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Case Report

Primary Malignant Melanoma of the Esophagus, Surgical Management. Case Report and Literature Review

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Abstract:

More than 100 years after the first record of esophageal melanoma in the literature, made by Baur in 1906, which was finally considered metastasis and not a primary malignant melanoma of the esophagus (MMPE), little is known about this pathology, with no overall 5-year survival rate. At the time of presentation of this case in 2022, the literature recorded approximately 400 cases of primary malignant melanoma of the esophagus, which corresponds to 0.2% of all esophageal neoplasms and, in terms of melanoma presentation sites, it occupies last place 0.5 to 1%, only preceded by anal canal melanoma. With the aim of contributing to the global casuistry, we present this case report of a 59-year-old woman with a primary malignant melanoma of the distal thoracic esophagus, treated at the Antioquia Oncology Center (COA). Envigado, Antioquia, Colombia, in light of the best evidence available in the literature and the scientific technical resources available at the institution.

Key words: melanin; melanocytes; melanosis; melanoma; lymph nodes; cancer; FDG PET-CT

Introduction

Melanoma is defined as a tumour originating in melanocytes, cells that produce melanin (pigment) and nevic cells (proliferation of pigmented cells). Melanoma can arise anywhere in the body, wherever melanocytes are found and by far the skin, it is the place where it most commonly occurs, followed by uveal melanoma, melanoma of the mucous membranes of the head and neck, digestive tract and genitourinary mucosa [1,2]. In all these locations, although they share the name of malignant melanoma (cancer, due to its local infiltrative capacity, potential lymphatic lymphatic dissemination, and distant metastatic hematogenous lymphatic dissemination), they are different entities from their neoplastic genesis, risk factors, biological behavior, management, and prognosis [3]. Although the mucous membranes can be the site of metastasis of skin melanoma, the epithelium of the mucous membranes can also be the primary origin of melanoma, despite the low melanin that originates in it. ***Primary malignant melanoma of the mucosa of the aero-digestive tract*** is rare, as opposed to the large extension of the hollow viscera and there is only a grouping of the most commonly reported locations, melanoma of the anal, rectal and esophageal canal, which represent 0.5 to 2.0% of all melanomas in the body, and increasingly, they cease to be anecdotal [4].

The **mucosa of the esophagus** is made up of a non-keratinized stratified squamous epithelium, which rests on a basement membrane that separates it from the lamina propria, rich in lymphoid cells. De La Pava and later Ohashi, demonstrated the presence of melanocytes in the esophageal mucosa, in up to 8% of the population studied [5,6]. **Melanocytosis** or **melanosis** (areas of pigmentation) of the esophageal mucosa is a benign condition, due to the increase of melanin granules in the cytoplasm of the melanocyte of the basement membrane, also considered a precursor lesion of malignancy in 30% of cases. In ***primary malignant melanoma of the esophagus (MMPE)*** the cellular behavior of malignancy is evident, atypia, cellular, promising nucleoli and increased mitosis [7]. The

incidence of **MMPE** is 0.0036 cases per million population, 0.1%-0.2% of all esophageal neoplasms [8,9]. The prognosis of MMPE is generally poor, with no overall survival of more than 5 years due to high regional lymph node involvement and distant metastatic 80% and 40%, respectively, at diagnosis [10].

The symptoms for **MMPE** are similar to those of benign conditions, gastroesophageal reflux, esophagitis, and less similar to dysphagia generated by squamous cell tumors and adenocarcinomas, in which endoluminal growth since its debut, requires upper gastrointestinal endoscopy and tumor identification; therefore, in the case of MMPE, its endoscopic identification is usually due to incidental findings of hyperpigmented lesions. in the esophageal lumen, which alert to suspicion [11, 12].

The sensitivity of endoscopic biopsies reaches 80% for the histological confirmation of MMPE, and is underdiagnosed in 15%, confusing it with a poorly differentiated carcinoma of the esophagus, especially cases of amelanocytic melanoma, which are approximately 26.9% of cases. This makes immunohistochemistry, S100, HMB-45, SOX 10 and Melan-A markers essential. The **diagnostic criteria** for primary melanoma of the esophagus are histological and clinical demonstration and the impossibility of demonstrating another possible site of primary melanoma, ahead in frequency [13, 14].

Case Presentation

A 59-year-old female, resident of Medellín, Fibromyalgia as the only personal history and pancreatic cancer in the mother as a family history. Consultation for epigastralgia and heartburn of a year and a half of evolution, without weight loss, the **esophagus-gastro-duodenoscopy** evidences, in the esophageal mucosa a longitudinal hyperpigmented macula at 30 cm from the dental arch, which extends up to 32 cm, with areas that become discretely raised, without significant decrease in esophageal lumen, very suggestive of melanoma. The biopsy report indicates a melanocytic lesion suspicious of melanoma; positive HMB-45, MELAN-A, SOX-10 immunohistochemistry stains confirm this.

Endoscopic ultrasonography **(EUS)** reports extensive melanocytic elevated lesion in the distal esophagus, with involvement of 50% of the circumference and 20% of the lumen; in ultrasound vision, hypoechogenic lesion involving from the second echolayer (muscularis mucosa) to the fourth echolayer (muscularis propria) contacting the adventitia in a central segment, without calcifications or cystic degeneration, measuring 12 x 6 mm with a length of 20 mm and with the presence of a 6.4 mm aortic lymph node; considering advanced neoplasm of the distal esophagus compatible with primary esophageal melanoma uT3-uN0-umM.

CT-FDG PET (positron emission tomography with fluorodeoxyglucose) showed hypermetabolic thickening, in the distal third of the esophagus with 4.5 SUVmax (units of metabolic value), without extraesophageal extension, lymph node or other distant hypermetabolic lesions.

The patient's general conditions are good, with ECOG 0 (*Eastern Cooperative Oncology Group*) non-smoking, sedentary, with a body mass index (BMI) of 23 kg/m2, good nutritional status. Thus, meeting criteria of resectability and operability for radical esophagectomy and gastric ascent, using the **Mc Kewon technique** (abdominal-thoracic and cervical approach) [8].

