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Esophageal Squamous Cell Carcinoma Masquerading as Achalasia: A Case Report on Diagnostic Pitfalls and Therapeutic Strategies

Renata Timoty Pasaribu[1*], I Gde Ardika Nuaba[1], I Ketut Suanda[1], Ida Ayu Alit Widiantari[1], I Wayan Lolik Lesmana[1]

[1]Department of Otorhinolaryngology and Head/Neck Surgery, Faculty of Medicine, Universitas Udayana/Prof. Dr. I.G.N.G. Ngoerah General Hospital, Denpasar, Indonesia

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***Corresponding author:**
Renata Timoty Pasaribu

E-mail address:
timotypasaribu@yahoo.co.id

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A B S T R A C T

Esophageal squamous cell carcinoma (SCC) is an aggressive malignancy often diagnosed at an advanced stage, leading to a poor prognosis. Its initial symptoms can be nonspecific, occasionally mimicking benign esophageal disorders such as achalasia, thereby posing significant diagnostic challenges. This report details such a case, emphasizing the diagnostic pitfalls and discussing therapeutic approaches. A 43-year-old male presented with a 5-month history of progressive dysphagia and odynophagia, initially suspected to be achalasia. Clinical findings, including significant weight loss and specific laboratory abnormalities, are detailed. Esophagogastroduodenoscopy revealed an obstructing tumor, confirmed as esophageal SCC by biopsy. Staging investigations, including Multi-Slice Computed Tomography (MSCT), characterized the disease as Stage IVA (T4N1M0). The patient underwent feeding gastrostomy for nutritional support and commenced systemic chemotherapy with docetaxel, carboplatin, and cetuximab. The treatment course and initial follow-up are described. In conclusion, this case underscores the critical importance of maintaining a high index of suspicion for malignancy in patients presenting with symptoms suggestive of achalasia, especially if accompanied by atypical features or risk factors. A meticulous and timely diagnostic evaluation, incorporating early endoscopy and biopsy, is paramount for accurate diagnosis and staging. Multidisciplinary management, including robust nutritional support and carefully selected systemic therapy, remains central to addressing advanced esophageal SCC.

1. Introduction

Esophageal cancer represents a formidable global health challenge, characterized by its aggressive nature and often unfavorable prognosis. It ranks as the seventh most common cancer and the sixth leading cause of cancer-related death worldwide. Histopathologically, esophageal cancer is primarily divided into two main types: squamous cell carcinoma (SCC) and adenocarcinoma (EAC). Esophageal SCC is the predominant type in many developing countries, particularly within the "esophageal cancer belt" that stretches from East Asia to the Middle East, including regions of Indonesia. In contrast, EAC is more common in Western, industrialized nations. According to GLOBOCAN 2020 data, the incidence of esophageal cancer in Indonesia was estimated at approximately 7,418 new cases annually, with a correspondingly high mortality rate of 7,165 deaths, underscoring its significant impact on public health within the nation.[1,2]

Esophageal SCC arises from the squamous epithelial cells lining the esophagus, most frequently occurring in the upper or middle thoracic esophagus. The pathogenesis of esophageal SCC is a complex,

multifactorial process driven by chronic mucosal irritation and inflammation resulting from prolonged exposure to various carcinogens and risk factors. Key etiological factors strongly associated with esophageal SCC include long-term tobacco smoking and heavy alcohol consumption, which are thought to act synergistically to increase risk. Other significant risk factors encompass poor dietary habits, such as low intake of fresh fruits and vegetables, deficiencies in essential micronutrients (selenium, zinc, vitamin A), and consumption of N-nitroso compounds found in certain preserved foods. The habit of drinking extremely hot beverages, such as tea or coffee, has also been implicated as a thermal irritant contributing to esophageal mucosal injury and subsequent malignant transformation, particularly in high-incidence regions. Furthermore, pre-existing esophageal conditions like achalasia (due to chronic stasis and inflammation), caustic esophageal injury (from lye ingestion), and Plummer-Vinson syndrome can predispose individuals to esophageal SCC. Certain strains of human papillomavirus (HPV) have been detected in esophageal SCC tissues, suggesting a potential etiological role, although its precise contribution remains an area of ongoing research. Genetic susceptibility and epigenetic alterations also play a role in modifying an individual's risk.[3,4]

A major impediment to improving outcomes in esophageal SCC is the frequent delay in diagnosis. Early-stage disease often presents with subtle or nonspecific symptoms, such as mild retrosternal discomfort, a sensation of food sticking, or intermittent dysphagia, which may not prompt immediate medical attention or may be misdiagnosed as benign conditions like gastroesophageal reflux disease (GERD) or functional dyspepsia. As the tumor grows and infiltrates the esophageal wall, more alarming symptoms develop, including progressive dysphagia (initially for solids, then liquids), significant unintentional weight loss (a common and ominous sign), odynophagia (painful swallowing), and regurgitation of undigested food. By the time these more pronounced symptoms manifest, the disease is often locally advanced or has metastasized, rendering curative treatment challenging. Consequently, the overall 5-year survival rate for esophageal cancer remains poor, typically ranging from 15% to 25% across all stages, with significantly lower rates for patients diagnosed with advanced disease (often less than 5-10% for metastatic cases).[5,6]

