Head & Neck

WILEY

CASE REPORT OPEN ACCESS

"Tension Chyle Leak": A Life-Threatening Sequela of Thoracic Duct Injury Following Resection of BRAF-Mutated Anaplastic Thyroid Carcinoma

Karim Botros[1] | Khashayar Esfahani[2] | Khalil Sultanem[3] | Jonathan D. Spicer[4] | Alex A. Mlynarek[1] | Michael P. Hier[1] | Marco A. Mascarella[1]

[1]Department of Otolaryngology Head and Neck Surgery, Jewish General Hospital, McGill University, Montreal, Quebec, Canada | [2]Department of Oncology, McGill University Health Centre, Montreal, Quebec, Canada | [3]Department of Radiation Oncology, McGill University Health Centre, Montreal, Quebec, Canada | [4]Department of Thoracic Surgery, McGill University Health Centre, Montreal, Quebec, Canada

Correspondence: Marco A. Mascarella (marco.mascarella@mcgill.ca)

Received: 6 August 2024 | **Revised:** 16 December 2024 | **Accepted:** 20 January 2025

Keywords: airway obstruction | anaplastic thyroid cancer | BRAF | chyle leak | thoracic duct

ABSTRACT

Background: Airway obstruction secondary to chyle leak is an exceptionally rare phenomenon. Here, we describe this complication in a patient with anaplastic thyroid carcinoma (ATC) undergoing consolidative surgery after BRAF-targeted therapy.

Methods: A 55-year-old man presented with a rapidly enlarging neck mass. Work-up was consistent with metastatic unresectable $BRAF^{V600E}$-mutant ATC. After a remarkable response to neoadjuvant dabrafenib and trametinib, he underwent curative-intent surgery with a right hemithyroidectomy and bilateral neck dissection. Within 48 h, he developed an expanding left neck mass with laryngeal obstruction due to a chyle leak.

Results: Despite surgical repair and maximal medical therapy, the leak persisted necessitating thoracoscopic ligation of the thoracic duct. Final pathology showed a completely excised residual tumor. The patient remains disease-free on long-term dabrafenib and trametinib.

Conclusions: BRAF-directed therapy has transformed the care of patients with mutated ATC. As more patients undergo consolidative surgery, increased vigilance is paramount in minimizing complications and their associated morbidity.

1 | Introduction

An iatrogenic chyle leak is a well-documented complication of neck surgery, particularly during dissection of the level IV nodal basin, with a risk of thoracic duct injury varying between 2% and 8% [1]. Chyle extravasation carries significant morbidity to the patient, including risk of metabolic disturbances, electrolyte imbalances, dehydration, immunosuppression, and local wound complications [1]. In this report, we present an atypical case of acute upper airway obstruction due to chyle leak, occurring 48 h after a right hemithyroidectomy with bilateral modified radical neck dissection for anaplastic thyroid carcinoma (ATC) in a patient treated with neoadjuvant dabrafenib/trametinib. Despite emergent intubation and exploration with ligation of thoracic duct tributaries, the high output chyle leak persisted necessitating thoracoscopic duct clipping. Although only one other documented case of chyle leak-related airway obstruction is reported, this is the first report of a high output chyle leak in a patient with ATC [2].

2 | Case Report

A 55-year-old gentleman presented with a rapidly enlarging right neck mass, dysphagia and dysphonia. On flexible

