DOI: https://doi.org/10.2298/SARH231003011V
UDC: 616.22-006.81

CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Transglottic laryngeal melanoma presented as severe dyspnea

Svetlana Valjarević[1,2], Anđelina Jovanović[1,2], Sanja Vučić[1], Ana Marija Tomić[2,3], Milan B. Jovanović[1,2]

[1]Zemun Clinical Hospital Center, Department of Otorhinolaryngology with Maxillofacial Surgery, Belgrade, Serbia;
[2]University of Belgrade, Faculty of Medicine, Belgrade, Serbia;
[3]University of Belgrade, Faculty of Medicine, Institute of Pathology, Belgrade, Serbia

SUMMARY

Introduction While mucosal melanoma of the head and neck remains an uncommon condition, its incidence has been on the rise in recent decades. Within the larynx, the supraglottis represents the most frequently affected subsite, followed by the glottis, with hoarseness being the predominant symptom. Given the tumor's aggressive behavior and its challenging location, it is often overlooked until it progresses to an advanced stage, which significantly worsens the prognosis.

Case report A 45-year-old male patient with stridorous breathing presented to the emergency room. An indirect laryngoscopy revealed a transglottic mass occupying the left piriform recess and the entire laryngeal inlet, leading to an exceptionally narrowed airway. Urgent tracheostomy was performed. Contrast-enhanced computed tomography of the neck identified an ulceroproliferative mass in the larynx, spanning the supraglottic, glottic, and subglottic regions, causing airway narrowing and extending into the left pyriform sinus. Laryngoscopy was performed, and biopsy of the laryngeal lesion confirmed a diagnosis of malignant melanoma. Unfortunately, the patient refused further surgical and oncological treatment, as well as additional diagnostic procedures. Four months after the initial diagnosis, the patient was lost to follow-up.

Conclusion Laryngeal melanoma is an uncommon condition that can necessitate an emergency tracheostomy. Since melanoma can be mistaken for other laryngeal malignancies, immunohistochemical analysis plays a crucial role in making an accurate diagnosis. Early detection of the disease is vital.

Keywords: melanoma; laryngeal tumor; stridor; tracheostomy

INTRODUCTION

Melanoma, which arises from the malignant transformation of melanocytes, is a type of cancer that is becoming increasingly common. Although head and neck mucosal melanoma (HNMM) is an uncommon malignancy, its incidence has been increasing in recent decades. [1, 2]. HNMM has an incidence of 1–4% of all melanomas and 0.03% of all cancer diagnoses [3]. The outlook for patients with this tumor is poor, as it tends to recur locally and metastasize to distant sites. Published five-year survival rates vary from 17.1 up to 40% [1, 4]. Mucosal melanomas affect males and females equally and are uncommon during the first three decades of life [4].

Mucosal melanoma can develop in various mucosal locations, but it is most detected in the head and neck region, as well as in the anogenital and visual tracts [5].

It is estimated that 40–60% of mucosal melanomas occur in the head and neck region. The most common sites of HNMM include the nasal cavities, paranasal sinuses, oral cavity, pharynx, and larynx [3, 6].

The most common subsite of mucosal melanoma in the larynx is supraglottis followed by glottis, with hoarseness of voice being the major symptom. A total of 60% of patients present with metastasis to neck lymph nodes, while another 60% develop distant metastases [7].

Symptoms of HNMM can be nonspecific, such as throat pain, hoarseness, or even asymptomatic. Due to the location and aggressive nature of this type of cancer, it often goes unnoticed until it has reached an advanced stage, resulting in a poor prognosis [3]. As a result, many patients are diagnosed late in the disease course when the cancer has already spread to other parts of the body.

Treating HNMM is an extremely arduous task because there is currently no therapeutic approach that has shown significant improvement in treatment outcomes [4].

Additionally, during the COVID-19 pandemic, it is expected that there will be delays in diagnosis and an increase in advanced cases of head and neck cancer due to disruptions in cancer screening and diagnosis [8]. The COVID-19 crisis has had a significant impact on every stage of the patient's journey from cancer diagnosis to treatment [9].

