CASE REPORT

Exophytic and Fungating Papillary Thyroid Carcinoma: A Rare and Complex Presentation of a Well-differentiated Malignancy

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ABSTRACT

Papillary thyroid carcinoma is the most common well-differentiated thyroid malignancy accounting for more than 80 to 90% of all thyroid tumors. It has an overall excellent prognosis owing to advances in screening via imaging and ultrasound-guided fine-needle aspiration biopsy, which have facilitated early detection, diagnosis, and surgical treatment followed by adjuvant radioactive iodine therapy. Exceptionally rare cases of papillary thyroid tumors may present with enormous growth due to delayed consultation and, thus, late diagnosis, posing a challenge to definitive management, quality of life, overall survival, and prognosis. We report a case of a 35-year-old woman who presented with a 4-year history of a bleeding exophytic and fungating anterior neck mass. Computed tomography showed a fungating mass arising from the left thyroid lobe that measured 14.1 x 14.0 x 11.1 cm with areas of necrosis and hemorrhage, left internal jugular vein thrombus formation, and compression of the left internal carotid artery. The mass causes a displacement of the trachea to the right side and multiple bilateral cervical lymphadenopathies. The patient was fully aware, and she consented to undergo wide excision, total thyroidectomy, neck dissection, and pectoralis major muscle flap reconstruction. However, she went into arrest intraoperatively attributed to massive pulmonary embolism. Papillary thyroid cancer is well known for its excellent prognosis. However, outcomes may not be favorable and can even be fatal in advanced and extensive cases. Although fungating papillary cancers are rare, they remain more common in the developing countries, where early detection and access to healthcare remains limited. They also represent a big challenge to surgeons. Even if the outcome was not good, we opted to report this case as there were many learning points. If only patients with good and excellent outcomes are reported in the literature, it will overestimate the treatment success of these complex cases.

Key Words: papillary thyroid cancer, thyroid malignancy, exophytic growth

INTRODUCTION

Thyroid cancer accounts for only 1% of all malignancies and is the most common endocrine malignancy. Papillary thyroid carcinoma (PTC) is the most common well-differentiated thyroid malignancy accounting for more than 80-90% of all thyroid tumors in iodine-sufficient areas across the globe.[1] It has an overall excellent prognosis owing to advances in screening via imaging and ultrasound-guided fine-needle aspiration biopsy (FNAB), which have facilitated early detection, diagnosis, and surgical treatment followed by adjuvant radioactive iodine therapy.[1] The most common presentation of PTC is a painless and slow-growing anterior neck mass with cervical lymphadenopathy and, in more advanced cases, hoarseness, dysphagia, and dyspnea.[2-11] Cutaneous metastases to the scalp (most common site), face, cervical neck, chest wall, abdomen, extremities, and ectopic

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thyroid tissue carcinoma have been reported as rare sites of involvement.[2-7]

Exceptionally rare cases of papillary thyroid tumors may present with enormous growth presenting as necrotic and fungating masses, a feature more commonly seen in anaplastic thyroid cancer.[8-11] These extreme forms of presentation of PTC are rarely seen and occur most often in the developing countries due to failure or inability of patients to seek early medical advice during the early course of the disease. A comprehensive literature search on PUBMED/MEDLINE was carried out for exophytic follicular thyroid carcinoma, but literature was limited only to case reports and case series.[2-11] Despite their extent and invasiveness, radical surgery and reconstruction techniques followed by radioactive iodine ablation are successful. Still, they remain a challenge to definitive management, quality of life, and overall prognosis.[11]

