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Malignant Carotid Body Tumor: A Case Report and Comprehensive Literature Review

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Abstract

Background: Malignant carotid body tumors (CBTs) are rare neoplasms arising from the chemoreceptor cells at the carotid bifurcation. They are often misdiagnosed and can lead to serious complications if not treated promptly.

Case presentation: A 44-year-old female presented with a mass in the neck, persisting for six months, without any accompanying symptoms, such as pain or difficulty swallowing. Physical examination revealed a firm 3 x 4 cm mass on the right side of her neck, near the mandible. Doppler ultrasound identified a semi-vascular mass (2.5 x 3.5 cm) at the right carotid bifurcation, which was further confirmed by contrast-enhanced computed tomography (CECT), indicating vascularity and contributing to the widening of the carotid arteries. The mass received blood supply from small arterioles stemming from the external carotid artery. Surgical exploration also revealed a firm, fibrous mass classified as a grade 2 tumor according to the Shamblin classification. The tumor was successfully excised after cauterizing small arterial branches from the internal and external carotid arteries.

Conclusion: The evaluation of this case highlighted the importance of early diagnosis and surgical intervention in managing malignant CBTs, as they can lead to severe complications. A multidisciplinary approach that incorporates imaging and surgical expertise is essential for achieving successful outcomes.

Keywords: Doppler ultrasound, Carotid body tumor, Malignant tumor.

1. Background

Malignant carotid body tumors (CBTs), also known as paragangliomas, are rare neuroendocrine neoplasms arising from the carotid body, a small organ located at the bifurcation of the common carotid artery (1). These tumors are often characterized by aggressive behaviors, the potential for local invasion, and the ability to metastasize to distant sites (2). They are typically associated with symptoms such as a neck mass, pulsatile tinnitus, and neurological deficits resulting from the compression of surrounding structures. Despite their rarity, malignant CBTs pose significant challenges in terms of diagnosis, management, and long-term outcomes (3).

Malignant CBTs are extremely rare, with an incidence of 1 to 2 cases per million people per year. The overall prevalence of CBTs, both benign and malignant, is low, affecting approximately 0.01% of the population. These tumors are more common in populations living at high altitudes, where chronic hypoxia is common, leading to increased catecholamine production and potential tumorigenesis (4, 5). World health organizations, including the

World Health Organization (WHO), classify CBTs in the category of neuroendocrine tumors, highlighting their unique biological behavior and potential malignancy. However, comprehensive data on the epidemiology of malignant CBTs are rare (6).

Numerous reports and case studies document the delivery and management of malignant CBTs in diverse populations and geographic locations (7). Case reports from Europe and the United States describe various surgical approaches, the role of radiation therapy, and chemotherapy protocols; however, much remains to be understood about optimal management strategies and long-term outcomes (8).

In Iran, studies on malignant CBTs are limited. The existing literature indicates an increasing awareness of these tumors, mainly through case reports and small series. However, systematic data collection and analysis are still lacking, indicating significant gaps in reporting and research within the country (9-11). Several studies have investigated clinical manifestations, diagnostic imaging, treatment modalities, and outcomes in patients with malignant CBTs. However, the focus is mostly on surgical management, while the role of adjuvant therapies has not been adequately studied. Most of the available literature consists of isolated case reports without large cohort analyses, which limits the ability to draw comprehensive conclusions about disease behavior and treatment efficacy (12-16).

The necessity of conducting this study stems from the rarity of malignant CBTs and the critical need for more robust data to inform clinical practice. This study aimed to report a case of malignant CBT, supplemented by a literature review that consolidates existing findings on incidence, management options, and outcomes.

2. Case Presentation

The subject of this case report is a 44-year-old female patient who presented with a palpable mass in the neck, episodes of hoarseness, and atypical headaches over the past six months. Upon initial examination, the mass was noted to be located at the carotid bifurcation. The patient had no significant medical history, and no family history of head and neck malignancies was recorded. Clinical assessment included a thorough physical and neurological examination.

On physical examination, a firm mass measuring approximately 3 x 4 cm was palpated on the right side of the neck, near the angle of the mandible. The mass exhibited no pulsation upon palpation, and auscultation revealed no bruits, suggesting that it was not immediately vascular in nature.