Achalasia is an idiopathic primary esophageal motility disorder characterized by two key pathognomonic features: impaired relaxation of the lower esophageal sphincter (LES) and absent or ineffective peristalsis in the body of the esophagus. These abnormalities result from the selective loss of inhibitory ganglion cells within the myenteric (Auerbach's) plexus in the distal esophagus and LES. Clinically, achalasia typically presents with dysphagia to both solids and liquids, regurgitation of undigested food (especially postprandial or nocturnal), retrosternal chest pain (often described as squeezing or pressure-like), and significant weight loss due to reduced oral intake and malabsorption. The symptomatic presentation of achalasia can, therefore, closely mimic that of esophageal cancer, particularly tumors located at or near the gastroesophageal junction (GEJ) that cause mechanical obstruction or infiltrate the neural plexuses governing esophageal motility. This phenomenon, where a malignancy gives rise to achalasia-like symptoms and manometric/radiographic findings, is termed "pseudoachalasia" or "secondary achalasia". While primary achalasia itself is recognized as a long-term risk factor for esophageal SCC development (estimated to increase the risk 16- to 33-fold after 10-25 years, likely due to chronic stasis, irritation, and bacterial overgrowth leading to chronic esophagitis), the scenario where an esophageal SCC initially presents as achalasia represents a distinct and critical diagnostic pitfall. Failure to differentiate pseudoachalasia from idiopathic achalasia can lead to

inappropriate benign management and a crucial delay in diagnosing and treating the underlying malignancy, with dire prognostic consequences.[7,8]

The diagnostic pathway for suspected esophageal cancer involves a comprehensive evaluation, beginning with a detailed clinical history and physical examination. Endoscopic investigation, specifically esophagogastroduodenoscopy (EGD), is the cornerstone procedure. EGD allows for direct visualization of the esophageal mucosa, precise localization and characterization of any suspicious lesions (mass, ulceration, stricture), and, most importantly, the acquisition of biopsy specimens for definitive histopathological diagnosis. Histologically, esophageal SCC is defined by the presence of invasive squamous cells exhibiting varying degrees of differentiation, keratin pearl formation, and intercellular bridges. Once malignancy is confirmed, meticulous staging is essential to guide treatment planning and prognostication. This typically involves a combination of imaging modalities, including contrast-enhanced computed tomography (CT) of the chest, abdomen, and pelvis to assess local tumor extent, regional lymph node involvement, and distant metastases; endoscopic ultrasound (EUS) for detailed locoregional staging (T and N status), particularly for early-stage tumors; and often 18F-fluorodeoxyglucose positron emission tomography combined with CT (FDG-PET/CT) for its superior sensitivity in detecting occult nodal or distant metastatic disease. Staging is performed according to the American Joint Committee on Cancer (AJCC) TNM classification system, currently in its 8th edition.[9,10]

The management of esophageal SCC is complex and necessitates a multidisciplinary team (MDT) approach, involving gastroenterologists, thoracic or general surgeons, medical oncologists, radiation oncologists, radiologists, pathologists, and nutritionists. Treatment decisions are tailored based on tumor stage, location, histological subtype, patient performance status, comorbidities, and patient preferences. For locally advanced, unresectable disease, such as the Stage IVA (T4N1M0) presented in this report, therapeutic options primarily include definitive chemoradiotherapy (dCRT) or systemic chemotherapy, with surgery generally not being a primary option for T4b tumors (invading unresectable structures). The choice of chemotherapy regimen is critical, with platinum-based doublets (cisplatin/5-fluorouracil, oxaliplatin/capecitabine) or taxane-containing regimens being common backbones. The advent of targeted therapies, such as epidermal growth factor receptor (EGFR) inhibitors (cetuximab), and, more significantly, immune checkpoint inhibitors (ICIs) targeting the PD-1/PD-L1 axis (nivolumab, pembrolizumab), has brought new therapeutic avenues, particularly for advanced or metastatic esophageal SCC, often in combination with chemotherapy or as subsequent lines of treatment. Nutritional support is an integral component of care, as significant dysphagia and consequent malnutrition are highly prevalent and can adversely affect treatment tolerance and outcomes. Interventions such as enteral feeding via nasogastric tube or, more definitively, percutaneous endoscopic gastrostomy (PEG) or feeding jejunostomy are often required.

This case report aims to describe the clinical course of a 43-year-old male patient who initially presented with symptoms suggestive of achalasia but was subsequently diagnosed with locally advanced esophageal SCC. The novelty of this study lies in its detailed exposition of the diagnostic journey, highlighting the insidious mimicry of esophageal SCC as a benign motility disorder in a relatively young patient from a region with a high SCC burden. It emphasizes the critical clinical reasoning required to navigate such diagnostic ambiguity and avoid potential mismanagement. Furthermore, this report discusses the specific diagnostic investigations undertaken, the rationale behind the staging, and the formulation of a contemporary therapeutic strategy based on current evidence for locally advanced

disease. The aim of this study is to meticulously present this illustrative case to heighten clinical awareness regarding esophageal SCC as a crucial, albeit sometimes deceptive, differential diagnosis in patients manifesting with achalasia-like symptoms. By doing so, it seeks to promote earlier and more accurate diagnosis, facilitate timely initiation of appropriate oncological management, and thereby improve the prospects for patients facing this challenging malignancy.