CASE PRESENTATION

A 35-year-old lady, married with six children, was admitted in our emergency room for her bleeding anterior neck mass presenting initially as a 4-year history of a gradually enlarging anterior neck mass measuring approximately 1 x 1 cm without associated hoarseness, dyspnea, dysphagia, and palpable lymph nodes. She had no eye symptoms, heat intolerance, weight loss, palpitations, jaundice, loose stools, and tremors, nor any hair changes, mental sluggishness, cold intolerance, weight gain, constipation, skin thickening, and edema. During the interim, she noted an increase in the size of the mass and beginning skin changes and overlying hyperpigmentation over the area of the said mass. She did not seek any form of medical consultation at this time. Over time, her anterior neck mass progressed to becoming an exophytic outgrowth, with overlying foul-smelling discharge and areas having occasional bleeding with spontaneous resolution prompting her to seek consult with our outpatient otorhinolaryngology clinic. Her initial head and neck physical examination revealed the following: a 13 x 11 x 6 cm exophytic, fungating and necrotic anterior neck mass with overlying skin induration, erythema, and areas of bleeding, with limitation in neck flexion and extension. A fine-needle aspiration biopsy (FNAB) was performed during the same consult, which showed a Bethesda Category III (atypia of undetermined significance) result. A core needle biopsy was then obtained to establish a definitive diagnosis given the aggressive nature of the mass and its incongruence between the physical exam findings and the FNAB results. The histopathologic considerations were malignant epithelial neoplasm with papillary features (considerations: 1. thyroid epithelial carcinoma, 2. metastatic adenocarcinoma). Immunohistochemistry studies were performed, which showed the following results: CK7: positive, strong, diffuse staining; CK20: negative; thyroglobulin: positive, weak, diffuse staining; TTF-1: positive, strong, diffuse nuclear staining and CDX2: negative, no staining. All of which were consistent with PTC.

A week before her admission, she developed persistent bleeding from the mass, eventually leading to the gradual onset of pallor and generalized body weakness, prompting her family members to bring her to our emergency room for further evaluation and management. At the time of her admission, she had a blood pressure of 90/60 mmHg, heart rate of 112 beats per minute, respiratory rate of 24 breaths per minute. She was afebrile, pale, and weak-looking. She had a 15 x 12 x 10 cm pale, exophytic, fungating, and necrotic mass with overlying skin changes and areas of bleeding that moves with deglutition, multiple hard cervical lymphadenopathies bilaterally, and limitation in neck flexion and extension (Figure 1). Furthermore, she had pale palpebral conjunctivae, tachycardia, strong and bounding pulses, pale palmar creases, and nail beds consistent with her admission hemoglobin level of 29 g/L. The rest of her systemic, gynecologic, and neurologic examinations were unremarkable. A summary of her baseline laboratory results and thyroid function tests can be found in Table 1.

Neck and chest computed tomography revealed a large, mixed attenuating, heterogeneously-enhancing fungating mass arising from the left thyroid lobe measuring 14.1 x 14.1 x 11.1 cm with areas of necrosis and hemorrhage. The mass causes a displacement of the trachea to the right side. Anteriorly, this is seen as a large fungating mass. Superiorly, it extends into the submandibular region at the level of C2-C3, enlarging the ipsilateral submandibular gland. Medially, it abuts the hyoid bone and thyroid cartilage but can be delineated from them. It displaces the sternocleidomastoid muscle on the left with no delineable plane of differentiation.

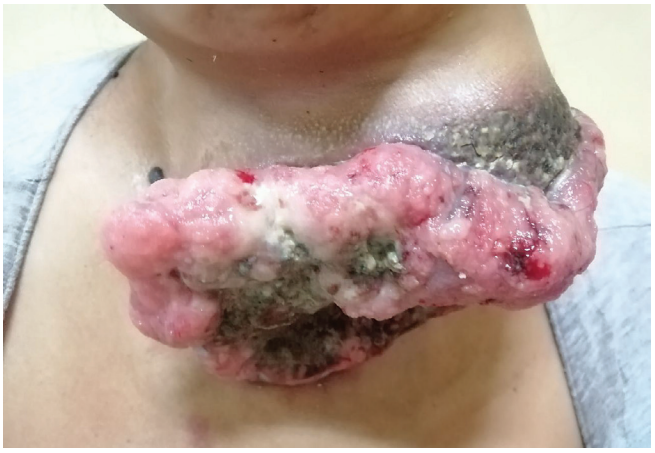

Figure 1. Anterior view showing a 15 x 12 x 10 cm pale, exophytic, fungating, and necrotic mass with overlying skin induration, hyperpigmentation, pinpoint areas of bleeding, necrotic regions with foul-smelling purulent discharge, multiple hard cervical lymphadenopathies bilaterally with limitation in neck flexion and extension.