In the first instance, the thoracic time approach is performed by right thoracoscopy with the intention of ruling out advanced unresectable or metastatic disease that may be underdiagnosed by imaging. We continued with a careful dissection of the esophagus in the posterior mediastinum, for which we sectioned the azygos vein prior to its entry into the inferior vena cava, using mechanical suture. Dissection also helps identify and preserve the chest duct. With this, we achieve ease for non-traumatic removal of the esophagus, minimize the risk of chylose fistula, in addition to preparing the space in the posterior mediastinum for gastric ascent, when the abdominal and cervical approach is continued. We continued with the mediastinal emptying of the at-risk lymph node stations, 2R – 4R – 3P – 3A – 7- 8 – 9R and 10R. (Figure 1-4).

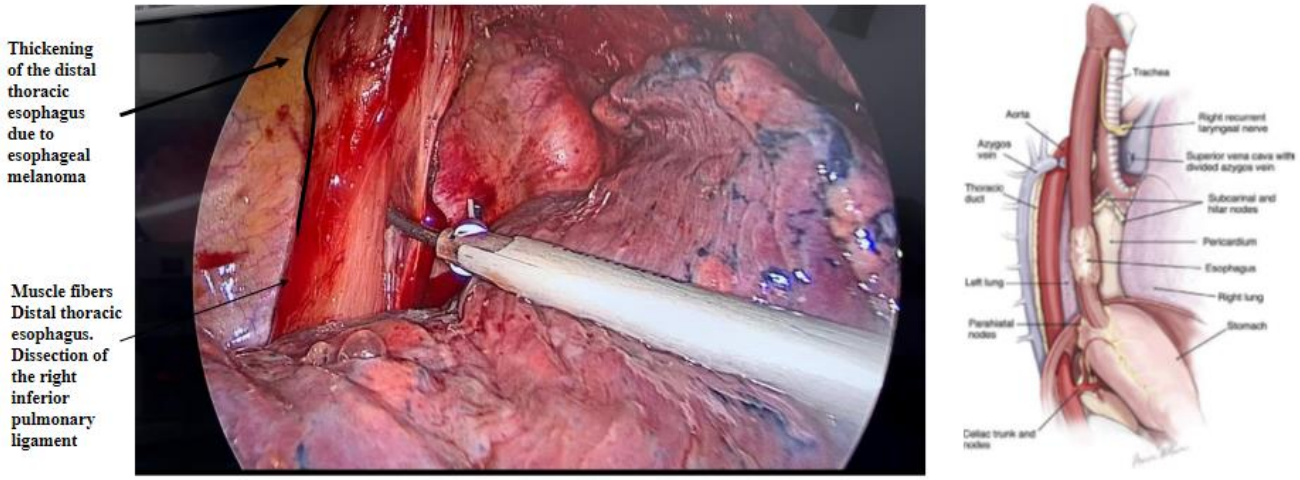

Figure 1. Thoracic time of esophagectomy. The left photograph shows right thoracoscopy, esophageal exposure and dissection in the posterior mediastinum. On the right illustration for the anatomical correlation taken from adult chest surgery second edition. David J. Sugarbaker. 2015.

Photographic archive. **Centro Oncológico de Antioquia. (COA)**

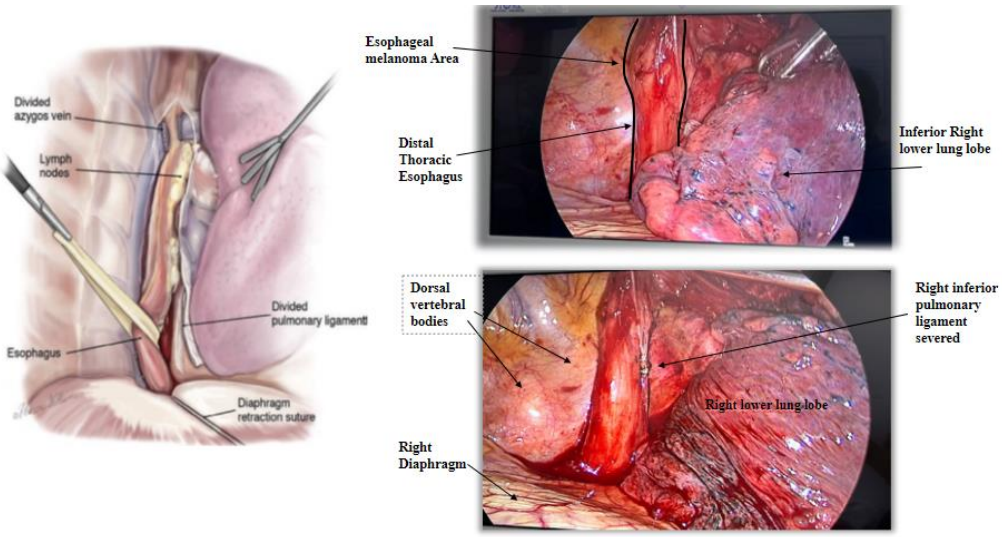

Figure 2. Thoracic time of esophagectomy. The photographs on the left, right thoracoscopy view, esophageal exposure and dissection. Photo archive. On the right, illustration for the anatomical correlation taken from adult chest surgery second edition. David J. Sugarbaker. 2015.

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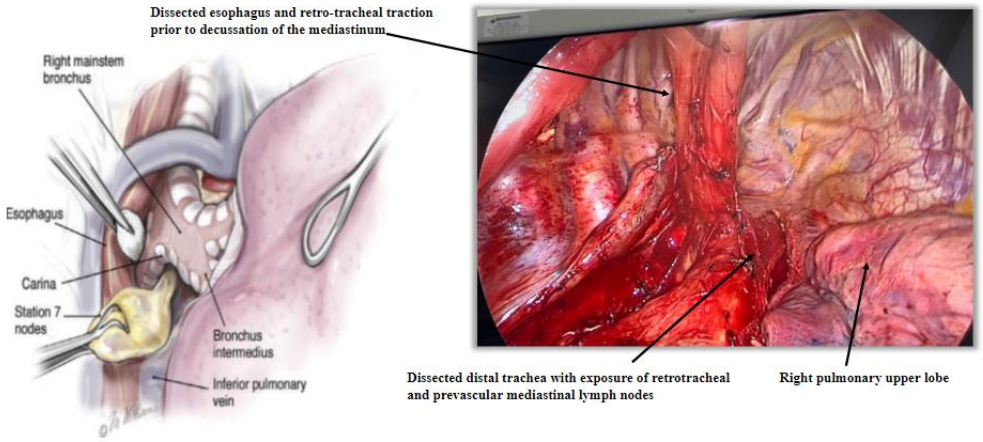

Figure 3. Thoracic time of esophagectomy. The photograph on the right shows right thoracoscopy, exposure and dissection of the upper mediastinal esophagus with exposure of mediastinal lymph nodes, prevascular and retrotracheal stations. On the left, illustration for the anatomical correlation taken from adult chest surgery second edition. David J. Sugarbaker. 2015.