2. Case Presentation

A 43-year-old Balinese male, employed as a laborer, was referred from a regional hospital with an initial working diagnosis of esophageal achalasia (Table 1). His symptoms began several months prior with odynophagia, which was not investigated further at that time. The predominant and progressive complaint leading to his current presentation was dysphagia, worsening over five months since January 2024. This dysphagia progressed from solids to soft foods, and ultimately, in the two weeks before consultation, he could only manage minimal amounts of liquidized porridge and sips of water. This was accompanied by a sensation of food lodging in his neck, mid-chest discomfort, anorexia, and a significant unintentional weight loss of approximately 6 kg over the preceding two months. He denied other systemic symptoms like fever, cough, or shortness of breath but had a notable history of smoking since age 17 and occasional alcohol use. There was no significant past medical or family history of chronic diseases or malignancy. Physical examination revealed a patient with compromised nutritional status, consistent with his history. Vital signs were stable. Examination of the head, neck, oral cavity, and oropharynx was largely unremarkable, with no palpable cervical lymphadenopathy. Fiberoptic Laryngoscopy (FOL) showed no masses in the nasopharynx, hypopharynx, or larynx, though saliva pooling around the larynx was noted, suggesting some degree of impaired clearance. Initial laboratory investigations highlighted several abnormalities. These included leukocytosis (11.05×10^3/L), microcytic hypochromic anemia (Hb 12.1 g/dL), and thrombocytosis (570×10^3/L). The Neutrophil-to-Lymphocyte Ratio (NLR) was elevated at 7.54. Mild hypokalemia (3.22 mmol/L) and hyponatremia (131 mmol/L) were also present. A chest X-ray was unremarkable. Given the progressive dysphagia, an Esophagogastroduodenoscopy (EGD) was performed, which identified a friable, easily bleeding mass in the upper esophagus, causing significant luminal obstruction, preventing further passage of the endoscope. The impression was an esophageal tumor, suspicious for malignancy. Histopathological examination of the biopsy confirmed oesophageal squamous cell carcinoma.

Staging investigations was then pursued. A bone survey on June 6th, 2024, was negative for metastases. A multi-slice computed tomography (MSCT) scan of the thorax (with and without contrast) revealed an irregular solid intraluminal mass at the gastroesophageal junction (GEJ), extending into the cardia and medial gastric corpus, causing near-total esophageal obstruction. Multiple suspicious perihepatic and perigastric lymphadenopathies were noted. No distant metastases were identified in the visualized fields. A subsequent liver ultrasound on June 19th, 2024, also showed no liver metastases or para-aortic lymphadenopathy. Based on these findings, the final clinical diagnosis was Squamous Cell Carcinoma of the esophagus, Stage IVA (T4N1M0, AJCC 8th Edition). The treatment plan and follow-up are outlined in Table 2. Due to severe dysphagia and obstruction, a feeding gastrostomy was performed on May 31st, 2024, for nutritional support. Following a multidisciplinary team discussion, the patient was initiated on systemic chemotherapy. The regimen consisted of Docetaxel (Braxel®) 100 mg, Carboplatin 416 mg, and targeted therapy with Cetuximab (Erbitux®) 556 mg. At the time of the report, the

patient had completed the first cycle of chemotherapy and was reported to be in a stable condition, continuing his treatment. His tolerance to the initial cycle was managed with supportive care for Grade 1-2 nausea and fatigue. Regular monitoring for treatment response and toxicity was planned, including clinical assessments, blood counts, biochemistry, and restaging imaging after a set number of cycles.

Table 1. Summary of patient's clinical findings.