Table 1. Baseline hematology, serum chemistry, and thyroid function tests

Hematology	09/16/2020 Admission	09/29/2020 7 units packed red cells / 4 units fresh frozen plasma	Normal values
WBC	6.80	8.70	4.5 - 11 x 10^9/L
RBC	2.46	4.45	4.2-5.4 x 10^{12}/L
Hgb	29	110	120-160 g/L
Hct	0.12	0.36	0.38-0.47
MCV	50.1	80.0	80-96 fL
MCH	11.7	24.8	27-31 pg
MCHC	233	310	320-360 g/L
RDW	27.0	26.9	11-16
PC	545	507	150-450 x 10^9/L

Chemistry	09/16/2020	Normal values
Creatinine	52 (eGFR: 119 mL/min)	46 - 92 umol/L
Na	134	137-145 mmol/L
K	3.8	3.5 - 5.1 mmol/L
Cl	107	98-107 mmol/L
Ca	1.80 (2.20)	2.10-2.55 mmol/L
Mg	0.92	0.7-1.00 mmol/L
AST	34	14-36 U/L
ALT	32	<35 IU/L
Alb	20	35-50 g/L
Iron	1.8	6.6 - 30.4 umol/L
dTIBC	49.76	47.4 - 89.0 umol/L
TSAT	3.61%	
Ferritin	10.2	6.24 - 137 ng/mL

Hormones	09/16/2020	Normal values
Free T4	9.45	9.01 – 19.05 pmol/L
Free T3	3.20	2.89 – 4.88 pmol/L
TSH	1.0867	0.35 – 4.94 mIU/mL

Enlarged and prominent lymph nodes were seen at the bilateral supraclavicular regions. Cut-off of the internal jugular vein on the left at the level of the C7-T1 and opacification of the left internal jugular vein was observed at the level of C7 likely represents thrombus formation (Figure 2). She was managed as a case of papillary thyroid cancer stage I (T4aN1bM0) and anemia from acute on top of chronic blood loss and iron deficiency. She underwent blood transfusion (total of 7 units of packed red blood cells and 4 units of fresh frozen plasma) to target a hemoglobin level of at least 100 g/L before surgery; started on ferrous sulfate and folic acid plus vitamin B complex supplementation; wound dressing, packing and control of bleeding. On her 7th hospital day, she had a markedly improved overall well-being and her hemoglobin at this time was already at 110 g/L. She underwent a wide excision, total thyroidectomy, bilateral

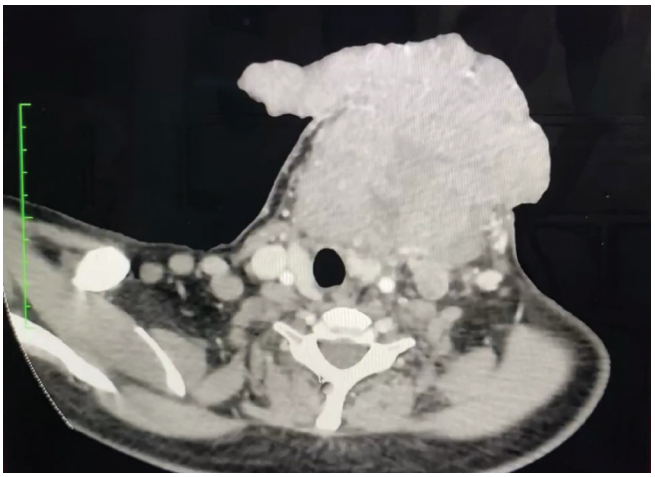

Figure 2. Neck CT with contrast coronal view at the C7-T1 showing a large, mixed attenuating, heterogeneously-enhancing fungating mass arising from the left thyroid lobe measuring 14.1 x 14.1 x 11.1 cm with areas of necrosis and hemorrhage. The mass causes a displacement of the trachea to the right side. Cut-off of the internal jugular vein on the left at the level of the C7-T1 and opacification of the left IJV is observed at the level of C7, representing thrombus formation.

radical neck dissection, and pectoralis major muscle flap under general anesthesia with long-term plans of radioactive iodine ablation, post-therapy whole-body scan, levothyroxine replacement and disease surveillance for recurrence. Unfortunately, during the 6th intra-operative hour, there was note of sudden decrease in end-tidal carbon dioxide levels, heart rate, and blood pressure during the ligation of the left internal jugular vein and went into arrest from obstructive shock from massive pulmonary embolism. She failed to be resuscitated following 30 minutes of advanced cardiac life support. Unfortunately, we could not document pulmonary embolism through computed tomography and pulmonary angiography due to limitations in terms of logistics as the patient went into sudden arrest intra-operatively. Pulmonary embolism as the cause of the patient's demise was diagnosed after accounting for the sudden onset, decreasing oxygen saturation levels in the background of an active malignancy with documented tumor thrombus on preoperative imaging.

