

Intravascular large B-cell lymphoma associated with sudden stridor arising from thyroid mucormycosis and concomitant bacterial infection

Dear Editor,

Mucormycosis is a life-threatening fungal infection that mainly affects immunocompromised patients. It typically has low prevalence, but fatality rate is as high as 50%.

We present a patient with intravascular lymphoma with secondary bacterial infection and invasive mucormycosis involving the thyroid gland, who experienced good outcomes following surgical decompression and prolonged intravenous antibiotics.

A 65-year-old man with diabetes and intravascular large B-cell lymphoma (IVLBCL) who had undergone 3 cycles of rituximab, cyclophosphamide, doxorubicin hydrochloride (hydroxydaunorubicin), vincristine sulfate (Oncovin) and prednisolone (R-CHOP) presented with sudden stridor due to bilateral vocal cord palsy.

Computed tomography scan revealed thyroid gland liquefaction with enlargement. Ultrasound showed that the entire gland was replaced by avascular heterogeneous content. He was clinically euthyroid and thyroid autoantibodies were negative. Tracheostomy was performed for prolonged intubation, and thyroid isthmusectomy was performed to obtain histology and culture samples.

Intraoperatively, necrotic yellowish serous material was seen upon exposure of the thyroid gland (Fig. 1A). Bilateral thyroid lobes were ischaemic with necrotic cricoid and tracheal cartilages but there was no frank pus. As the overall tracheal cartilage framework was

deemed stable, resection of these necrotic cartilages was withheld. The thyroid isthmus biopsy showed necrotic tissue only, while cultures and bacterial, fungal and *hsp65* gene sequencing were negative.

Post-procedure, he had persistent sepsis. A multi-disciplinary team involving otorhinolaryngology, infectious diseases and endocrinology determined the thyroid necrosis to be the likely nidus for infection and total thyroidectomy was performed. Histology revealed extensively necrotic thyroid tissue with sheets of large cells, suggestive of necrotic tumour tissue with therapy effects. Within necrotic areas, dense neutrophilic infiltrates with foreign body giant cell reaction were also noted, raising the possibility of concomitant secondary infection. Immunohistochemical staining for B-cell lymphoma markers were negative on the extensively necrotic tissue. Intraoperative cultures grew *Klebsiella* and *Proteus*. Gomori methenamine silver (GMS) stain was performed only after review of histology for multidisciplinary meeting. This showed broad (5–25µm), pleomorphic, ribbon-like, pauci-septate hyphae with tendency for right-angle-branching, in keeping with Mucorales. Areas suggestive of angioinvasion (Fig. 1B) were also seen, revealing the concomitant cause for acute thyroid necrosis. Due to extensive necrosis, ghost outlines of pale stained *Mucor* hyphae were initially missed on haematoxylin and eosin (HE) stain. This emphasises the importance of performing GMS stain on necrotic tissue for their identification. Although uncertain whether

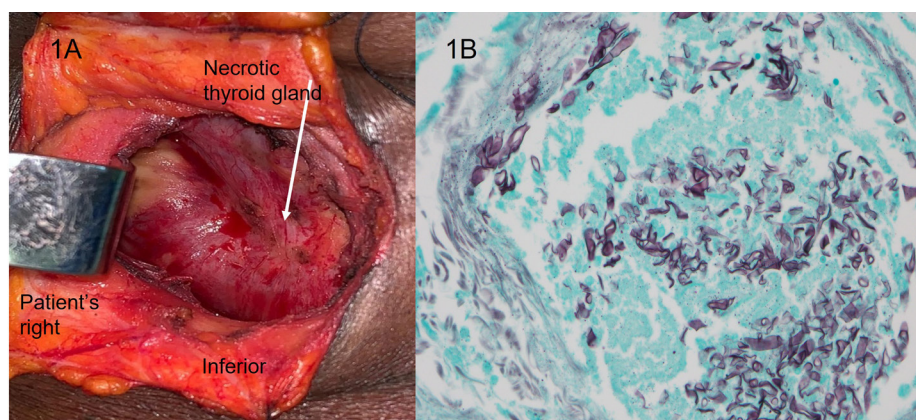


Fig. 1A. Intraoperative photo showing the necrotic thyroid gland (arrow), with the retractor placed on patient's right. Fig. 1B. Grocott methenamine silver stain showing extensively necrotic tissue from thyroid parenchyma with likely vessel wall with invasive fungal elements featuring pleomorphic, ribbon-like, pauci-septate hyphae with the tendency for right-angle-branching, in keeping with Mucorales.

mucormycosis may merely be a contaminant, this is unlikely, in view of angioinvasion noted within the thyroid parenchyma and localisation within the central necrotic areas.