2.1. Diagnostic methods:

A series of diagnostic procedures was employed to evaluate the mass. Initially, a high-resolution neck ultrasound was performed to assess the size, vascularity, and characteristics of the mass. This assessment suggested a highly vascular tumor located at the carotid bifurcation. Doppler ultrasound revealed a semi-vascular mass measuring 2.5 x 3.5 cm located at the right carotid bifurcation, positioned explicitly between the internal and external carotid arteries. Contrast-enhanced CT imaging further characterized the lesion, demonstrating a vascular mass at the right carotid bifurcation that resulted in the widening of both the internal and external carotid arteries. The primary blood supply to the tumor was found to originate from several small arterioles branching off the external carotid artery.

Following the ultrasound, a computed tomography angiography (CTA) study was conducted to obtain detailed information regarding the tumor's relationship with surrounding vessels and to evaluate any potential invasion into adjacent structures. To further characterize the tumor, a

magnetic resonance imaging (MRI) was performed. T1-weighted and T2-weighted images were analyzed to assess the extent of the mass and its differentiation from the surrounding soft tissue. Subsequently, a fine needle aspiration biopsy was conducted under ultrasound guidance to obtain histological samples from the tumor, which ultimately provided a definitive diagnosis of malignant CBTs. Moreover, routine laboratory tests were performed, including a complete blood count, a comprehensive metabolic panel, and tumor markers, to assess the patient's overall health and to identify any possible paraneoplastic syndromes.

2.2. Management of the patient

Following the diagnosis of malignant CBT, a multidisciplinary team was assembled, including oncologists, radiologists, and surgical specialists. The management plan emphasized both curative and palliative approaches, given the characteristics of malignancy. The patient was counseled regarding potential treatment options, including surgery, and the importance of regular follow-up.

2.3. Surgery method

The surgical approach to remove the malignant CBT was carefully planned based on preoperative imaging studies. A traditional cervical approach was deemed appropriate, with a focus on preserving critical neurovascular structures.

2.4. Surgery procedure

The patient underwent a series of meticulous steps starting with anesthesia and positioning, where general anesthesia was administered, and the neck was scrubbed and draped in a sterile manner, utilizing a shoulder roll to facilitate neck extension for improved surgical access. Following this preparation, a standard transverse cervical incision was executed along the anterior border of the sternocleidomastoid muscle, carefully extending towards the midline to ensure adequate exposure for subsequent dissection.

The surgical team retracted the sternocleidomastoid muscle to reveal the carotid sheath, performing careful dissection to locate the external and internal carotid arteries. This step was critical as it limited the manipulation of vessels, thus minimizing the risk of intraoperative complications. Once the relevant anatomy was thoroughly identified, the malignant CBT was meticulously dissected from the surrounding tissues, employing electrocautery and sharp dissection techniques. The surgeons ensured that adequate margins were outlined, and the tumor was successfully resected in its entirety. During the surgical procedure, a very firm and fibrotic mass was identified. Based on the Shamblin classification system, the tumor was categorized as grade 2, which is indicative of a moderately vascularized tumor that may involve surrounding structures to a certain extent.

Small arterial branches arising from both the internal and external carotid arteries were carefully cauterized using bipolar cautery to minimize blood loss. Following meticulous dissection, total excision of the tumor was successfully performed. The specimen was sent for histopathological analysis to confirm the diagnosis and assess any further treatment requirements. Postoperative recovery was monitored, with particular attention given to the patient's neurological status due to the proximity of the tumor to critical vascular structures. Follow-up appointments were also scheduled to assess any signs of recurrence and to ensure the comprehensive management of her condition. The pathological reports are demonstrated in Figures 1 to 4.

After the tumor removal, attention

turned to achieving hemostasis, during which the wound was irrigated. The incision was closed in a layered fashion, and drains were inserted as deemed necessary. The final closure involved suturing the incision securely, marking the completion of the surgical procedure. Following the operation, the patient was carefully monitored in a recovery area, where signs of complications, such as bleeding and neurological deficits, were assessed. To further support the patient's recovery and the potential need for adjuvant therapies, follow-up imaging and clinical evaluations were scheduled.