CASE REPORT

A 45-year-old male presented to the emergency room complaining of hoarseness, dysphagia, left-sided otalgia, and fatigue for more than

Received • Примљено: October 3, 2023
Revised • Ревизија: January 23, 2025
Accepted • Прихваћено: January 26, 2025
Online first: January 28, 2025

Correspondence to:
Anđelina JOVANOVIĆ
Zemun Clinical Hospital Center
Department of Otorhinolaryngology with Maxillofacial Surgery
Vukova 9
11000 Belgrade
Serbia
andjelinakjosevski@yahoo.com

four months. His medical history revealed prolonged consumption of tramadol tablets due to opiate withdrawal treatment and smoking one pack of cigarettes per day for 25 years. Upon examination, the patient was conscious but tachypneic with inspiratory stridor in a seated position, and oxygen saturation was 90% while breathing room air. Indirect laryngoscopy revealed a transglottic ulceroproliferative, reddish-colored mass occupying the left piriform recess and nearly obstructing the entire laryngeal inlet, resulting in a severely narrowed airway. Although no palpable neck nodes were detected, laryngeal malignancy was suspected, and the initial assessment indicated a high likelihood of difficult intubation. The patient was promptly taken to the operating room, where an awake tracheostomy was performed under local anesthesia using 25 mL of lidocaine (40 mg / 2 mL). A 10.0 mm tracheostomy cannula was successfully placed, securing the airway. The patient remained hemodynamically stable with an oxygen saturation of 98%.

Blood tests revealed an elevated white cell count (14.7×10^9/L) with neutrophilia (11.7×10^9/L), raised C-reactive protein (12.3 mg/L), and anemia (erythrocytes 4.01×10^{12}/L, hemoglobin 11.7 g/dL, hematocrit 0.357 L/L, mean cell hemoglobin concentration 328 g/L). Other blood tests, including liver function tests, were normal, and virology screening excluded HIV, hepatitis B virus, and hepatitis C infection.

Contrast-enhanced computed tomography (CT) of the neck revealed a laryngeal ulceroproliferative mass 35.7 mm × 31.3 mm × 63.4 mm in its diameter, involving the supraglottic, glottic, and subglottic regions, causing airway narrowing and extending into the left pyriform sinus (Figure 1). An additional high-resolution head CT scan demonstrated no signs of malignancy and involutional brain parenchymal volume loss. Chest radiography revealed normal findings, and no distant metastases were found on thorax CT and abdomen ultrasound. The patient underwent a laryngoscopy which confirmed clinical and CT findings. A massive laryngeal ulceroproliferative mass completely narrowed airway, occupying left hypopharynx with infiltration of the medial and anterior wall of the left pyriform sinus. The posterior wall of hypopharynx, postcricoid region and right pyriform sinus appeared without tumor infiltration. Biopsy was performed and a malignant melanoma was confirmed. Oesophagoscopy findings were normal, and an attentive intraoral examination revealed no notable findings. The histopathological examination revealed strong nuclear positivity for *SOX10* (Sry-related HMg-Box gene 10), a sensitive and specific marker of malignant melanoma, as well as weaker microphthalmia transcription factor (MITF) positivity (Figure 2). Considering all the performed diagnostics as well as clinical findings, our patient was staged as T4N0M0.

Unfortunately, the patient refused further surgical and oncological treatment, as well as additional diagnostic procedures. He was discharged from the hospital and regularly followed up for tracheostomy care but consistently refused further medical treatment. On the last control, he was in a normal state of consciousness, but his physical condition

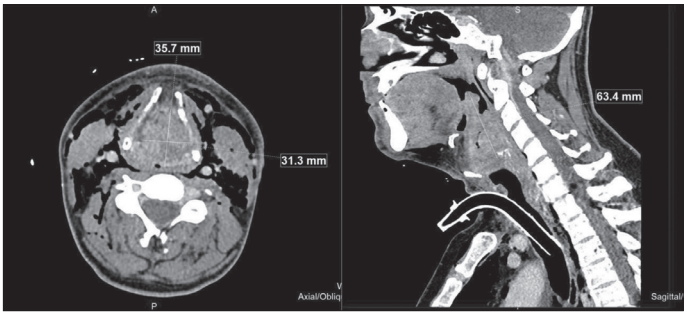

Figure 1. Contrast-enhanced computed tomography image of the neck reveals ulceroproliferative laryngeal mass with airway narrowing; tracheostomy tube is in the correct position