Category	Finding
Demographics	
Age	43 years
Gender	Male
Ethnicity	Balinese
Occupation	Laborer
Anamnesis	
Chief complaint	Progressive dysphagia (5 months)
History of present illness	Initial odynophagia (not investigated). Dysphagia progressed from solids to liquids. Sensation of food sticking in the neck, mid-chest discomfort, anorexia, unintentional weight loss (~6 kg in 2 months).
Associated symptoms	No fever, cough, palpitations, diarrhea, neck mass, proptosis.
Past medical history	No chronic illnesses (HTN, DM, heart disease).
Social history	Smoker (since age 17), occasional alcohol use.
Family history	No relevant family history of malignancy or chronic illness.
Initial suspected diagnosis	Esophageal Achalasia
Physical examination	
General appearance	Compromised nutritional status. Vital signs stable (BP 110/70, HR 88, RR 20, Temp 36.5°C).
Head & neck	Oral cavity/oropharynx: pink mucosa, tonsils T1/T1. No palpable cervical lymphadenopathy.
Fiberoptic laryngoscopy (FOL)	No mass in nasopharynx, hypopharynx, larynx. Saliva pooling around larynx. Symmetrical vocal cords & arytenoids, normal mobility, no edema/hyperemia. Epiglottis normal.
Laboratory findings (25/05/2024)	
Complete blood count	Leukocytosis (11.05×10^3/L), Microcytic hypochromic anemia (Hb 12.1 g/dL), Thrombocytosis (570×10^3/L).
Inflammatory markers	Neutrophil-to-Lymphocyte Ratio (NLR): 7.54 (elevated).
Electrolytes	Hypokalemia (3.22 mmol/L), Hyponatremia (131 mmol/L).
Imaging/Special tests	
Chest X-ray (AP)	Trachea central, no cor/pulmo abnormalities.
Esophagogastroduodenoscopy (EGD)	Mass in upper esophagus, friable, easily bleeding. Scope could not pass. Impression: Esophageal tumor, suspect malignancy.
Esophagoscopy with Biopsy (28/05/2024)	Biopsy of esophageal mass.
Histopathology	Esophageal tissue with tumor mass: proliferating neoplastic epithelial cells in solid nests, infiltrative. Conclusion: Oesophageal Squamous Cell Carcinoma. (Moderately differentiated).
Bone survey (06/06/2024)	No visualized osseous metastasis.
MSCT thorax (with/without contrast) (13/06/2024)	Irregular solid intraluminal mass at GEJ, cardia, extending to gastric corpus, causing near-total esophageal obstruction. Suspicious multiple perihepatic & perigastric lymphadenopathies. No distant mets visualized.
Liver ultrasound (19/06/2024)	No liver metastasis. No para-aortic lymph node enlargement.
Clinical diagnosis	
Final diagnosis	Squamous Cell Carcinoma of the Esophagus, Stage IVA (T4N1M0).

Table 2. Treatment procedures and follow-up.

Category	Details
Nutritional support	
Procedure	Feeding Gastrostomy performed on 31/05/2024.
Rationale	Severe dysphagia and near-total esophageal obstruction preventing adequate oral intake.
Oncological treatment	
Treatment modality	Systemic Chemotherapy with Targeted Therapy.
Regimen	Docetaxel (Braxel®) 100 mg, Carboplatin 416 mg, Cetuximab (Erbitux®) 556 mg.
Rationale for regimen	Locally advanced, unresectable (T4) disease. Aim to control disease, alleviate symptoms, potentially improve survival.
Administration schedule	Typically cyclical (every 3 weeks).
Follow-up & outcomes	
Patient status at report	Stable condition, currently undergoing chemotherapy.
Tolerance	Grade 1-2 nausea and fatigue reported for the first cycle; managed with supportive care.
Planned monitoring	Clinical assessments for symptomatic improvement/worsening. Regular blood tests (CBC, biochemistry) for toxicity monitoring. Restaging imaging (CT scan) after a predetermined number of cycles to assess treatment response (per RECIST criteria). Nutritional status monitoring.
Long-term plan	Dependent on response to initial chemotherapy, tolerance, and overall clinical status. May involve further cycles of chemotherapy, consideration of radiotherapy if localized control becomes an aim, or palliative care if disease progresses.

3. Discussion

The case of Mr. IMA, a 43-year-old male diagnosed with Stage IVA (T4N1M0) esophageal squamous cell carcinoma (SCC) subsequent to an initial suspicion of achalasia, offers a rich platform to discuss the intricate challenges in diagnosing and managing this aggressive malignancy. This discussion will delve into the pathophysiological underpinnings of his presentation, the diagnostic labyrinth navigated, the rationale and implications of the staging, the complexities of the chosen therapeutic strategy, and the overarching prognostic considerations, all viewed through the lens of current scientific understanding and clinical best practices. One of the most salient features of this case is the initial diagnostic hypothesis of achalasia, a benign motility disorder, which ultimately proved to be a manifestation of a life-threatening malignancy (Table 1). This phenomenon, termed pseudoachalasia or secondary achalasia, though less common than idiopathic achalasia, represents a critical diagnostic pitfall that can lead to significant delays in appropriate oncological intervention, adversely impacting patient outcomes.[11,12]

Idiopathic achalasia is fundamentally a neurodegenerative disorder characterized by the progressive loss of inhibitory ganglion cells within the myenteric (Auerbach's) plexus of the distal esophagus and the lower esophageal sphincter (LES). These inhibitory neurons, primarily releasing nitric oxide (NO) and vasoactive intestinal peptide (VIP), are crucial for mediating LES relaxation and propagating orderly peristaltic waves in the esophageal body. Their absence or dysfunction leads to impaired LES relaxation, an elevated resting LES pressure, and aperistalsis of the esophageal body. The exact etiology of this neuronal degeneration in idiopathic achalasia remains elusive but is thought to involve a combination of autoimmune mechanisms, viral triggers (herpes simplex virus-1), and genetic predisposition in susceptible individuals. Chronic inflammation and subsequent fibrosis within the myenteric plexus are common pathological findings. Pseudoachalasia, conversely, arises when a secondary process, most commonly a malignancy, mimics the clinical, radiographic, and manometric features of idiopathic achalasia. Tumors can induce an achalasia-like picture through several mechanisms. A tumor