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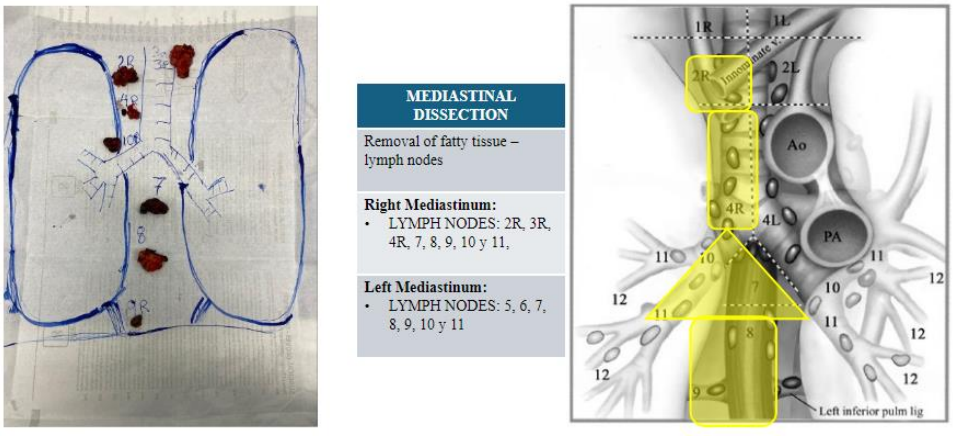

Figure 4. Thoracic time of esophagectomy. The photograph on the right shows the systematic mediastinal emptying performed for the patient. It is illustrated on paper and sent with these references to the pathology laboratory. On the left, representation of the gaglionic stations at risk and emptying target for esophageal melanoma. Taken from Thoracic Surgery in Adults Second Edition. David J. Sugarbaker. 2015.

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The second surgical stage was advanced via laparotomy for the gastric tube. The "tubulization" of the stomach is made with the greater curvature, making gastric section from proximal, at the level of the gastric fundus below the cardia, to guarantee greater length of the gastric tube, while providing safe margins on the gastroesophageal junction. The irrigation of the new gastric tube with the right and left gastroepiploic artery is guaranteed by extreme care of the greater omentum and preservation of the small gastric vessels at the level of the angularis incisure, for the gastric antrum coming from the right gastric artery. (Figures 5 and 6).

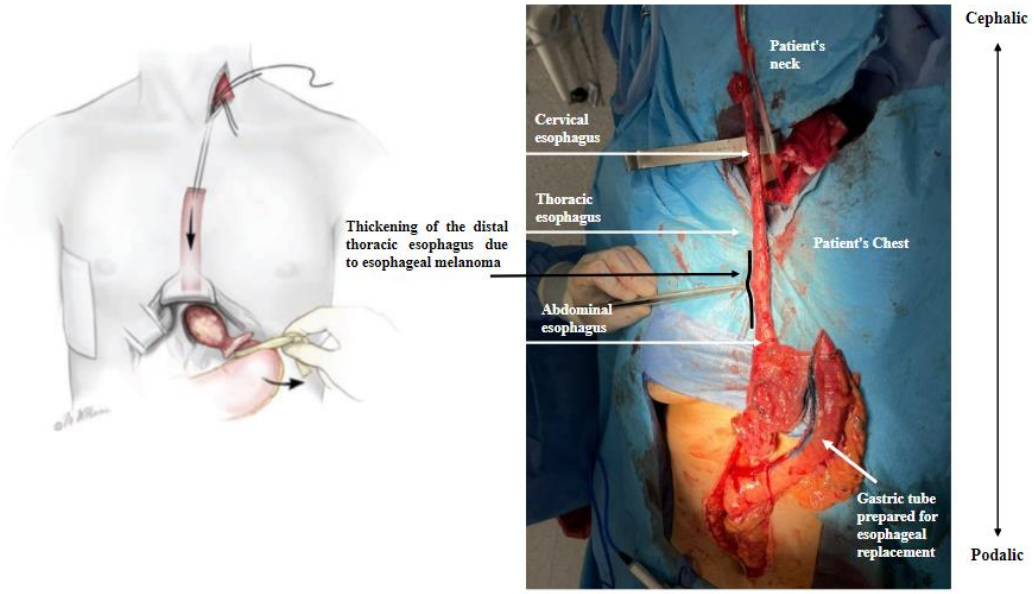

Figure 5. The photograph on the right shows the patient's triple approach, cervical, thoracic and abdominal, to control the same portions of the esophagus, removing the esophagus via the abdomen once mediastinal and cervical release has been achieved. On the left, illustration for the anatomical correlation taken from adult chest surgery second edition. David J. Sugarbaker. 2015.