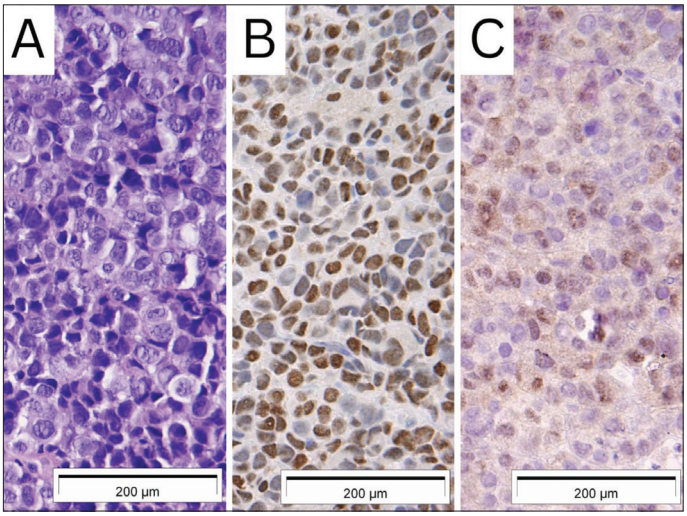

Figure 2. A – Tumor cells are large, epithelioid, with abundant eosinophilic cytoplasm and prominent nucleoli; hematoxylin and eosin stain, original magnification × 400; B – tumor cells show strong nuclear SOX10 positivity; C – tumor cells also show as weaker microphthalmia transcription factor positivity; original magnification × 400

was in rapid decline. Four months after the initial diagnosis, the patient was lost to follow-up.

All procedures were carried out in compliance with the institutional and/or national research committees' ethical standards, as well as the 1964 Helsinki Declaration and its revisions or similar ethical standards. The patient provided written permission to publish all shown material.

DISCUSSION

Mucosal melanoma of the larynx is an exceptionally rare malignancy, however, there has been a trend of rising incidence over the past few decades [3, 10].

The cause of HNMM remains unclear, but it is not believed to be linked to excessive UV exposure. Instead, contributing factors include poor-fitting dentures, physical injury, smoking, and a family history of the disease.

Our patient's family health history revealed no cases of melanoma, but he had a history of chronic heavy smoking. Mucosal melanoma is uncommon in patients under 65 years, however in the presented case, the patient was 45 years old [11].

The intricate anatomical arrangement of the head and neck coupled with the lack of early-stage symptoms present significant obstacles for both the diagnosis and treatment of malignant melanoma. Laryngeal melanoma may be presented as an unusual sensation in the patient's throat, hoarseness, or dyspnea [5]. Our patient had a significant clinical presentation with stridor and massive laryngeal infiltration.

The differential diagnosis of laryngeal masses, based on their clinical appearance, includes a variety of malignant and benign lesions, such as squamous cell carcinoma, neuroendocrine carcinoma, lymphoma, paraganglioma, and chronic granulomatous conditions of the larynx [12]. Laryngeal melanoma, as in our case, may arise as an amelanotic lesion. Hence, accurate diagnosis may be challenging, and priority must be placed on histologic assessment [3]. We underline that the clinical presentation of the tumor mass in the larynx in our patient did not arouse suspicion of mucosal melanoma. Histology analysis shows melanin abundant tumor cells altering from polyhedral to pleomorphic shapes with notable mitotic activity. Verification is performed with immunohistochemistry using S100 protein and melanocyte markers- MART1/Melan A, tyrosinase, HMB45, MITF. Protein S100 exhibits the highest sensitivity, while HMB45 shows the greatest specificity [13]. In the study of Suresh et al. [4], 90.2% of cases showed positivity both to S100 and HMB45. The absence of p16 has been reported in 74% of patients with mucosal melanoma.

Based on immunohistochemistry, it is not possible to distinguish between primary and metastatic melanoma [13]. Based on nodularity and primary submucosal localization, it is possible that malignant melanoma in this study is presented as metastasis. However, since a part of the tumor's surface was necrotic, it cannot be reliably ruled out that the larynx was the primary location.

Despite advancements in therapy modalities, HNMM still remains a rare oncologic condition with a dismal prognosis [12]. Primary mucosal melanoma is associated with an extremely poor prognosis due to its invasive growth and tendency to present at an advanced stage [7, 14]. As an outcome, no categorical treatment strategy was adopted for this entity.

Treatment for mucosal melanoma can include surgery, radiotherapy, chemotherapy and, latterly, target therapy and immunotherapy.