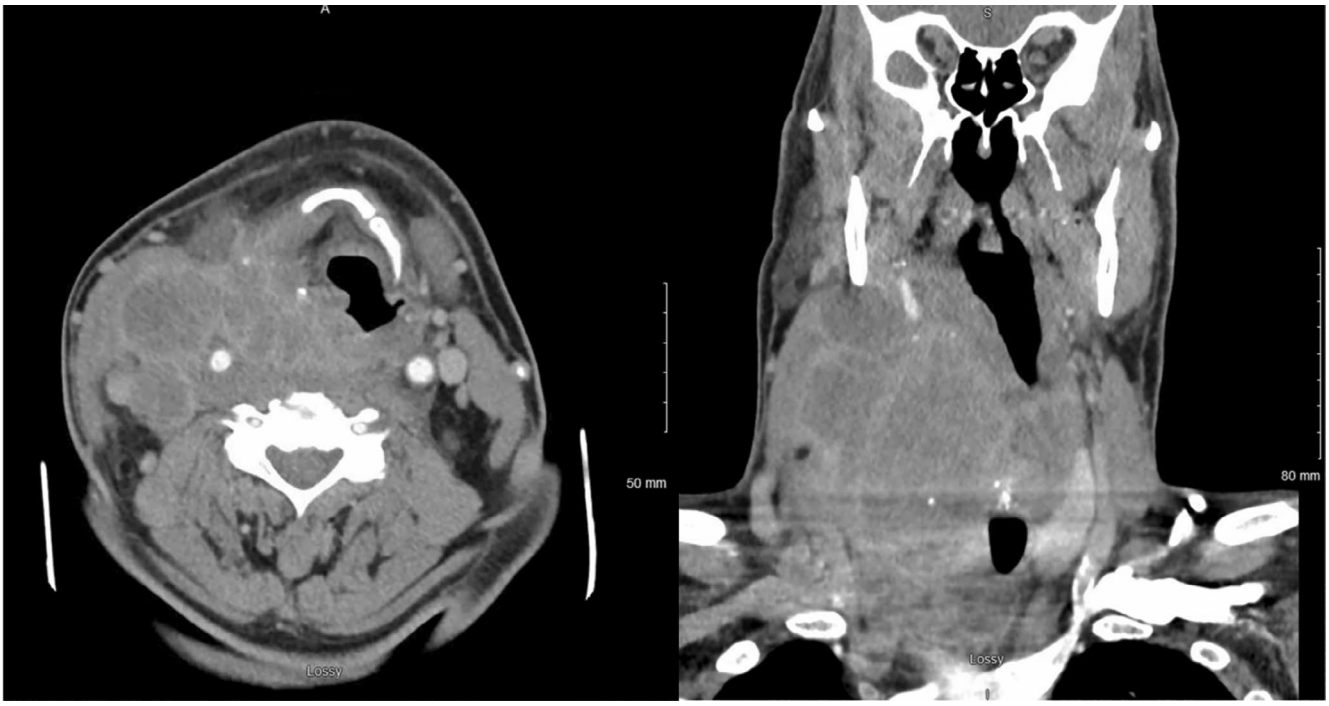

FIGURE 1 | Pre-treatment contrast-enhanced CT images of the neck showing advanced locoregional disease with obliteration of the right internal jugular vein and anterolateral deviation of the aerodigestive tract.

laryngoscopy, significant external compression of the airway was appreciated, and the right vocal cord was fixed. CT imaging revealed a large mass of the right thyroid gland encasing a portion of the common carotid artery, trachea and extending down to the anterior mediastinum with multiple adenopathy (Figure 1). Following needle biopsy, the patient was diagnosed with cT4N1bM1 $BRAF^{V600E}$-mutant anaplastic thyroid cancer. Following 8 weeks of dabrafenib and trametinib (DT), near complete radiologic and metabolic resolution was obtained in the neck and complete response at distant sites. At this time, following multidisciplinary team discussion, appropriate counseling, and informed consent, the patient elected for consolidative surgery. He underwent definitive locoregional control with a right hemithyroidectomy, right central and bilateral modified radical neck dissections (MRND II-V). Of note, the dissection planes were scarred akin to patients undergoing surgery after neoadjuvant chemotherapy. The right recurrent laryngeal nerve was grossly involved by tumor and was sacrificed. The internal jugular vein was thrombosed secondary to direct tumor invasion and was resected down to the jugular-subclavian junction. The sternocleidomastoid muscles were adherent to bulky nodal disease bilaterally and were partially resected. A small chyle leak was identified intra-operatively, following which the thoracic duct was clipped and suture ligated with no evidence of residual leak. The patient was extubated and started on a full-fluid diet postoperatively. On postoperative day 2, milky fluid was noted in the drains. Several hours later, the patient developed a sudden left neck swelling and inspiratory stridor. Flexible laryngoscopy revealed laryngeal obstruction (Figure 2). The patient underwent emergent intubation and neck exploration; a large amount of chyle was evacuated. Lymphatic tributaries originating from the base of the left level 4 neck were repaired by suture ligation and application of fibrin sealant with a sternocleidomastoid myofascial flap. Despite local control, intravenous octreotide and total parenteral nutrition (TPN), a high output chyle leak (> 1000 mL/day) persisted. Four days from his emergent takeback to the operating theater, the patient required thoracoscopic ligation of the thoracic duct. Several complications prolonged his ICU course, including delirium, saddle pulmonary embolism, and ventilator-associated pneumonia. Remarkably, the patient made a full recovery and was discharged home after a 6-week admission.