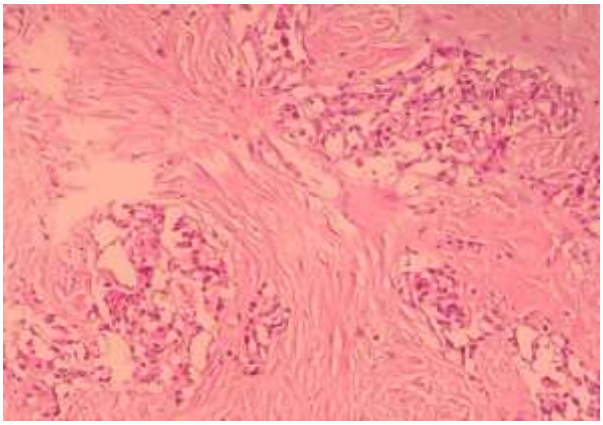

Figure 1. Tumor cells between fibrosis

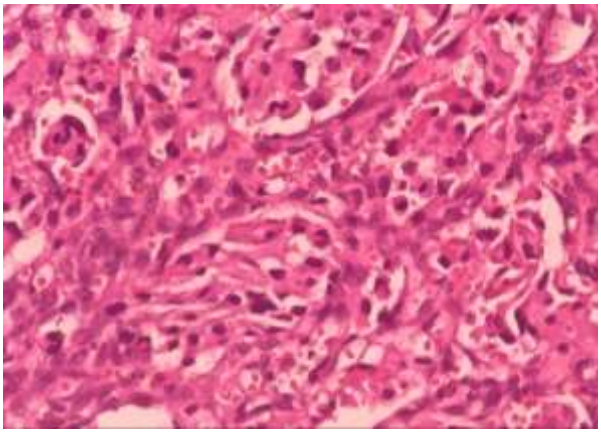

Figure 2. Tumor cells with acidophilic cytoplasm (Zellballen pattern)

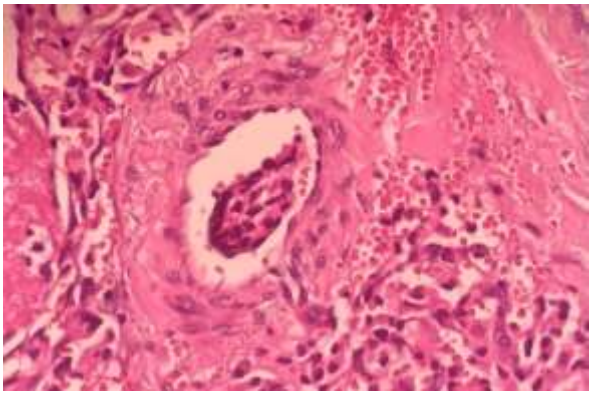

Figure 3. Tumor cells between neural cells

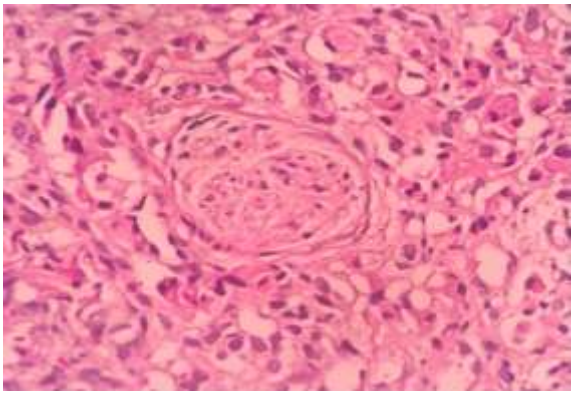

Figure 4. Vascular invasion by tumor cells

3. Discussion

3.1: A Comprehensive approach to the carotid body tumors:

3.1.1: Carotid body

The carotid body is a small, pea-sized cluster of chemoreceptors and supporting cells located at the bifurcation of the common carotid artery, where it divides into the internal and external carotid arteries.

This critical peripheral chemoreceptor plays a vital role in regulating respiratory and cardiovascular function by detecting changes in blood chemistry, particularly in oxygen (O_2) levels, carbon dioxide (CO_2) levels, and pH. As an integral component of the body's homeostatic mechanisms, the carotid body plays a crucial role in maintaining oxygenation and acid-base balance, thereby ensuring that tissues receive an adequate blood supply during varying physiological states (17, 18).