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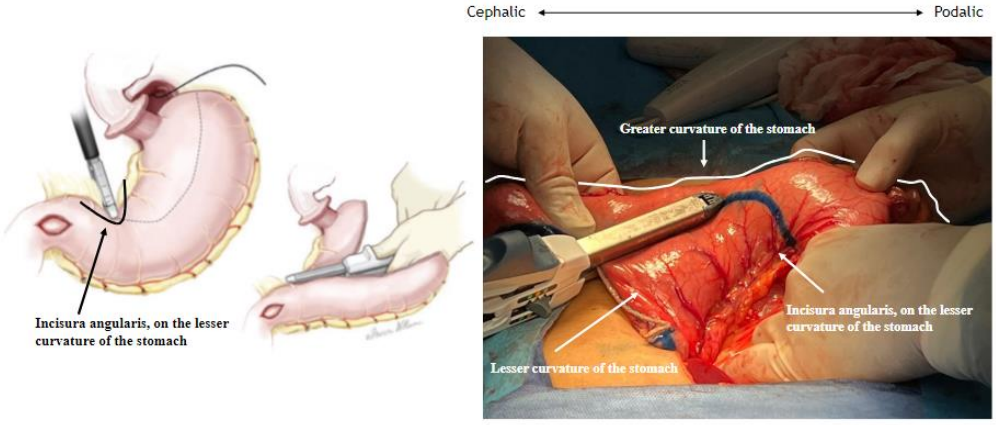

Figure 6. In the photograph on the right, creation of the gastric tube, through "tubulization" of the stomach with the greater curvature. Irrigation of the new gastric tube with the left gastroepiploic tube is guaranteed, for the ascent and replacement of the esophagus. The white dotted line exposes all the use of the greater curvature of the stomach to gain greater length. The illustration on the left shows how the section recommends from proximal, immediately after the gastroesophageal junction, note how to be careful with the preservation of gastric vessels at the level of the incisura angularis to preserve irrigation. Taken from adult chest surgery second edition. David J. Sugarbaker. 2015.

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By means of a left cervicotomy, the cervical esophagus is exposed, here we make a section of the esophagus, and we tie a long thread that serves as a guide for the removal of the esophagus via the abdomen and also for the ascent of the gastric tube through its traction, again via cervical. We performed a terminus-lateral anastomosis of the gastric esophagus, at the level of the neck with manual suturing and left a cervical drain. (Figure 7).

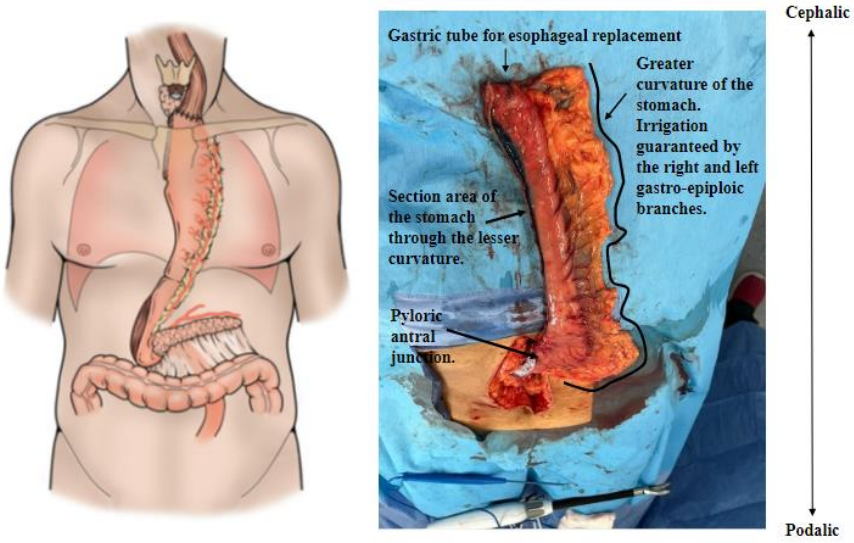

Figure 7. In the photograph on the right, gastric tube, "neoesophagus". Note the prioritization and extreme care of the omentum that protects the greater curvature of the stomach and with it the right and left gastro-epilois that guarantees irrigation. In our team we omitted piloproplastica on the left correlation of gastric rise. Illustration taken from Operative Thoracic Surgery. Edited by Larry R Kaiser MD. FIFTH EDITION. 2006 Edward Arnold (Publishers).

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The total surgical time was 3 hours with estimated bleeding of 500cc without complications. He did not require red blood cell transfusion or vasopressor support. The time for monopulmonary ventilation was 45 minutes, immediate postoperative extubation, clinical surveillance in the intensive care unit, early initiation of peripheral parenteral nutrition (PPN) and assisted early ambulation. On the fourth postoperative day, a chest CT scan, with esophageal protocol, routinely, ruled out mediastinal anastomotic leakage, pleural or pulmonary complication. She started a liquid diet with tolerance and removal of the right chest tube.

On the eighth postoperative day, the patient presented tachycardia, signs of deep surgical site infection (ISO) in the neck, due to pus leaking from the left cervical drain, empirical antibiotic therapy was initiated, oral treatment was suspended, and the nutritional intake was continued by total parenteral (TPN). The elevated amylase in the drain confirms saliva, concluding low-output cervical esophageal anastomotic fistula, we continued conservative management, consisting of cervical drain fistula cannulation, broad-spectrum antibiotic therapy and exclusive TPN. Two weeks after the diagnosis of the fistula, its production ceased, a liquefied diet began, TPN was dismantled and he was discharged on the 26th postoperative day.

The **pathology report** identifies involvement by invasive melanoma, epithelioid type (mucosal melanoma). Tumor size of 3 x 1 cm, without ulceration, invading up to the submucosa, with high mitotic activity, with up to 38 mitoses in 10 fields of high magnification, no perineural invasion, no lymphovascular invasion, no necrosis, no intratumoral lymphocytes, no satelitosis. Resection margins were negative and wide

proximal, distal and radial to more than 3.5 cm. Associated melanoma in situ was found. In lymph node dissection, 27 lymph nodes were identified, 3 of them with metastatic involvement, two in the right cardial station and one in the minor curvature. The largest nodal tumor deposit was 6 mm, with extra-nodal extension present, of 3 mm. Immunohistochemistry S-100, HMB-45, Melan-A, SOX-10 were positive. Non-mutated BRAF biological profile. (Figure 8-10).