Post-mortem, the gross specimen was sent for histopathologic examination and was signed out as a case of PTC, conventional variant, 12.5 cm in greatest tumor dimension with extension into the skin and subcutaneous tissue, positive for intratumoral and peritumoral lympho-vascular space invasion and no definite perineural invasion; two perithyroidal and three supraclavicular lymph nodes were positive for tumor (Figure 3). The study was carried out following the principles outlined in the 2008 Declaration of Helsinki. Informed consent was obtained from the patient before the beginning of the study.

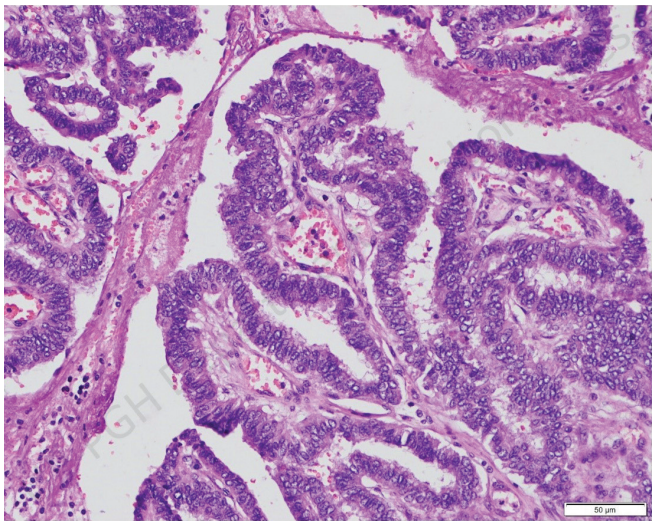

Figure 3. On higher magnification (H & E staining, 100X), the tumor-forming complex, branching, randomly oriented papillae with fibrovascular cores tumor cells are shown. Nuclear enlargement, elongation and overlapping, chromatin clearing, chromatin margination with ground glass nuclei or the classic Orphan Annie nuclei are also demonstrated, as well as the nuclear membrane irregularities showing irregular nuclear contour, nuclear grooves, and nuclear pseudoinclusions.

DISCUSSION

PTC is the most common epithelial thyroid tumor, accounting for more than 80 to 90% of all thyroid tumors in the iodine-sufficient areas globally, with Asian women having the highest incidence.[1] The prognosis of PTC is generally excellent, with 10-year overall survival rates exceeding 90%. However, studies have shown that among Asians, Filipinos have consistently been reported as the ethnic group with the highest incidence of thyroid cancer. Furthermore, thyroid cancer among Filipinos was also observed to be more aggressive and recurrent.[1] In sporadic cases, papillary thyroid cancers may assume enormous dimensions due to late diagnosis and an overall lack of access to healthcare and treatment, which remains common in developing countries like the Philippines and, in worst scenarios, the patient's negligence of the problem and refusal of treatment.[2-11] A summary of similar cases, disease presentation, management, and outcomes are presented in Table 2.

A fungating form of cancer occurs due to combined malignant proliferation and central necrosis of the tumor, leading ultimately to foul-smelling necrotic skin lesions that exude fluids and can bleed profusely.[2-7] The most common forms of cancer presenting as fungating masses are breast cancer (62%), followed by head and neck cancers (24%), cancers of the back and genitalia. Locoregional control of these advanced cancers is exceptionally challenging. It requires a multidisciplinary team approach with adequate physical and mental patient support owing to the nature of their visible progressive cancers.[11] For the case of our patient, despite the fungating nature and presentation, which is more consistent with poorly-differentiated thyroid tumors such as anaplastic thyroid carcinoma characterized by marked pleomorphism, high mitotic activity, sarcomatoid changes, presence of giant cells as well as epithelial and squamous tumor nests, all microscopic and immunohistochemical findings were consistent with PTC (100% reactivity in PTC, 0% reactivity in anaplastic carcinoma): positive and diffuse staining for CK7, thyroglobulin, and TTF-1, all of which are absent in anaplastic carcinoma.[12]