According to the study by Grant-Freemantle et al. [12], distant metastasis and local recurrence are the main contributors to mortality in HNMM. It was found that distant metastasis plays a more prominent role in mortality. The study also showed that survival rates were lower with primary radiotherapy compared to surgery alone, indicating that radiotherapy alone is less effective than surgery alone. However, radiotherapy can be highly effective in achieving long-term local control.

The application of postoperative radiotherapy, including its plan and dose, remains a topic of debate. In a study by Lu et al. [11], which included 288 patients with mucosal melanoma who underwent surgery, radiotherapy did not show an improvement in overall survival or disease-specific survival.

On the other hand, a systematic review conducted by Jarrom et al. [15] that focused on mucosal melanoma in the upper airways system determined that postoperative radiotherapy could enhance locoregional control of the disease. A study by Pincet et al. [2] also showed that primary or adjuvant radiotherapy provides a benefit on local control and overall survival.

The outcomes of recent treatment modalities, such as immunotherapies, have not brought about significant improvements in the prognosis of mucosal melanoma. However, these modalities provide new possibilities for the treatment of inoperable tumors or as adjuvant post-surgery treatments. Despite this, radical surgical procedures remain a fundamental component of mucosal melanoma treatment. It should be noted that targeted mutations vary between cutaneous and mucosal melanoma, which means that the treatment benefits are comparatively lesser. Also, response rates after surgical treatment are lower than those seen in patients with cutaneous melanoma (19% *vs*. 33%) [16, 17].

It is recommended that the initial and most effective treatment for mucosal melanoma is a complete resection with negative margins [16].

Managing mucosal melanoma is an extremely challenging task, and studies have not yet provided a clear statement regarding the role of radiotherapy and novel systemic treatments [17]. A study by Patel et al. [18] found that the only independent predictors of outcome in HNMM are clinical stage at presentation, tumor thickness greater than 5 mm, vascular invasion on histologic examination, and

Table 1. The brief literature review of glottic laryngeal mucosal melanoma in Europe

Cases	Author	Year	Country	Treatment	Follow-up
1	Cremonesi [19]	1956	Italy	Radiotherapy and neck dissection	No details
2	Lorentz [20]	1979	Germany	Partial laryngectomy and radiotherapy	No details
3	Hussain and Whitehead [21]	1989	United Kingdom (UK)	Radiotherapy	No recurrence identified at 24 months follow-up
4	Duwel and Michielssen [22]	1996	Belgium	Total laryngectomy	No details
5	Asare-Owusu et al. [23]	1999	UK	Radiotherapy	No recurrence identified at 24 months follow-up
6	Szmeja et al. [24]	2000	Poland	Total laryngectomy, neck dissection, and radiotherapy	No details
7	**Current case**	**2021**	**Serbia**	**None**	**No details**

the development of distant metastasis. In our case report, delayed presentation made urgency for tracheostomy. Total laryngectomy was advised, but the patient's refusal made the treatment impossible.

So far, literature review revealed only 60 cases of laryngeal melanoma and 18 of them were in glottic subregion [7]. In Europe, there have been six reported melanomas of the glottis, while the last one was recorded more than 20 years ago. Of all these cases, three patients had a combined treatment of radiotherapy and surgical treatment, while another three underwent monotherapy. Only two patients who were treated with radiotherapy attended regular examinations and it was noted that they did not have a recurrence of the disease during the two years follow-up (Table 1). It is evident that there is no categorical strategy for the treatment of these malignancies even in advanced European countries. It is also observed that most patients, four out of six, do not have a recorded history of follow-up after the treatment, just like in our case.

Laryngeal melanoma is a rare condition that may require emergency tracheostomy. Since melanoma can be mistaken for other laryngeal malignancies, immunohistochemical analysis plays a crucial role in making an accurate diagnosis. Early detection of the disease is vital. The recommended first-line treatment is radical surgery followed by postoperative radiotherapy for optimal locoregional control. Despite advances in treatment modalities, laryngeal melanoma still carries a poor prognosis with an exceptionally low five-year overall survival rate.

ACKNOWLEDGMENT

The authors acknowledge support of the Ministry of Science, Technological Development and Innovation of the Republic of Serbia, grant No. 451-03-66/2024-03/200110, subgrant entitled "Development of artificial intelligence models based on the random forest algorithm for the detection of discrete structural changes in the cell nucleus" (head of the subgrant Prof. Igor Pantić).

Conflict of interest: None declared.