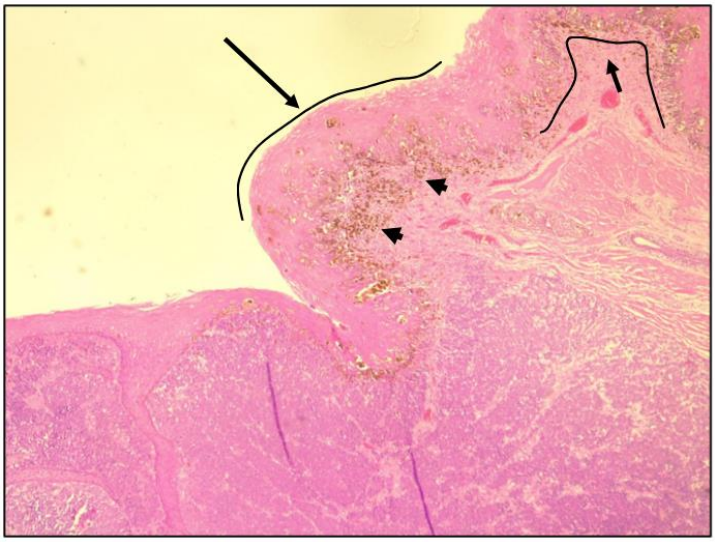

Figure 8. Hematoxylin and eosin staining. Cut at 100x.

Esophageal mucosa with preserved squamous lining long arrow and lamina propria (short arrow). Mucosa and submucosa occupied by cells with intracytoplasmic melanocytic pigment (arrowhead). Photographic archive. **Centro Oncológico de Antioquia. (COA)**

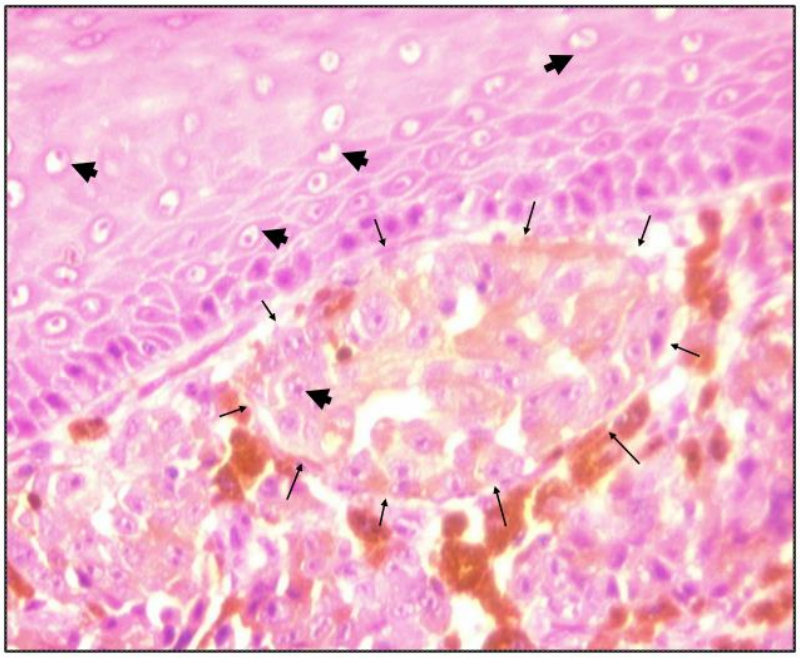

Figure 9. Hematoxylin and eosin staining, section at 400x.

Neoplastic cells forming nests (circled by arrows) with increased mitotic activity and protruding nucleoli (arrowheads). Photographic archive. **Centro Oncológico de Antioquia. (COA)**

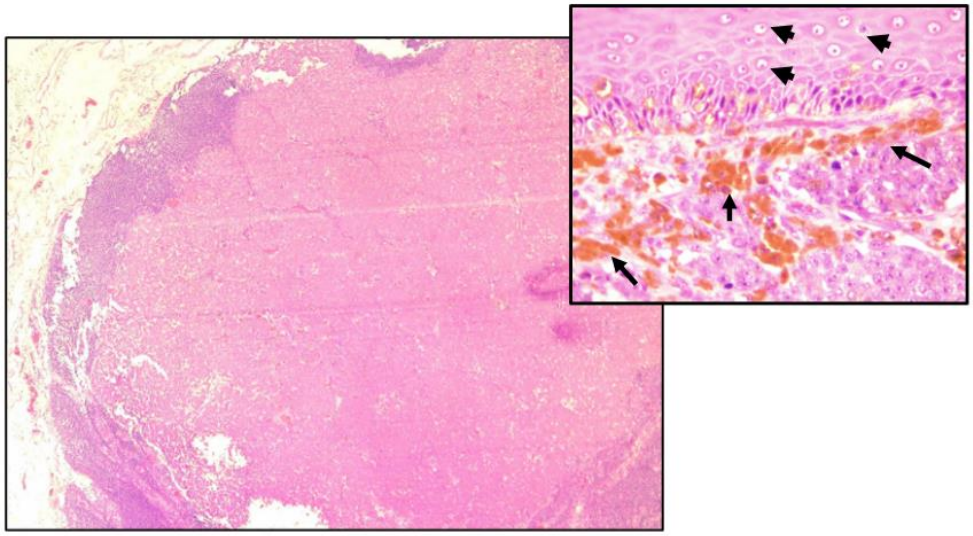

Figure 10. Hematoxylin and eosin staining of section of lymph node involved by melanoma at 100x and magnification at 400x. Cells with polygonal epithelioid morphology with prominent nucleoli, mitosis (arrowhead) and intracytoplasmic melanin pigment (arrow).

Photographic archive. **Centro Oncológico de Antioquia. (COA)**

In the third postoperative month, the patient was evaluated by clinical oncology, considering him outside the therapeutic window for the initiation of adjuvant, which only provided discreet results and opted for clinical surveillance. The patient was admitted to the emergency room in the fifth postoperative month with resting dyspnea and heartburn. In upper **gastrointestinal endoscopy**, a wide esophagogastric anastomosis with suture material was found at 17 cm of the dental arch, with no evidence of endoluminal lesions. In the proximal third of the body of the gastric tube there are 2 submucosal hyperpigmented lesions of 4mm 5mm. Biopsies are taken, which report melanosis, and malignant melanoma is ruled out. (Figure 11). At the sixth postoperative month, he was admitted to the emergency room with medium-exertion dyspnea. Chest CT scans identified carcinomatous pulmonary lymphangitic dissemination. He did not initiate specific palliative oncological management and died in the seventh month postoperatively.