A thorough preoperative diagnostic evaluation should be emphasized with excluding anaplastic thyroid cancer as the first step. Evaluation is performed through a combination of clinical, radiological, and histopathologic assessment (FNAB, punch biopsy, and immunohistochemical staining). Management-wise, large fungating well-differentiated cancers are sporadic and represent a unique challenge to surgeons requiring wider excision margins, proximity to vital and vascular anatomic structures, greater intraoperative blood loss, and higher morbidity and mortality rates and functional cosmesis.[11] Surgery remains the first-line management if the patient's general condition permits. It leads to maximum benefit for more effective radioactive iodine ablation and radiotherapy treatment, a better quality of life, and longer overall survival.[11]

Other preoperative modalities that can be used to address the tumor burden include the application of selective embolization of thyroid arteries (SETA) before surgery. SETA has been used in other countries to decrease the blood flow to the thyroid by selectively blocking the superior thyroid and one of the inferior thyroid arteries preoperatively. It has been used in cases of extensive well-differentiated thyroid cancers, anaplastic thyroid carcinoma, large-sized toxic goiters refractory to medical and radioactive iodine ablation therapy, extensive non-toxic cervicomediastinal goiters, and in cases of amiodarone-induced thyrotoxicosis.[13-17] SETA is evaluated using a combination of technical and clinical success. The technical success of embolization is defined as the occlusion of the targeted vessels. However, only one inferior thyroid artery should be embolized to avoid hypoparathyroidism. On the other hand, the vascular supply of other vital structures such as the esophagus, trachea, and recurrent laryngeal nerves do not depend on thyroid arteries and are not likely to be affected by SETA. The clinical success of embolization is defined as a decrease in the expected blood loss during surgery and/or facilitated tumor removal and/or reduced surgical complication and/or palliation of the symptoms associated with tumor presence.[13-18] SETA has several potential advantages before thyroidectomy, which include better visualization of the surgical field with decreased overall surgical complication rate as an effect of limited

Table 2. Summary of cases of exophytic thyroid cancer, disease presentation, management, and treatment outcomes

Year and Country	Case Presentation	Primary or Recurrence	Management	Outcome
2004 Canada[2]	Case A: 71/F with fleshy outgrowth at the scalp confirmed to be PTCA, with lung and bone metastases	Recurrence Total thyroidectomy 6 years prior	Radical resection and RAI (total 400 + 200 mCi)	Mortality from disease progression
	Case B: 82/F with 4 cm hyperpigmented papule on the neck	Recurrence Total thyroidectomy 11 years prior	Radical resection	Alive
2005 Malaysia[3]	Case A: 66/F with a 40-year history of enlarging anterior neck mass with ulceration and discharge	Primary	Resection and skin grafting	Alive
	Case B: 52/F with an ulcerating and fungating mass	Recurrence Total thyroidectomy 6 years prior for PTCA, RAI, and RT	Radical resection, deltopectoral graft, and RAI	Alive
2005 Turkey[4]	75/F with a 10-year history of gradually enlarging anterior neck mass with overlying skin erythema	Primary	Complete surgical extirpation, total thyroidectomy, modified radical neck dissection followed by RAI	Alive
2005 Japan[6]	64/F with an enlarging anterior neck mass, facial and right arm swelling	Primary	Total thyroidectomy, resection of the IJV and subclavian vein. Median sternotomy with dislocation of the left sternoclavicular joint. En-bloc resection of the tumor, SVC was reconstructed with a graft	Alive
2012 Greece[7]	72/F with a 7-year history of gradually enlarging anterior neck mass, now with ulcerations and bleeding	Primary	Hemostasis of bleeding No consent for surgery and RAI	Mortality
2012 Turkey[8]	72/F with a 2-year history of a gradually enlarging buccal mass → ectopic PTCA	Primary	Lip splitting, total excision of the mass, total thyroidectomy, and RAI	Alive
2015 India[9]	58/F with a 20-year history of a fungating anterior neck mass with ulcerations, foul-smelling discharge, and maggots	Primary	Wide excision, total thyroidectomy, neck dissection, skin flap, and RAI	Alive
2018 India[10]	40/F with an exophytic and bosselated mass 12 x 10 cm	Recurrence Nodulectomy 15 years ago	En bloc resection of the mass and lymph node dissection	Alive
2018 India[11]	72/M with a 10-year history of multiple neck swelling and ulcerations	Primary	Total thyroidectomy, modified radical neck dissection, central neck dissection, and skin flap, and RAI	Alive

intraoperative bleeding, shortening of the overall procedure time, and increasing the chances of complete surgical resection. One significant consequence of the procedure is the massive increase of thyroglobulin (Tg) concentration and moderate increase of free thyroid hormones brought about by the ischemic necrosis of the thyroid gland following embolization of arterial supply.[13-14] Massive Tg increase can theoretically cause acute respiratory distress syndrome, and hence, performing thyroidectomy within 36 hours from SETA has become a common practice.[13]