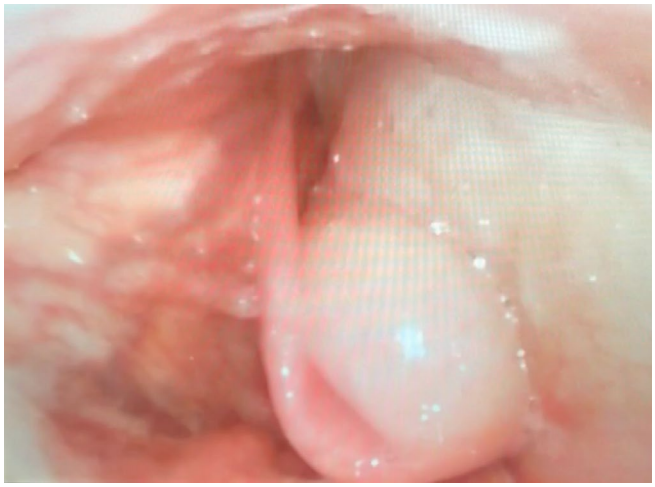

FIGURE 2 | View of the glottis on postoperative day 2 showing near complete external compression of the airway in the context of an expanding left-sided neck swelling and high-volume chylous drain output.

Review of final postoperative pathology revealed a small residual tumor focus consisting of mixed anaplastic (minor)

and papillary (major) thyroid carcinoma with widely negative margins. Of 74 harvested lymph nodes, only 4 harbored metastatic conventional papillary thyroid carcinoma (ypT3N1b). Approximately 8 weeks postoperatively, the patient resumed targeted therapy with dabrafenib and trametinib, which was recommended to continue indefinitely. Over a year since initiation of treatment, the patient remains disease free.

3 | Discussion

Anaplastic thyroid cancer is a rare and aggressive malignancy known to carry a poor prognosis. Recent advances in targeted therapy have led to a paradigm shift in the management of several cancers harboring compatible genetic alterations [3]. Exploiting the BRAF V600E mutation—which is present in approximately 40% of patients diagnosed with ATC—has markedly improved patient outcomes [3]. In this report, we presented a patient with initially unresectable cT4bN1bM1 $BRAF^{V600E}$-mutated ATC. The patient had a dramatic response to DT therapy experiencing near complete metabolic response. After 8 weeks of treatment, he was a candidate for consolidative surgery through which an R0 resection was achieved. Despite the favorable postoperative pathology, an exceedingly rare and life-threatening complication jeopardized his recovery: an acute airway obstruction from a high output chyle leak.

Typically, the onset of a chyle leak coincides with the initiation of enteral feeds [1]. In our patient's case, the rate of chyle extravasation and degree of mass effect were rather striking for a patient on a fluid diet. Even more so, the progression of swelling despite the presence of two Jackson-Pratt drains decompressing the neck was equally unusual. What is more atypical is that the leak was not mitigated by local surgical intervention. In retrospect, several risk factors rendered this patient at a particularly elevated risk of thoracic duct injury. First of all, he was overweight (pre-operative BMI 38.8 kg/m^2). Obesity is a recognized risk factor for the development of high-output chyle leaks. Perhaps the strongest predictor of thoracic duct injury in his case however, was the caudal and lateral extent of disease [2]. In a review of 436 consecutive MRNDs by Dunlap et al., when controlling for the pathologic indication, chyle leak was found to be significantly more frequent in the endocrine group than in the non-endocrine group (7.7% vs. 1.1%, respectively, $p = 0.003$) [4]. The increased prevalence of level IV disease and extensive dissection typically required within the territory of the thoracic duct in endocrine pathology were hypothesized as potential explanations for this observation. Intraoperative identification of chyle was another statistically significant predictor of postoperative chyle leak in the same study ($p = 0.027$). This was despite the authors' efforts to immediately address the thoracic duct in those cases [4]. Indeed, our patient combined all the aforementioned risk factors. He had ATC with extensive cervical lymphadenopathy and intraoperative chyle leak. Interestingly, on histologic examination, all four lymph nodes harboring metastasis (of 74 harvested nodes) were in the left level II-IV specimen.