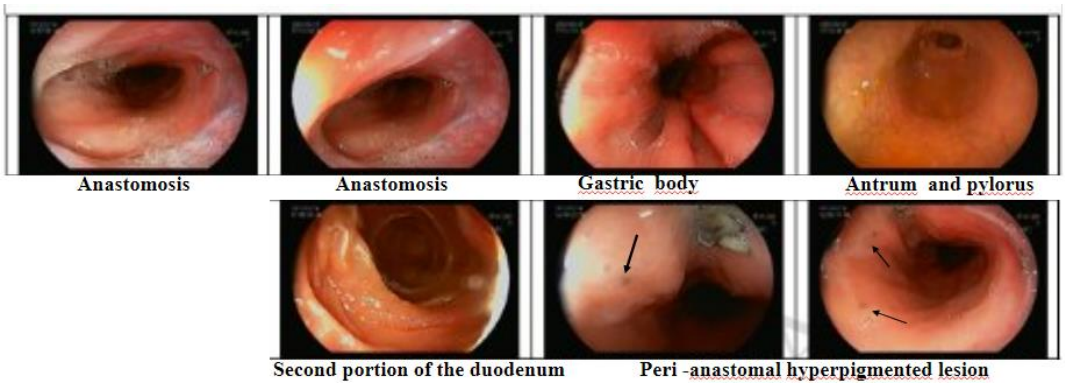

Figure 11. Upper gastrointestinal endoscopy, 5 months after esophagectomy and gastric ascent. Two 4mm or 5mm hyperpigmented lesions are identified on the proximal mucosa of the gastric tube (arrows).

Photographic archive. **Centro Oncológico de Antióquia. (COA)**

Discussion:

We bring to discussion some factors that make **MMPE** (Primary Malignant Melanoma of the Esophagus) a disease with a poor short-term prognosis and on which we can act in search of better results. On the one hand, the lack of serosa in the esophagus, the copious network of lymphatic channels and the behavior of the melanoma cell leads to an incidence of up to 60% of regional lymph node involvement, from superficial invasion into the esophageal mucosa [15]. In our clinical case, we found this behavior, where the depth of the melanoma reached only the submucosa and presented three lymph nodes involved out of 27 harvested, in the lymphadenectomy that accompanied the radical esophagectomy. Despite the proven value of **PET-CT-FDG (Positron Emission Tomography with Fluorodeoxyguse)** for the rule out of distant lymph node and metastatic disease, given the avidity of the melanoma cell by FDG; [16] In our case, the PET CT with FDG showed no evidence of hypermetabolic lymph nodes or alteration in their morphology. The group of authors of this review consider that its limitation to presume preoperative regional lymph node involvement lies in the small size of the melanoma cell, and the low nodal tumor volume, which do not alter the morphology of the lymph node or produce increased metabolic activity [17]. On the other hand, the **EUS (endoscopic ultrasonography)** [18], did not come close to the correct staging of tumor size, nor preoperative lymph node, which I consider uT3uN0.

In **histological evaluation**, criteria such as the associated instu component, in proximity to mucosal invasive melanoma, radial pattern of mixed epithelioid and fusiform growth, guide the consideration of primary malignant melanoma of the esophagus [19-21]. **Immunohistochemistry stains** are conjunctural for diagnosis; Protein S-100, HMB-45, Melan-A, SOX-10 were positive, confirming melanoma and ruling out the presence of squamous cell carcinoma, adenocarcinoma, or poorly differentiated neuroendocrine tumors, and especially useful in cases of amelanic melanoma [22]. S-100 overexpression, as well as in cutaneous melanoma, provides a poor prognosis factor. In our case, 38 mitoses were identified by 10 high-power fields; Another independent adverse prognostic factor [23-25]. The absence of BRAF mutation eliminates a therapy option for this molecular target [26].

Lymph node involvement, apart from staging, is the most important independent adverse prognostic factor in non-metastatic disease. In mucosal melanoma of the digestive tract, radical lymphadenectomy has a low impact in terms of **overall survival (OS)** [8,27,28] and may offer unacceptable morbidity, especially in anorectal melanoma.29 Wang's retrospective analysis [12]. of 76 patients with surgical management of MMPE, with **periesophageal, mediastinal and celiac axis lymphadenectomy**, identified lymph node involvement in 66% of patients, not demonstrated preoperatively; which brings us back to the consideration of initial clinical substratification in most cases. We perform periesophageal, mediastinal and perigastric lymphadenectomy; 3 of 26 lymph nodes were involved by tumor. Lymphadenectomy did not leave sequelae such as chylose fistula, nor pleural, pulmonary or mediastinal morbidity. The patient in our clinical case died seven months after surgery, due to pulmonary metastatic recurrence with lymphangitic dissemination, corroborating the low impact of lymphadenectomy on OS. What lymphadenectomy did help with was knowing the real lymph node involvement that allowed better staging, prognosis and indication of postoperative adjuvant. In our practice of esophageal surgery, we do not routinely perform thoracic duct ligation, but we do section of the azygos vein and careful mediastinal dissection, thoracic route, under direct vision, which has decreased, the occurrence of **chylous fistula** or **chylothorax** that can cause blind traumatic dissection of the esophagus, when only the transhiatal and cervical Orringer route is implemented [30-32]. As for the dreaded **anastomotic fistula** [33], in our institutional experience, it has been partial undone, without severe clinical repercussions and its control is achieved with conservative measures or endoscopically placed stent requirements.