A study by Dedecjus and colleagues showed that among the 20 patients with large well-differentiated thyroid cancers who underwent SETA preoperatively, SETA effectively limited blood flow through the thyroid arteries confirmed immediately after embolization by angiography, CT scan, and ultrasound examination.[13] There was a massive increase in serum Tg concentration following SETA (130.9 ± 48.89 vs. 15.441.26 ± 41.895.9 ng/mL, respectively, $P < 0.003$), increase of free thyroid hormone concentrations (FT4 15.01 ± 3.1 vs. 20.15 ± 4.55 pmol/L, respectively, $P < 0.052$) and (FT3 4.79 ± 0.88 vs. 6.1 ± 8.5 pmol/L, respectively, $P < 0.008$). Although five cases had developed a hematoma, six had a fever, and five had pain, no major complications were observed. The study also compared thyroidectomies performed after SETA to a similar population of 20 patients who underwent thyroidectomy without prior SETA. There was noted a significant decrease of the operating time (123 ± 24 min vs. 95.8 ± 26 min, respectively, $P < 0.01$), intraoperative blood loss (138.2 ± 29.2 mL vs. 49.9 ± 12.7 mL, respectively, $P < 0.0001$) and drainage in the first 24 hours (160 ± 25 mL vs. 92 ± 9 mL, respectively, $P = 0.00$).[13] SETA is an attractive preoperative minimally invasive and safe neoadjuvant procedure in patients with large well-differentiated thyroid cancers who are at risk of developing massive intraoperative bleeding following extensive surgery. However, the modality is not readily available in our setting and requires extensive technical expertise.

Going back to the case of our patient, a tumor thrombus was demonstrated in the left internal jugular vein at the C7-T1 vertebral level. The first principle is to always differentiate between tumor thrombus and traditional thrombus (also called a bland thrombus) through pertinent radiographic features of tumor thrombi such as invasion and extension into the vessel contiguous with the malignant mass, marked contrast enhancement, and high uptake fluorodeoxyglucose on positron emission tomography. Filling defects within the affected vessel are seen in both tumor and bland thrombus. More importantly, tumor thrombi are not expected to respond to anticoagulation.[13] Although prophylactic anticoagulation is warranted from the hypercoagulable state from active malignancy, we opted not to do anticoagulation for her case after weighing the risks of massive bleeding versus the benefits and presence of tumor thrombus.

Given the rarity of fungating well-differentiated thyroid cancers, the available literature is mostly case reports and series, and most of these are documented in developing countries.[2-11] Majority of reports have shown that despite the fungating nature of these papillary thyroid cancers, they tend to have more favorable outcomes through a combination of thorough preoperative evaluation and optimization, surgical removal and reconstruction followed by radioactive iodine ablation, levothyroxine suppression, and continued close surveillance and monitoring.[11]

CONCLUSION

In summary, the timely diagnosis and treatment of thyroid cancer are essential. Although large and fungating thyroid masses are rare as initial clinical presentations, they remain more common in developing countries, where early detection and access to healthcare remains limited. Furthermore, these large fungating masses represent a unique challenge to surgeons for adequate preoperative optimization, total thyroidectomy, and wider margins of resection and debulking followed by adjuvant radioactive iodine ablation, levothyroxine suppression, and continued close surveillance and monitoring to achieve a better quality of life and longer overall survival. For the case of our patient, even if the outcome was not good, we still opted to report this case as there were many significant learning points, and we would likely see more of these cases, especially in our setting and practice. Lastly, if only patients with good and excellent outcomes are reported in the literature, it would lead to an overestimated treatment success of these complex cases.

Statement of Authorship

All authors participated in the conceptualization of work, acquisition, and analysis of data, drafting and revising, and final approval of the version to be published.

Author Declaration

All authors declared no conflicts of interest.

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