In exploring other predisposing factors for recalcitrant thoracic duct injury, one has to consider the effect of neoadjuvant DT therapy on post-surgical wound complications. Trametinib, a mitogen-activated protein kinase (MEK) inhibitor, is thought to antagonize wound healing through its anti-angiogenic properties [5]. This has led to the recommendation to hold it 5–7 days preoperatively, with dabrafenib being continued until the day of surgery [5]. In our patient's case, DT were both stopped 7 days before surgery, which should have theoretically minimized the risk of trametinib-mediated wound disruption. The rapidity of response to DT rather than their direct biologic action could have precipitated the refractory leak. The altered lymphatic drainage of the neck due to bulky compressive disease and its subsequent brisk resolution with BRAF-targeted therapy may have placed the thoracic duct and its tributaries in a vulnerable state.

Halawani et al. described what we believe is the first report of acute airway obstruction related to postoperative chyle leak [2]. As in our case, their patient was also undergoing head and neck endocrine surgery, albeit for benign disease. Similarly, the development of an airway-threatening swelling began in the immediate postoperative phase (< 24 h). Unlike our case however, simple suture ligation of a transected thoracic duct was sufficient to resolve the leak, and their patient was discharged home 3 days later [2].

The treatment of $BRAF^{V600E}$-mutated ATC is rapidly changing. A once uniformly fatal disease is now showing promise in those afflicted with this mutation and responding to DT. Neoadjuvant DT followed by localized therapy in responders confers possible long term disease control [5]. Optimal radical surgery to resect residual locoregional disease is essential in select patients to reduce the risk of local failure [6]. This case report highlights the challenges that can arise due to tumor extent and underscores the potential gravity of lymphatic injury in head and neck surgery. Prompt detection and management of chyle leaks are crucial in sparing the patient undue morbidity and mortality [1]. In high-risk patients where an intraoperative leak is encountered, conservative measures, including strict dietary fat restriction, should be immediately implemented while more invasive surgical intervention is contemplated. As is true to all operative complications; prevention is the best medicine. This rests upon intimate familiarity with the regional anatomy and embryology of the surgical bed at hand [1].

Data Availability Statement

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

References

1. D. Leović, M. Pastorčić Grgić, I. Gugić Radojković, I. Blivajs, L. Matoc, and K. Gršić, "Management of Chyle Leak Following Head and Neck Surgery: Review of Current Treatment Strategies and Algorithmic Approach to the Treatment," *Acta Clinica Croatica* 61, no. Suppl 4 (2022): 88–95, https://doi.org/10.20471/acc.2022.61.s4.11.

2. H. M. Halawani, S. Bakkar, S. F. Jamali, F. Khalifeh, and S. G. Abi, "Life Threatening Presentation of Thoracic Duct Injury Post Thyroid Surgery; a Case Report," *International Journal of Surgery Case Reports* 34 (2017): 40–42, https://doi.org/10.1016/j.ijscr.2017.03.003.

3. X. Zhao, J. R. Wang, R. Dadu, et al., "Surgery After BRAF-Directed Therapy Is Associated With Improved Survival in BRAFV600EMutant Anaplastic Thyroid Cancer: A Single-Center Retrospective Cohort Study," *Thyroid* 33, no. 4 (2023): 484–491, https://doi.org/10.1089/thy.2022.0504.

4. Q. Dunlap, M. Bridges, K. Nelson, et al., "Predictors for Postoperative Chyle Leak Following Neck Dissection, a Technique-Based Comparison," *Otolaryngology and Head and Neck Surgery* 165, no. 5 (2021): 667–672, https://doi.org/10.1177/0194599821993815.

5. S. Hamidi, R. Dadu, M. E. Zafereo, et al., "Initial Management of BRAF V600E-Variant Anaplastic Thyroid Cancer: The FAST Multidisciplinary Group Consensus Statement," *JAMA Oncology* 10 (2024): 1264–1271, https://doi.org/10.1001/jamaoncol.2024.2133.

6. J. R. Wang, M. E. Zafereo, R. Dadu, et al., "Complete Surgical Resection Following Neoadjuvant Dabrafenib Plus Trametinib in *BRAFV600E*-Mutated Anaplastic Thyroid Carcinoma," *Thyroid* 29, no. 8 (2019): 1036–1043, https://doi.org/10.1089/thy.2019.0133.