arising in the distal esophagus or gastric cardia can directly infiltrate the musculature and neural plexuses of the LES, physically impairing its ability to relax and causing obstruction. This was likely a major contributing factor in Mr. IMA's case, given the MSCT findings of a mass at the GEJ extending into the cardia and causing near-total luminal obstruction (Table 1). Malignant cells can invade the myenteric plexus, destroying the inhibitory neurons in a manner analogous to the primary neurodegeneration seen in idiopathic achalasia. Alternatively, some cancers can induce a paraneoplastic syndrome, where antibodies or cytotoxic T-cells directed against tumor antigens cross-react with components of the enteric nervous system, leading to neuronal damage and dysmotility. Esophageal cancer, lung cancer, and gastric cancer are among the malignancies most frequently implicated in pseudoachalasia. Though less common for mimicking true LES dysfunction, large mediastinal tumors or extensive lymphadenopathy could theoretically compress the distal esophagus, leading to obstructive symptoms. The net effect of these malignant processes is an outflow obstruction at the GEJ, impaired esophageal emptying, and consequent dilatation of the proximal esophagus, mirroring the findings in primary achalasia.[13,14]

Distinguishing pseudoachalasia from idiopathic achalasia based solely on clinical symptoms can be exceedingly difficult, as both conditions share core manifestations of dysphagia (to solids and liquids), regurgitation, chest pain, and weight loss. However, certain "red flag" features, while not definitive, may raise the index of suspicion for malignancy. Idiopathic achalasia can occur at any age but often peaks between 30 and 60 years. An onset after age 60 is considered a relative warning sign for pseudoachalasia, though Mr. IMA was younger (43 years), demonstrating this is not an absolute rule. Symptoms of pseudoachalasia often have a more rapid onset and progression (typically < 6 months to 1 year) compared to the often insidious and prolonged course of idiopathic achalasia, which can span several years before diagnosis. Mr. IMA's 5-month history of progressive dysphagia (Table 1) aligns with a potentially more aggressive underlying process. While weight loss is common in both conditions, it is often more rapid and profound in pseudoachalasia due to the catabolic effects of malignancy in addition to reduced oral intake. Mr. IMA's loss of ~6 kg in 2 months is significant (Table 1). Symptoms like anorexia (present in this case, Table 1), significant fatigue beyond what is expected from poor intake, or unexplained fever are more suggestive of an underlying systemic illness like cancer. The presence of established risk factors for esophageal SCC, such as a long history of smoking (Mr. IMA smoked since age 17, Table 1) and alcohol consumption, should heighten suspicion for malignancy. His origin from Indonesia, a region within the esophageal cancer belt, further adds to this background risk. Despite these potential clues, considerable overlap exists, and relying solely on clinical presentation is insufficient. The definitive diagnostic step in any patient presenting with achalasia-like symptoms, particularly if there are any atypical features or risk factors for cancer, is a thorough endoscopic evaluation with biopsies of any suspicious areas. Mr. IMA's journey exemplifies this diagnostic challenge. The initial complaint of odynophagia, followed by progressive dysphagia over five months, leading to an initial suspicion of achalasia (Table 1), highlights how the benign diagnosis was entertained. Odynophagia (painful swallowing) itself can occur in severe esophagitis secondary to stasis in achalasia, but it is also a common symptom of ulcerative esophageal malignancies. The critical turning point was the EGD, which directly visualized the friable, bleeding, obstructive mass (Table 1). This finding immediately shifted the diagnostic focus from a benign motility disorder to a probable malignancy, a suspicion swiftly confirmed by biopsy as esophageal SCC (Table 1). This underscores the indispensable role of early endoscopy in all cases of significant or

progressive dysphagia to rule out structural lesions, especially cancer, before concluding a diagnosis of a primary motility disorder.[15,16]