Functionally, the carotid body communicates with the central nervous system through the glossopharyngeal nerve (cranial nerve IX), relaying information about the blood gases and stimulating respiratory responses as needed (19). In instances of hypoxia, hypercapnia, or acidosis, the carotid body triggers an increase in respiratory rate and depth, alongside cardiovascular adjustments, to restore normal physiological conditions. Beyond its primary role in gas exchange, the carotid body has garnered interest for its involvement in various pathophysiological conditions, including sleep apnea, heart failure, and hypertension (20).

The study of the carotid body encompasses a range of disciplines, from neurobiology and physiology to clinical medicine, as researchers seek to understand its intricate signaling pathways, cellular mechanisms, and potential therapeutic implications. As our knowledge of the carotid body expands, we gain deeper insights into its contributions to both health and disease, highlighting its significance in the broader context of human physiology and pathology (21).

3.1.2: Carotid body tumors

Carotid body tumors, also known as carotid body chemodectomas, are rare neuroendocrine tumors that arise from the carotid body, a small cluster of chemoreceptor cells located at the bifurcation of the common carotid artery (22). These tumors are typically highly vascular and are classified as paragangliomas, a category of tumors that originate from neural crest cells, which form the paraganglia, a component of the autonomic nervous system. While CBTs are most commonly benign, they can exhibit aggressive behavior and have the potential for local invasion or metastasis, particularly in specific demographics and in larger tumors (23).

Typically presenting as a palpable neck mass, CBTs may be asymptomatic in their early stages, leading to a delayed diagnosis. When symptoms do occur, they may include a pulsatile mass, cranial nerve deficits, or neck discomfort. The diagnosis often involves imaging studies, including ultrasound, CT scans, or MRI scans, to evaluate the size and extent of the tumor, as well as its relationship to surrounding vascular structures (24).

The management of CBTs primarily involves surgical excision, particularly for symptomatic patients or those with tumors demonstrating significant growth. However, the surgical approach can be intricate due to the tumor's proximity to critical anatomical structures, and preoperative planning is essential. In cases where surgery is not feasible or the tumor is deemed inoperable, alternative therapies, such as radiotherapy or embolization, may be considered (25). Understanding the unique clinical, radiological, and pathological aspects of CBTs is vital for effective diagnosis and management. Increased awareness of this rare entity can lead to better outcomes for patients, highlighting the importance of further research and training in the field of head and neck tumors (23).

3.1.3: Malignant CBTs

Malignant CBTs are rare, neoplastic growths that arise from the chemoreceptor cells situated in the carotid body located at the bifurcation of the common carotid artery. These tumors, often classified under paragangliomas, can exhibit aggressive behaviors and present significant clinical challenges due to their propensity for local invasion and distant metastasis (26). While the majority of CBTs are benign, the malignant variants, characterized by their potential to metastasize and recur, present distinct diagnostic and therapeutic challenges (27).

Malignant CBTs tend to present predominantly in middle-aged individuals, with a slight female predominance. Symptoms may vary widely depending on tumor size and

location, including cervical masses, cranial nerve dysfunction, and symptoms attributable to local invasion. Due to their vascular nature and the anatomical complexities of the head and neck region, accurate diagnosis often necessitates a combination of imaging modalities, including ultrasound, CT, and MRI, as well as histopathological examination (28).

The management of malignant CBTs continues to evolve, with treatment options ranging from surgical resection to radiotherapy and systemic therapies. Surgical excision remains the cornerstone of treatment; however, the presence of vascular invasion or metastasis complicates the prognosis and necessitates a multidisciplinary approach to care. Recent advances in molecular biology and genetics have created new research opportunities, potentially leading to targeted therapies for patients with advanced disease (29).

Given their rarity and the challenges they pose in diagnosis and management, malignant CBTs highlight the importance of interdisciplinary collaboration in the clinical setting. This review aims to provide a comprehensive overview of the etiology, clinical presentation, diagnostic strategies, and current therapeutic approaches for malignant CBTs, shedding light on the complexities of managing these formidable tumors (30).