The **final pathological staging** of esophageal melanoma represented a serious dilemma. If we use the **TNM (Tumor, Nodes, Metastatases)** for esophageal cancer, we would have for our case, a pT1b (by invasion to the submucosa) N2 (metastasis in three-six lymph nodes) M0. Clinical stage IIIB, if it was squamous cell carcinoma and IVA if it was adenocarcinoma [34]. But clearly, because it is melanoma, it does not apply. The most approximate staging, in terms of its poor prognosis, is that offered **by TNM for mucosal melanoma of the head and neck** [35] which starts from pT3 (mucosal tumors or in the immediately underlying tissue) N0 without lymph node disease and N1 if there is lymph node involvement, without taking the number of nodes involved. With the latter, our patient had a clinical stage IVA (pT3N1M0). It should not be forgotten that the TNM of melanoma of the mucosa of the head and neck only takes into account the locations, oral cavity, pharynx and larynx, excluding the esophagus,36 again leaving a void for the correct staging of the **MMPE.**

The **postoperative adjuvant strategy** is a priority, despite its low results. The publication of Sabanathan in 1989 [11]. reported an overall survival of 10 months and Gao in 2016 [37]. Almost 30 years apart, he continued to show poor results, with an OS of 18.1 months, with postoperative chemotherapy schemes, dacacarbazine, nimustine, vincristine, cisplatin, and interferon. The action on the known molecular targets in melanoma has not been superior in melanoma of the mucosa and digestive tract either; oncogenic mutations such as **BRAF** (serine/threonine). **NRAS** (neuroblastoma RAS viral oncogene) and **KIT** (tyrosine protein kinase), present in up to 30% of patients with cutaneous melanoma, are only found in less than 5% of mucosal melanoma [38, 39]. **Immunotherapy** seems to have better results and show promise, check point inhibitors on cytotoxic T lymphocyte-associated protein 4 (**CTLA-4**; ipilimumab and

tramelimumab), those that act on the programmed cell death receptor (**PD-1**; nivolumab and pembrolizumab) and those targeting programmed cell death ligand 1 (**PD-L1**; atezolizumab, avelumab, and durvalumab) [40]. The work of Hamid et al., on the efficacy of pembrolizumab as monotherapy in patients with advanced mucosal melanoma, showed a median overall survival of 11 months and the objective response rate was 22%. [40, 41] Our patient in the clinical case did not receive specific adjuvant oncological management in the postoperative period or as palliative oncological management at the diagnosis of pulmonary metastatic relapse. Something similar is found in Schizas' systematic review [42]. Out of 91 patients with MMPE, 85 (91%) underwent radical esophagectomy and only 22.1% of the patients managed to arrive in adequate conditions for adjuvant management. The median time to recurrence was six months, and disease-specific mortality was 43%.

Conclusion:

Along with the diagnosis, defining the clinical stage of primary malignant melanoma of the esophagus (**MMPE),** establishing prognosis and the indicated management of this rare pathology, expose the need for these case reports that open the discussion on what is known and add to future systematic reviews. For the time being, the best available evidence should be used, local surgical oncological control, esophagectomy and regional lymphadenectomy, followed by rapid postoperative nutritional and pulmonary rehabilitation, and the patient should be taken to adjuvant with immunotherapy.

References:

1. Cheng L, Guo ZY, Lei L, Wang WX, Xu CW, Fang MY. (2020). Treatment and prognosis of primary malignant melanoma of the esophagus. *Transl Cancer Res*; 9(7):4141-4147.
2. Siegel RL, Miller KD, Jemal A. (2016). Cancer statistics, 2016. *CA Cáncer J Clin* 2016; 66:7-30.
3. Kibbi N, Kluger H, Choi JN. (2016). Melanoma: Clinical Presentations. *Cancer Treat Res*; 167:107-129.
4. Mihajlovic M, Vlajkovic S, Jovanovic P, Stefanovic V. (2012). Primary mucosa melanomas: a comprehensive review. *Int J Clin Exp Pathol* ; 5:739- 753.
5. De La Pava S, Nigogosyan G, Pickren JW, Cabrera A. (1963). Melanosis of the esophagus. *Cancer*; 16:48-50
6. Ohashi K, Kato Y, Kanno J, Kasuga T. (1990). Melanocytes and melanosis of the oesophagus in Japanese subjects--analysis of factors eff ecting their increase. *Virchows Arch A Pathol Anat Histopathol*; 417(2):137-143.
7. Lohmann CM, Hwu WJ, Iversen K, Jungbluth AA, Busam KJ. (2003). Primary malignant melanoma of the oesophagus: a clinical and pathological study with emphasis on the immunophenotype of the tumours for melanocyte diff erentiation markers and cancer/testis antigens. Melanoma Res; 13(6):595-601.
8. Wang S, Tachimori Y, Hokamura N, Igaki H, Kishino T, Kushima R. (2013). Diagnosis and surgical outcomes for primary malignant melanoma of the esophagus: a single-center experience. *Ann Th orac Surg*; 96(3):1002-1006
9. Westwood DA, Macemon JB, Coulter GN, ChalmersWatson TA, Roberts RH. (2011). Primary oesophageal malignant melanoma. *J Gastrointest Surg Off J Soc Surg Aliment Tract*; 15(7):1286-1288
10. Li B, Lei W, Shao K, Zhang C, Chen Z, Shi S, et al. (2007). Characteristics and prognosis o fprimary malignant melanoma of the esophagus. *Melanoma Res*; 17(4):239-242.
11. Sabanathan S, Eng J, Pradhan GN. (1989). Primary malignant melanoma of the esophagus. *Am J Gastroenterol*; 84(12):1475-1481.
12. Wang X, Kong Y, Chi Z, et al. (2019). Primary malignant melanoma of the esophagus: A retrospective analysis of clinical features, management, and survival of 76 patients. *Thorac Cancer*; 10:950-956.
13. Joob AW, Haines GK 3rd, Kies MS, Shields TW. (1995). Primary malignant melanoma of the esophagus. *Ann Th orac Surg*; 60(1):217-222
14. Tacastacas JD, Bray J, Cohen YK, et al. (2014). Update on primary mucosal melanoma. *J Am Acad Dermatol*; 71:366-375.
15. Schwimmer J, Essner R, Patel A, Jahan SA, Shepherd JE, Park K, et al. (2000). A review of the literature for whole-body FDG PET in the management of patients with melanoma. Q J Nucl Med Off Publ Ital Assoc *Nucl Med AIMN Int Assoc Radiopharmacol IAR*; 44(2):153-167.
16. Charu Jora, Promila Pankaj, Ritu Verma, Anjali Jain, Ethel S. Belho. (2015). Department of Nuclear Medicine and PET/CT, Mahajan Imaging Centre, Sir Ganga Ram Hospital, New Delhi, India. Primary malignant melanoma of the esophagus. *Indian Journal of Nuclear Medicine* Vol. 30: Issue 2April-June.
17. Jiaqi Zeng, Lin Zhu, Guanzhou Zhou, Fei Pan, Yunsheng Yang. (2023). Prognostic models based on lymph node density for primary gastrointestinal melanoma: a SEER population-based analysis. *BMJ Open*. oct 5; 13(10): e073335.
18. La Selva D, Kozarek RA, Dorer RK, et al., (2020). Primary and metastatic Melanoma of the GI tract: clinical presentation, endoscopic findings, and patient outcomes. *Surg Endosc*; 34:4456–4462.
19. Allen AC, Spitz S. (1953). Maglignant melanoma. A clinicopathological analysis of the criteria for diagnosis and prognosis. Cancer; 6:1-45.
20. Boni L Benevento A, Dionigi G, et al. (2002). Primary malignant melanoma of esophagus: *A case report surg endosc*; 16:359.360.
21. Laura Granel – Villach, et al. (2016). Primary esophageal melanoma: a case description. *Spanish Journal of Digestive Diseases*. Vol 108 N° 10. Pp 666-669.
22. Bisceglia M, Perri F, Tucci A et al. (2011). Primary malignant melanoma of the esophagus: a clinicopathologic study of a case with comprehensive literature review. *Adv Anat Pathol*; 18: 235–252.
23. Uetsuka H, Naomoto Y, Fujiwara T. (2004). Primary malignant melanoma of the esophagus: long-term survival following preand postoperative adjuvant hormone/chemotherapy. *Dig Dis Sci*; 49: 1646–1651.
24. Nagore E, Oliver V, Botella-Estrada R, et al. (2005). Prognostic factors in localized invasive cutaneous melanoma: high value of mitotic rate, vascular invasion and microscopic satellitosis. *Melanoma Res*; 15:169-177.
25. Barnhill RL, Katzen J, Spatz A, et al. (2005). The importance of mitotic rate as a prognostic factor for localized cutaneous melanoma. *J Cutan Pathol*; 32:268-273.
26. Francken AB, Shaw HM, Thompson JF, et al. (2004). The prognostic importance of tumor mitotic rate confirmed in 1317 patients with primary cutaneous melanoma and long follow-up. *Ann Surg Oncol*; 11:426-433.
27. Xu X, Chen L, Guerry D, et al. (2012). Lymphatic invasion is independently prognostic of metastasis in primary cutaneous melanoma. *Clin Cancer Res*; 18:229-237.
28. Volpin E, Sauvanet A, Couvelard A, Belghiti J. Primary malignant melanoma of the esophagus: a case report and review of the literature. *Dis Esophagus*; 15: 244–249.
29. Ciarrocchi A, Pietroletti R, Carlei F, et al., (2017). Extensive surgery and Lymphadenectomy do not improve survival in primary Melanoma of the Anorectum: results from analysis of a large database (SEER). *Colorectal Dis*; 19:158–164.
30. Nicola Martucci, MD, Maura Tracey, RN, Gaetano Rocco. (2015). Postoperative Chylothorax. *Thorac Surg Clin* 25,523–528.