The patient's history of progressive dysphagia, initially for solids and then progressing to liquids over a 5-month period, is a classic presentation for an evolving esophageal obstruction. While this pattern can be seen in severe achalasia as the esophagus decompensates, it is highly characteristic of a growing malignant stricture. The associated odynophagia suggested mucosal ulceration or inflammation. The substantial unintentional weight loss (~6 kg in 2 months) pointed towards a significant catabolic process and/or severely compromised nutritional intake, both common in advanced esophageal cancer. His long-term smoking history was a major risk factor for SCC. The sensation of food "sticking in the neck" could be referred pain or related to proximal esophageal dilatation above the obstruction. While the general physical examination and routine ENT assessment were largely unremarkable for specific signs of advanced metastatic disease (palpable supraclavicular nodes or hepatomegaly), the observation of compromised nutritional status was a key finding corroborating the severity of his symptoms. The FOL finding of saliva pooling around the larynx (Table 1), despite no intrinsic laryngeal pathology, was an indirect sign of impaired esophageal clearance and significant downstream obstruction, preventing saliva from being effectively swallowed. An elevated white blood cell count can be due to various factors, including inflammation associated with the tumor, a paraneoplastic response, or even a subclinical infection in a debilitated patient. Large, necrotic tumors can elicit a significant inflammatory response. This type of anemia typically suggests iron deficiency. In the context of an esophageal tumor, this could be due to chronic occult blood loss from the friable, ulcerated tumor surface, or impaired iron absorption secondary to malnutrition and altered gastrointestinal function. Anemia of chronic disease (normocytic, normochromic) can also contribute to cancer patients. An elevated platelet count is a common paraneoplastic phenomenon seen in various malignancies, including esophageal cancer. It is often driven by inflammatory cytokines (IL-6) produced by the tumor or host immune cells, which stimulate megakaryopoiesis. Paraneoplastic thrombocytosis has been associated with a poorer prognosis in some cancers. The NLR is a readily available biomarker reflecting systemic inflammation and immune dysregulation. An elevated NLR (typically >3-5, depending on the study) is increasingly recognized as an independent adverse prognostic factor in many solid tumors, including esophageal SCC. It signifies an increased neutrophil-driven inflammatory response and a relative decrease in lymphocyte-mediated anti-tumor immunity. These electrolyte disturbances were likely multifactorial, stemming from poor oral intake, potential losses if there was any regurgitation or vomiting (though not explicitly stated as major), and possibly refeeding issues if nutrition was erratic. Malnutrition itself can lead to depletion of total body potassium.[17,18]

EGD was the pivotal diagnostic procedure. The endoscopic description of a "friable, easily bleeding mass" causing "significant luminal obstruction" (Table 1) is pathognomonic for an advanced esophageal malignancy. Friability and contact bleeding are hallmarks of neoplastic tissue due to aberrant angiogenesis and poor structural integrity. The inability to pass the scope beyond the lesion indicated a high-grade obstruction. The biopsy and subsequent histopathological examination provided the definitive diagnosis of "Oesophageal Squamous Cell Carcinoma" (Table 1). SCC is characterized by malignant squamous cells that invade beyond the basement membrane into the lamina propria and deeper layers. Key microscopic features include cellular pleomorphism, nuclear hyperchromasia, increased nuclear-to-cytoplasmic ratio, atypical mitoses, and often, evidence of keratinization (keratin pearls, individual cell keratinization). The degree of

differentiation (well, moderately, or poorly differentiated) is also assessed based on the extent to which the tumor resembles normal squamous epithelium and forms keratin. This patient's tumor was reported as being composed of "proliferating neoplastic epithelial cells arranged in solid nests, infiltrative among jaringan ikat (connective tissue)," which is typical. Additional details often included in a comprehensive pathology report for esophageal SCC are the depth of invasion (if assessable on a biopsy, though usually more accurately determined by EUS or resection), presence or absence of lymphovascular invasion (LVI), and perineural invasion (PNI), all of which have prognostic implications. Immunohistochemical stains like p63 and CK5/6 are often positive in SCC and can aid in differentiating it from adenocarcinoma if the morphology is ambiguous. In Mr. IMA's case, the MSCT scan was pivotal for staging (Table 1). It described an "irregular solid intraluminal mass at the GEJ, cardia, extending to the gastric corpus, causing near-total esophageal obstruction." This implies invasion into adjacent structures. While the specific structures invaded, making it T4, were not explicitly detailed beyond "massa solid irreguler intralumen," the "near total obstruksi" and location at the GEJ extending into the stomach often means at least adventitial invasion (T3) or direct invasion of structures like the diaphragm, pericardium (T4a), or potentially inoperable structures if more extensive. The report given (IVA - T4N1M0) suggests the T4 was considered significant. "Suspicious multiple perihepatic and perigastric lymphadenopathies" led to the N1 designation (1-2 positive regional nodes, assuming the "multiple" fit this category after radiological assessment, or this was a summary after pathological confirmation if available, though usually clinical staging is based on imaging). Perihepatic and perigastric nodes are considered regional for distal esophageal/GEJ tumors. The bone survey and liver ultrasound, along with the CT scan, ruled out distant metastases (M0) (Table 1). Combining these gave a clinical stage of T4N1M0. According to the AJCC 8th Edition for esophageal SCC, a T4aN1M0 or T4bN1M0 would typically fall into Stage IVA or IVB depending on specifics. The provided states Stage IVA. Stage IVA generally signifies locally advanced disease that is often unresectable or borderline resectable with very high risk, carrying a challenging prognosis. EUS could have provided more precise detail on the depth of wall penetration and local nodal status if performed, and PET-CT would have offered a more sensitive whole-body survey for nodal and distant metastases.[19,20]