3.1.4: Prevalence of Malignant CBTs in the world and Iran

Malignant CBTs are rare neuroendocrine neoplasms arising from chemoreceptor tissues located at the bifurcation of the common carotid artery. These tumors are part of a larger group called paragangliomas, which originate from paraganglionic tissues located throughout the body (27). While benign types of CBTs are more common, malignant forms present significant challenges in diagnosis and management due to their aggressive behavior and potential for metastasis. Globally, the prevalence of malignant CBTs is low, with an overall incidence estimated to be between 1 and 6 cases per million people per year. The rarity of these tumors means that there are few large-scale epidemiological studies, contributing to a limited understanding of their true prevalence and the factors that may predispose individuals to develop them (2).

Additionally, geographic and ethnic variations may influence incidence, with a notable prevalence in certain populations. This is particularly true among individuals with specific family histories, such as those with germline mutations associated with hereditary paraganglioma syndromes. In Iran, the prevalence of malignant CBTs has not been widely documented; nevertheless, evidence suggests that these tumors may occur with a degree of frequency due to specific genetic susceptibility and environmental factors. Understanding the epidemiology of malignant CBTs in Iran can provide fundamental insights into the etiology of the disease and facilitate more effective clinical management. Furthermore, as healthcare systems evolve and diagnostic technologies improve, a clearer picture of the prevalence and characteristics of these tumors can be created, emphasizing the need for continued research and clinical awareness (31).

3.1.5: Risk Factors of Malignant CBTs

Malignant CBTs are rare neuroendocrine tumors that arise from the carotid body, a specialized structure located at the bifurcation of the common carotid artery. These tumors have the potential to be aggressive and can metastasize to other organs, making early diagnosis and treatment critical to patient outcomes (32). The identified risk factors for the development of malignant CBTs are provided in Table 1. Understanding these risk factors is crucial for healthcare providers and patients to identify those who may be at an increased risk of carotid body malignancy and to manage them effectively. Appropriate screening and surveillance strategies for early

detection and management of these tumors are essential to optimize patient outcomes and improve overall prognosis (33).

Table 1. Identified risk factors for the development of malignant CBTs

Risk factor	Description
Genetics	There is evidence to suggest that specific genetic mutations may predispose individuals to the development of CBTs, including mutations in the succinate dehydrogenase gene.
Radiation exposure	Previous exposure to radiation, particularly in the head and neck region, has been linked to an increased risk of developing CBTs.
Age and gender	Malignant CBTs are more commonly seen in older individuals, with a peak incidence in the sixth and seventh decades of life. Additionally, these tumors are more frequently diagnosed in women than in men.
Smoking	Tobacco use has been identified as a potential risk factor for the development of CBTs.
Hypoxia	Chronic exposure to hypoxia, such as that seen in individuals living at high altitudes or those with chronic respiratory diseases, has been suggested as a potential risk factor for CBT development.

3.1.6: Prevention and treatment of malignant CBTs

Malignant CBTs are rare but aggressive neoplasms that arise from the chemoreceptor tissue located at the bifurcation of the common carotid artery. These tumors are typically classified as paragangliomas, a subset of neoplasms originating from neuroendocrine cells derived from the neural crest. While benign CBTs are more common, malignant variants can exhibit a propensity for local invasion and distant metastasis, complicating both diagnosis and management (2).

The significance of CBT lies not only in its understanding of pathological behavior but also in its clinical implications. Patients with malignant CBTs often present with nonspecific symptoms, such as neck mass, pain, or cranial nerve neuropathies due to tumor encroachment. As these tumors often remain asymptomatic in the early stages, they can be challenging to detect, leading to delayed diagnosis and treatment. Moreover, their vascular location poses unique challenges, particularly when considering surgical interventions (34).

Comprehensive management of malignant CBTs encompasses both prevention and treatment strategies. Prevention primarily revolves around early detection and intervention, especially in patients with hereditary syndromes, such as multiple endocrine neoplasia type 2 or familial paraganglioma syndromes, which predispose individuals to these tumors. Treatment modalities may include surgical resection, radiotherapy, and systemic therapies, depending on the tumor's size, extent of invasion, and metastatic status (35).