REFERENCES

1. Ong CV, Samlowski W. Neoadjuvant ipilimumab plus nivolumab therapy as a potential organ preservation strategy in mucosal melanoma: case report. Front Oncol. 2024;14:1301424. [DOI: 10.3389/fonc.2024.1301424] [PMID: 38549929]
2. Pincet L, Lambercy K, Pasche P, Broome M, Latifyan S, Reinhard A. Mucosal Melanoma of the Head and Neck: A Retrospective Review and Current Opinion. Front Surg. 2021;7:616174. [DOI: 10.3389/fsurg.2020.616174] [PMID: 33585548]
3. López F, Rodrigo JP, Cardesa A, Triantafyllou A, Devaney KO, Mendenhall WM, et al. Update on primary head and neck mucosal melanoma. Head Neck. 2016;38(1):147–55. [DOI: 10.1002/hed.23872] [PMID: 25242350]
4. Suresh S, George N, Janardhan D, George P, Patil S, George CK, et al. Mucosal Melanomas of the Head and Neck—a Tertiary Cancer Centre Experience. Indian Journal of Surgery. 2020;82(4):625–31. [DOI: 10.1007/s12262-020-02082-5]
5. Bezerra Toscano de Mendonça U, Guimarães Soffientini J, Ficher Barbosa V, Cozer K. Mucosal Melanoma of the Head and Neck: From Diagnosis to Treatment. Melanoma. IntechOpen; 2021. [DOI: 10.5772/intechopen.93804]
6. García AM, Parra-Lara LG, Mendoza-Urbano DM, Bravo JC, Zambrano Harvey Á. Survival of patients with mucosal melanoma in Cali, Colombia: a retrospective cohort study. BMC Cancer. 2024;24(1):886. [DOI: 10.1186/s12885-024-12371-x] [PMID: 39044133]
7. Nam YS, Bullock MJ, Forner D, Rigby MH, Corsten M, Trites JRB, et al. A case report: Primary malignant melanoma of the glottic larynx – A very rare entity. Otolaryngology Case Reports. 2023;28:100542. [DOI: 10.1016/j.xocr.2023.100542]
8. Kiong KL, Diaz EM, Gross ND, Diaz EM Jr, Hanna EY. The impact of COVID-19 on head and neck cancer diagnosis and disease extent. Head Neck. 2021;43(6):1890–7. [DOI: 10.1002/hed.26665] [PMID: 33650276]
9. Riera R, Bagattini ÂM, Pacheco RL, Pachito DV, Roitberg F, Ilbawi A. Delays and Disruptions in Cancer Health Care Due to COVID-19 Pandemic: Systematic Review. JCO Glob Oncol 2021;7:311–23. [DOI: 10.1200/GO.20.00639] [PMID: 33617304]
10. Zhou L, Duan M, Huang X. Primary Transglottic Mucosal Melanoma of the Larynx, a Very Rare Entity. American Journal of Biomedical Science & Research. 2020;10(1).AJBSR.MS.ID.001475. [DOI: 10.34297/AJBSR.2020.10.001475]
11. Lu Z, Zhou Y, Nie G, Miao B, Lu Y, Chen T. Prognostic Nomograms for Predicting Overall Survival and Cancer-Specific Survival in Patients with Head and Neck Mucosal Melanoma. Int J Gen Med. 2022;15:2759–71. [DOI: 10.2147/IJGM.S352701] [PMID: 35300129]
12. Grant-Freemantle MC, Lane O'Neill B, Clover AJP. The effectiveness of radiotherapy in the treatment of head and neck mucosal melanoma: Systematic review and meta-analysis. Head Neck. 2021;43(1):323–33. [DOI: 10.1002/hed.26470] [PMID: 32926490]
13. Lourenço SV, Fernandes JD, Hsieh R, Coutinho-Camillo CM, Bologna S, Sangueza M, et al. Head and neck mucosal melanoma: a review. Am J Dermatopathol. 2014;36(7):578–87. [DOI: 10.1097/DAD.0000000000000035] [PMID: 24423929]
14. Falcone R, Verkhovskaia S, Di Pietro FR, Poti G, Samela T, Carbone ML, et al. Primary Mucosal Melanoma: Clinical Experience from a Single Italian Center. Curr Oncol. 2024;31(1):588–97. [DOI: 10.3390/curroncol31010042] [PMID: 38275835]
15. Jarrom D, Paleri V, Kerawala C, Roques T, Bhide S, Newman L, et al. Mucosal melanoma of the upper airways tract mucosal melanoma: A systematic review with meta-analyses of treatment. Head Neck. 2017;39(4):819–25. [DOI: 10.1002/hed.24652] [PMID: 27898196]
16. Mao L, Qi Z, Zhang L, Guo J, Si L. Immunotherapy in Acral and Mucosal Melanoma: Current Status and Future Directions. Front Immunol. 2021;12:680407. [DOI: 10.3389/fimmu.2021.680407] [PMID: 34149718]
17. Yentz S, Lao CD. Immunotherapy for mucosal melanoma. Ann Transl Med. 2019;7(Suppl 3):S118. [DOI: 10.21037/atm.2019.05.62] [PMID: 31576325]
18. Patel SG, Prasad ML, Escrig M, Singh B, Shaha AR, Kraus DH, et al. Primary mucosal malignant melanoma of the head and neck. Head Neck. 2002;24(3):247–57. [DOI: 10.1002/hed.10019] [PMID: 11891956]
19. Cremonesi G. An unusual case of primary melanotic sarcoma of the larynx. Minerva Otorinolaringol. 1956;6(6):333–40. [Article in Italian] [PMID: 13418549]
20. Lorentz E. [Malignant melanoma of the larynx (author's transl)]. HNO. 1979;27(8):275–7. [Article in German] [PMID: 521338]
21. Hussain SS, Whitehead E. Malignant melanoma of the larynx. J Laryngol Otol. 1989;103(5):533–6. [DOI: 10.1017/s0022215100156816] [PMID: 2666540]
22. Duwel V, Michielssen P. Primary malignant melanoma of the larynx. A case report. Acta Otorhinolaryngol Belg. 1996;50(1):47–9. [PMID: 8669272]
23. Asare-Owusu L, Shotton JC, Schofield JB. Adjuvant radiotherapy for primary mucosal malignant melanoma of the larynx. J Laryngol Otol. 1999;113(10):932–4. [DOI: 10.1017/s0022215100145633] [PMID: 10664714]
24. Szmeja Z, Kruk-Zagajewska A, Kaczmarek J, Zieli´nski L, Majewski P. [Primary malignant melanoma of the larynx]. Otolaryngol Pol. 2000;54(2):173–6. [Article in Polish] [PMID: 10961077]