Postoperatively, patient's fever lysed and wound healed. Prolonged courses of intravenous piperacillin/tazobactam and meropenem were administered until inflammatory markers trended downwards. Nasoendoscopy performed 1 month postoperatively showed mobile vocal cords bilaterally. He was successfully decannulated 2.5 months later. During his follow-up, he did not encounter airway complications such as subglottic stenosis. Unfortunately, he succumbed to lymphoma relapse 2 years later.

Acute suppurative thyroiditis is rare due to the gland capsule, high iodide content, rich blood supply, and extensive lymphatic drainage. Potential risk factors include pre-existing thyroid disease, congenital anomalies and immunosuppression.¹ Treatment consists of antibiotics, drainage, and partial or total thyroidectomy.

Our patient had IVLBCL with likely thyroid gland involvement. IVLBCL is a rare variant of diffuse large B-cell lymphoma. It is characterised by malignant lymphoid proliferation within blood vessels but without circulating neoplastic cells.² This often poses a diagnostic challenge. Additionally, it is aggressive and may involve any organ.³ Although immunohistochemical staining for lymphoma in our patient was negative, this may be explained by extensive tumour necrosis and 3 cycles of anti-CD20/rituximab before resection. The rapid progression and necrosis after commencing chemotherapy was consistent with tumour lysis syndrome of IVLBCL involving the entire thyroid gland,⁴ which subsequently got infected secondary to his immunosuppressed state.

Acute invasive mucormycosis is extremely rare in the thyroid gland but is associated with high mortality. Most reported cases had thyroid involvement in the context of disseminated infection while isolated thyroid involvement is rare.⁵ To the best of our knowledge, there are 12 reported cases involving the thyroid gland, of which only 2 are isolated within the gland.

The first patient is a 79-year-old man with chronic lymphocytic leukemia who underwent ibrutinib 2 months prior to presentation of a rapidly progressive neck mass and dysphonia. Imaging and biopsy revealed extensive necrotic thyroid with sternocleidomastoid invasion.⁵ He underwent surgical debridement and prolonged course of liposomal amphotericin-B and Posaconazole. The disease was eradicated successfully; however, left vocal cord palsy persisted.

The second patient was a 52-year-old man on long-term immunosuppressant for renal allograft transplant.⁶ He presented acutely with fever and neck swelling. This progressed to hoarseness and right vocal cord palsy within 4 days, and stridor with bilateral cord palsy within another 6 hours. A tracheostomy was planned for, but he succumbed to cardiac arrest. Post-mortem examination revealed thyroid gland mucormycosis with severe angioinvasion.

These cases illustrate the rapidity invasive mucormycosis progresses and the potential for upper airway compromise due to vocal cord palsy from thyroid gland involvement. However, the diagnosis of mucormycosis is often only established post-mortem.⁷ The gold standard for diagnosis is still tissue biopsy. Mucorales grow within 1–7 days on most fungal culture media. However, culture has low sensitivity of 50% due to the friable nature of fungal hyphae. Evidence of thyroid gland liquefaction post-chemotherapy should raise suspicion about possible lymphoma involvement or opportunistic infections. Hence, evaluation with special stains for invasive fungal infections should be considered in immunocompromised hosts. Current treatment guidelines recommend a combination of antifungal therapy, surgical debridement, and correction of risk factors.⁸ In our patient, rapid improvement was seen following thyroidectomy, with resolution at confirmation of mucormycosis.

Current literature has shown 2 other case reports of vocal cord paralysis resulting from acute suppurative thyroiditis. Bukvic reported a 75-year-old patient with resolution of thyroid abscess after surgical drainage and intravenous antibiotics. However, right vocal cord paralysis persisted.⁹ Additionally, Boyd reported a 41-year-old patient with resolution of thyroid abscess and left vocal cord paralysis following intravenous antibiotics and drainage.¹⁰

In our patient, total thyroidectomy, instead of drainage, was performed to remove the nidus of infection and relieve compression. Resolution of bilateral cord paralysis with successful decannulation suggests that early surgical intervention to obtain source control could potentially reverse cord paralysis.

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