), which is an unusual finding in hematologic malignancies, but has been previously reported in patients with AML.[9] Elevated inflammatory markers, including CRP and ESR, have been demonstrated in AML and other hematologic malignancies.[10] Of note, elevations in certain inflammatory markers such as serum ferritin and IL-6 have been associated with a poor prognosis in AML patients, although these findings were not demonstrated in our case.[11]

There have been only three prior cases of extramedullary AML involving the trachea reported in the literature.[12–14] Of these reports, one patient was found to have tracheobronchial myeloid sarcoma, with a known history of AML that preceded the tracheal findings. CT chest revealed diffuse involvement of the mediastinum by a mass that had invaded the right lung; bronchoscopy revealed widening and submucosal infiltration of the main carina, with pinkish-white, distinctively raised parallel columns of submucosal infiltration that obliterated the right upper lobe and intermedius bronchi. Our operative findings demonstrated similar findings of pinkish-white submucosal nodular infiltration, though distinct columns were not identified. Histology and immunohistochemistry of the submucosal tissue confirmed a myeloid origin. Subsequent bone marrow examination revealed multilineage dysplasia, and cytogenetic studies showed complex abnormalities including 5q deletion.[12] This patient was treated with induction chemotherapy with complete response achieved, and thereafter was placed on maintenance therapy with azacitidine.

There were two patients with no known history of AML who initially presented with symptoms of airway obstruction. In one case, after discovery of tracheal stenosis, an elevated white blood cell count with ≥20% blasts and cytopenia were noted on laboratory studies, raising suspicion for underlying systemic disease. Tracheal biopsy and bone marrow evaluation confirmed the diagnosis of AML.[13] Interestingly, in the other case, blood counts were within the normal range despite the presence of symptomatic airway obstruction. Bronchoscopy revealed cauliflower-like neoplasms with an irregular surface around the central airway beginning 5 cm from the glottis, as well as friable, red, hemorrhagic mucosa with 60% stenosis of the airway. These findings prompted biopsy, with histopathology revealing atypical primitive appearing cells initially felt to be small cell carcinoma, and immunohistochemistry positive for myeloid markers. Subsequent bone marrow evaluation confirmed the diagnosis of AML.[14] On DLB, our patient demonstrated irregular tissue of the large airways that appeared similarly to the findings in the aforementioned cases.

Pinkish-white submucosal infiltrating lesions may be a diagnostic clue for tracheal AML; however, due to limited data, this remains a postulation. Additional reports of DLB findings in tracheal AML may uncover characteristic findings that can provide guidance to further clinical studies and evaluation.

4 | CONCLUSION

Hematologic malignancies such as AML can initially present with extramedullary tracheal manifestations. Diagnosis of AML can be made via laboratory findings followed by bone marrow evaluation for morphologic assessment. In particular, tracheal AML appears to present with irregular, pinkish-white submucosal infiltrating lesions, which may serve as a helpful clue in the differential diagnosis of an unusual airway lesion. Comprehensive airway evaluation including biopsy is crucial in guiding proper diagnosis in these atypical cases, and appropriate, broad differential diagnosis and workup should be performed to understand the extent of possible multiple system involvement.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

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