Трансглотични меланом гркљана представљен отежаним дисањем

Светлана Ваљаревић[1,2], Анђелина Јовановић[1,2], Сања Вучић[1], Ана Марија Томић[2,3], Милан Б. Јовановић[1,2]

[1]Клиничко-болнички центар „Земун“, Одељење оториноларингологије са максилофацијалном хирургијом, Београд, Србија;
[2]Универзитет у Београду, Медицински факултет, Београд, Србија;
[3]Универзитет у Београду, Медицински факултет, Институт за патологију, Београд, Србија

САЖЕТАК

Увод Иако је меланом слузокоже главе и врата ретка болест, његова учесталост расте последњих деценија. Најчешћа локализација меланома ларинкса је супраглотис, затим глотис, а главни симптом је промуклост. Због локализације и агресивне природе ове врсте рака, често остаје асимптоматски све док не достигне узнапредовали стадијум болести, што резултира лошом прогнозом.

Приказ болесника Пацијент, стар 45 година, са отежаним дисањем, примљен је у хитну службу. Индиректна ларингоскопија открила је трансглотичну масу која заузима леви пириформни синус и скоро цео улаз у ларинкс, што је довело до изузетно суженог дисајног пута. Урађена је хитна трахеотомија. Контрастном компјутеризованом томографијом врата откривена је улцеропролиферативна маса ларинкса која обухвата супраглотис, глотис и субглотис са сужењем дисајних путева и ширењем у леви пириформни синус. Учињена је и директна ларингоскопија, а биопсијом је потврђен малигни меланом ларинкса. Нажалост, пацијент је одбио даље хируршко и онколошко лечење, као и додатне дијагностичке процедуре. Четири месеца након постављања дијагнозе пацијент је престао да долази на контроле.

Закључак Меланом ларинкса је ретко стање које може захтевати хитну трахеотомију. Пошто се меланом може заменити са другим малигнитетима ларинкса, имунохистохемијска анализа игра кључну улогу у постављању тачне дијагнозе. Рано откривање болести је од виталног значаја.

Кључне речи: меланом; тумор ларинкса; стридор; трахеотомија