31. Janani S. Reisenauer. Et al. (2018). Treatment of Postsurgical Chylothorax. *Ann Thorac Surg*; 105:254–262.
32. Mark B. Orringer. (2005). Transhiatal Esophagectomy without Thoracotomy. Operative Techniques in thoracic and cardiovascular surgery. *Elsevier*; 1522-2942/05.
33. Braghetto M. I, Figueroa G. M, Sanhueza P. B, Valladares H. H, Cardemil H. G, Cortés L. S, et al. (2018). Oncological evolution and prognosis of esophageal anastomotic fistulas in the treatment of esophageal cancer. Comparative study according to gastric tube ascent route. *Chilean Journal of Surgery*. 70(1):19-26.
34. Thomas W. Rice. et al. (2017). 8th edition AJCC/UICC staging of cancers of the esophagus and esophagogastric junction: application to clinical practice. *Ann Cardiothorac Surg*; 6(2):119-130.
35. Amin M, Edge S, Greene F, et al. (2017). TNM system staging for Mucosa Melanoma of the head and neck. *AJCC Cancer Staging Manual 8th ed. New York*: *Springer*.
36. Haiyan Sun. Et al. (2022). Clinicopathological Features, Staging Classification, and Clinical Outcomes of Esophageal Melanoma: Evaluation of a Pooled Case Series. *Front. Oncol*., Volume 12.
37. Gao S, Li J, Feng X, Shi S, He J. (2016). Characteristics and surgical outcomes for primary malignant melanoma of the Esophagus. *Sci Rep*; 6: 23804.
38. Badakhshi H, Wang Z-M, Li R-J, et al. (2021). Survival and Prognostic Nomogram for primary gastrointestinal Melanoma (PGIM): A population-based study. *Anticancer Res*; 41:967–974.
39. Kohoutova D, Worku D, Aziz H, et al. (2021). Malignant Melanoma of the gastrointestinal tract: symptoms, diagnosis, and current treatment options. Cells; 10:327. 10.3390/cells10020327
40. Hamid, O.; Robert, C.; Ribas, A.; Hodi, F.S.; Walpole, E.et al. (2018). Antitumour activity of pembrolizumab inadvanced mucosal melanoma: A post-hoc analysis of KEYNOTE-001, 002, 006. *Br. J. Cancer*, 119, 670–674
41. Apolle R, Rehm M, Bortfeld T, Baumann M, Troost E G C. (2017). The clinical target volume in lung, head-and-neck, and esophageal cancer: lessons from pathological measurement and recurrence analysis. *Clin Transl Radiat Oncol*; 21(3): 1–8
42. D. Schizas, K. S. Mylonas, G. Bagias, A. Mastoraki, M. Ioannidi, P. Kanavidis, N. Hasemaki, I. Karavokyros, D. Theodorou, T. Liakakos. (2019). Esophageal melanoma: a systematic review and exploratory recurrence and survival analysis. *Diseases of the Esophagus* 32,1–9

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