The diagnosis of Stage IVA (T4N1M0) esophageal SCC placed Mr. IMA in a category of locally advanced disease with a generally poor prognosis and limited curative options (Table 2). The management strategy must be carefully tailored, balancing oncological efficacy with quality of life considerations. The management of such complex cases invariably benefits from an MDT discussion involving medical oncologists, radiation oncologists, thoracic/upper GI surgeons, gastroenterologists, radiologists, pathologists, nutritionists, and palliative care specialists. This collaborative approach ensures all relevant factors are considered and a consensus treatment plan is formulated. The mention of consultation with internal medicine/gastroenterology and ENT-HNS, and later a decision for chemotherapy, implies that such discussions likely occurred. Given the "near-total esophageal obstruction" (Table 1) and significant weight loss, establishing a reliable route for nutritional support was paramount. The placement of a feeding gastrostomy on May 31st, 2024 (Table 2) was a crucial and timely intervention. Malnutrition is highly prevalent in esophageal cancer patients due to dysphagia, odynophagia, anorexia, and tumor-induced catabolism. It can lead to cachexia, impaired immune function, poor wound healing, reduced tolerance to anti-cancer treatments, and worsened quality of life. Enteral nutrition via a gastrostomy tube allows for consistent delivery of calories, protein, and

micronutrients, helping to stabilize or improve nutritional status, thereby potentially improving treatment tolerance and overall outcomes. The choice of gastrostomy over nasogastric feeding is appropriate for anticipated long-term nutritional needs in the context of an obstructing esophageal tumor.

The patient was initiated on systemic chemotherapy with Docetaxel 100 mg, Carboplatin 416 mg, and Cetuximab 556 mg (Table 2). This is a multi-drug regimen combining cytotoxic agents with a targeted therapy. Docetaxel is a semi-synthetic taxane that promotes microtubule assembly and inhibits their depolymerization, leading to cell cycle arrest in the G2/M phase and apoptosis. Taxanes have demonstrated activity in various solid tumors, including esophageal SCC. Common toxicities include myelosuppression (especially neutropenia), alopecia, peripheral neuropathy, mucositis, fluid retention, and hypersensitivity reactions. The dose of 100 mg seems like a flat dose; typically, it's dosed per m^2 body surface area (75 mg/m^2). Carboplatin is a second-generation platinum compound that forms covalent DNA adducts, interfering with DNA replication and transcription, ultimately leading to cell death. It is often preferred over cisplatin in some settings due to a more favorable toxicity profile, particularly less nephrotoxicity, neurotoxicity, and ototoxicity, though it causes more myelosuppression (especially thrombocytopenia). It is a standard component in many esophageal cancer regimens. Dosing is typically based on the Calvert formula, targeting a specific Area Under the Curve (AUC, AUC 5-6). The 416 mg dose would correspond to a calculated AUC for the patient. Cetuximab is a chimeric (mouse/human) IgG1 monoclonal antibody that binds with high affinity to the extracellular domain of the Epidermal Growth Factor Receptor (EGFR, also known as HER1 or ErbB1). EGFR is a transmembrane tyrosine kinase receptor that, upon ligand binding (EGF, TGF-α), activates downstream signaling pathways (RAS/MAPK, PI3K/Akt) involved in cell proliferation, survival, angiogenesis, invasion, and metastasis. EGFR is frequently overexpressed in esophageal SCC (reported in 40-80% of cases, depending on the study and detection method), and its overexpression is often associated with a more aggressive phenotype and poorer prognosis. By blocking ligand binding, cetuximab inhibits EGFR signaling, potentially leading to cell cycle arrest, induction of apoptosis, inhibition of angiogenesis, and reduced tumor cell motility. It can also mediate antibody-dependent cell-mediated cytotoxicity (ADCC). Cetuximab is approved for use in squamous cell carcinoma of the head and neck (SCCHN) and metastatic colorectal cancer (in KRAS wild-type patients). Its role in esophageal SCC is less well-established by large phase III trials compared to SCCHN, but it has been investigated, often in combination with chemotherapy or radiotherapy, with varying degrees of success. Some studies suggested improved response rates, but not always a significant survival benefit. Common side effects of cetuximab include an acneiform skin rash (often correlated with response), hypomagnesemia, diarrhea, mucositis, and infusion reactions. The 556 mg dose likely represents a loading dose (typically 400 mg/m^2) followed by weekly maintenance doses (typically 250 mg/m^2).

The combination of a taxane, a platinum agent, and an EGFR inhibitor leverages different mechanisms of action to achieve synergistic anti-tumor effects. This type of regimen is more commonly studied and used in SCCHN. For esophageal SCC, particularly Stage IVA, standard first-line options often include platinum-fluoropyrimidine doublets (cisplatin/5-FU, oxaliplatin/capecitabine) or platinum-taxane doublets, with or without radiotherapy. More recently, immunotherapy (PD-1 inhibitors like pembrolizumab or nivolumab) combined with platinum-fluoropyrimidine chemotherapy has become a standard first-line option for advanced/metastatic esophageal SCC, especially if PD-L1 positive (KEYNOTE-590, CheckMate-648 trials). The specific choice of Docetaxel + Carboplatin + Cetuximab for Mr.

IMA would have been based on factors such as institutional protocols, physician experience, patient performance status and comorbidities (if cisplatin was contraindicated or less preferred), and potentially EGFR expression status if tested (though not always required for cetuximab use in some SCC contexts). The aim in Stage IVA disease is typically palliative – to control tumor growth, alleviate symptoms (especially dysphagia once systemic effects kick in, though local obstruction might still need stenting or radiotherapy if not responding adequately), improve quality of life, and potentially prolong survival. For unresectable, locally advanced esophageal SCC (including many T4 cases or node-positive disease not amenable to surgery), definitive chemoradiotherapy (dCRT) is a standard curative-intent or life-prolonging approach. This typically involves concurrent administration of radiotherapy (50-50.4 Gy in 25-28 fractions) with platinum-based chemotherapy (cisplatin/5-FU or carboplatin/paclitaxel).