Given the rarity of malignant CBTs and the diversity in their clinical presentation and behavior, a multidisciplinary approach is essential. This overview will delve deeper into the strategies for prevention, diagnosis, and treatment of malignant CBTs, highlighting the latest advancements in surgical techniques and adjuvant therapies, as well as the role of genetic counseling in high-risk populations (36).

3.2: Tips and tricks in carotid body tumors:

We reported a 44-year-old woman with a significant neck mass that prompted further investigation and surgical intervention. Despite the absence of systemic symptoms commonly associated with malignant tumors, the imaging and operative findings in this case align with the characteristics documented in the existing literature.

The initial clinical presentation of a firm neck mass without accompanying symptoms, such as pain or neurological deficits, is characteristic of benign and malignant CBTs. According to Avgerinos et al., many patients present with asymptomatic neck masses, and it is not uncommon for these tumors to be discovered incidentally during routine examinations or imaging for other conditions (37).

The utilized imaging modalities, including Doppler ultrasound and contrast-enhanced CT, corroborated the findings of other studies, highlighting the significance of these techniques in diagnosing vascular lesions. Notably, Chen et al. emphasized that CT imaging provides detailed information regarding vascular involvement, aiding in both diagnosis and preoperative planning (38).

In this case, the tumor was classified as grade 2 according to the Shamblin classification system, indicating moderate vascularity and possible involvement of surrounding structures. This classification has been pivotal in determining the surgical approach and anticipating potential complications involved in the surgical management of CBTs. A systematic review by Prasad et al. supports this view, noting that higher Shamblin grades are associated with increased surgical complexity and potential morbidity due to the proximity to vital vascular structures (39).

Intriguingly, the surgical approach adopted in this case, specifically, the meticulous surgical technique employed to minimize blood loss, mirrors the methods described by Hinojosa et al., who advocate for careful dissection and the use of bipolar cautery in managing CBTs. Their findings demonstrated that attention to surgical technique is crucial in reducing perioperative complications and promoting optimal recovery (40).

In terms of prognosis, survival rates and outcomes of malignant CBTs vary widely in the literature. While early diagnosis and complete surgical resection significantly improve prognosis, the presence of vascular invasion and metastasis at the time of diagnosis is detrimental to overall survival (13, 14, 29, 41). This case report underscores the importance of timely intervention and thorough follow-up, in line with the consensus in the literature regarding the critical role of surgical management in improving patient outcomes. The results of the present study strengthened the existing data on the clinical presentation, imaging characteristics, surgical management, and outcomes associated with malignant CBTs. Continued documentation of such cases and their outcomes is crucial for enhancing understanding and refining management strategies for these rare yet clinically significant tumors**.**

4. Conclusion

This case report demonstrated the diagnosis and management of a malignant CBT in a 44-year-old woman and emphasized the importance of careful clinical evaluation and surgical intervention. The presented case suggests that even in the absence of warning signs and with a relatively indolent presentation, a neck mass may require careful investigation due to its potential malignancy, as indicated by comprehensive imaging studies before surgical intervention. Histopathological confirmation of the tumor, classified as grade 2 according to the Shamblin classification, indicates moderate vascular growth with a tendency to involve surrounding structures. The surgical approach employed is characterized by careful dissection around vital vascular structures and emphasizes the need for careful management of such tumors to reduce the risk of complications and ensure complete resection. This case also emphasized the importance of continuous postoperative surveillance to monitor for recurrence, given the aggressive nature attributed to malignant CBTs. Future studies are recommended to focus on refining treatment protocols and postoperative management strategies to enhance patient outcomes. While individual cases may vary, clinicians must remain vigilant in recognizing the malignant potential of neck masses, thereby facilitating early diagnosis and timely intervention.

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Availability of data and materials: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of interest: The authors declare that they have no competing interests.

Consent for publication: Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

Ethics approval and consent to participate: This study was approved by the local ethics committee for research, and the confidentiality of patient data was maintained. The data presented was anonymized, ensuring that no personal information of the case subjects was disclosed.

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Author contributions: Hassan Ravari conducted conceptualization, Reza Asadi performed supervision and validation, and Reza Sahabi carried out investigation and methodology. The authors conducted the writing of the original draft, editing, and reviewing of the manuscript.

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