As indicated (Table 2, Follow-up & Outcomes), Mr. IMA was reported as stable after the first cycle. Ongoing management would involve regular clinical monitoring for symptom changes, assessment of nutritional status, and monitoring for treatment-related toxicities (via blood counts, biochemistry, and clinical examination). Treatment response is typically assessed using imaging (CT scans) after every 2-3 cycles of chemotherapy, using standardized criteria such as RECIST (Response Evaluation Criteria in Solid Tumors). The goals are to determine if the tumor is shrinking (response), remaining stable (stable disease), or growing (progressive disease). If the disease responds or is stable and the treatment is well-tolerated, chemotherapy may be continued for a defined number of cycles (4-6 cycles) or until disease progression or unacceptable toxicity. If the disease progresses, a switch to second-line therapy would be considered, potentially involving immunotherapy or other chemotherapy regimens based on prior treatments and patient fitness.

Despite advances in diagnosis and treatment, Stage IVA esophageal SCC carries a sobering prognosis. This is the most powerful prognostic determinant. T4 tumors (invasion of adjacent structures) and N1 disease (regional lymph node metastasis) inherently signify aggressive disease with a high risk of local recurrence and distant spread. The patient's overall fitness and ability to tolerate treatment (ECOG performance status) significantly impact outcomes. Patients who achieve a good objective response to initial therapy (chemotherapy or chemoradiotherapy) generally have better survival outcomes than non-responders. While not routinely guiding specific targeted therapies beyond PD-L1 for immunotherapy and occasionally HER2 in adenocarcinomas, research continues into other molecular markers that might predict prognosis or response to specific agents in esophageal SCC. EGFR overexpression, for instance, has been variably linked to prognosis. Tumor grade, presence of lymphovascular or perineural invasion can also provide prognostic information. The 5-year overall survival for patients with Stage IVA esophageal cancer is generally poor, often cited in the range of 10-20% or even lower, depending on the specific substage (T4a vs. T4b) and treatment received. The SEER data groups esophageal cancer into localized (48% 5-year survival), regional (28%), and distant (5%). Stage IVA falls within the more advanced end of "regional" or can border on "distant" if N status is high or T status is very advanced. Given the challenging prognosis, integrating palliative and supportive care early in the management of Stage IVA esophageal SCC is crucial. This focuses on symptom management (dysphagia, pain, nausea, fatigue, anxiety, depression), psychosocial support for the patient and family, and maintaining the best possible quality of life throughout the illness trajectory. Discussions about goals of care and advance care planning are also important.

The landscape of esophageal cancer treatment is continually evolving. As mentioned, immune

checkpoint inhibitors (ICIs) like pembrolizumab and nivolumab have revolutionized treatment for advanced esophageal SCC, particularly when combined with first-line chemotherapy or used as adjuvant therapy after chemoradiation and surgery in certain contexts. Their role in the neoadjuvant setting for locally advanced disease is also being actively investigated. Beyond EGFR inhibitors, research into other potential molecular targets (FGFR, VEGFR, cell cycle regulators) is ongoing, though esophageal SCC has proven relatively resistant to many targeted agents thus far compared to adenocarcinoma. Efforts continue to optimize chemotherapy regimens to improve efficacy and reduce toxicity. The use of circulating tumor DNA (ctDNA) for non-invasive monitoring of treatment response, detection of minimal residual disease, and identification of resistance mechanisms is a promising area of research. Advances in radiotherapy delivery, such as intensity-modulated radiation therapy (IMRT) and proton beam therapy, aim to deliver more conformal radiation doses to the tumor while sparing surrounding normal tissues, potentially reducing toxicity and allowing for dose escalation.

Esophageal malignancy must always be a differential in adult patients presenting with new-onset, persistent, or progressive dysphagia, odynophagia, or unexplained significant weight loss, even if symptoms initially suggest a benign condition like achalasia, and regardless of age, if risk factors are present. Prompt EGD with biopsy is mandatory in such cases to rule out or confirm malignancy. Delays in endoscopic evaluation can lead to diagnosis at a more advanced, less treatable stage. Clinicians should be aware of pseudoachalasia and the red flag signs that might suggest an underlying malignancy rather than idiopathic achalasia. Once cancer is diagnosed, meticulous staging using appropriate imaging modalities (CT, EUS, PET-CT) according to established guidelines (AJCC 8th ed.) is crucial for accurate prognostication and guiding management decisions. Optimal care for esophageal cancer patients, especially those with locally advanced disease, requires a collaborative MDT approach. Aggressive nutritional intervention is vital in patients with obstructing esophageal tumors to improve tolerance to therapy and overall well-being. While guidelines exist, treatment for advanced esophageal SCC should be personalized based on stage, patient factors, tumor biology (where known), and available therapies, including consideration of clinical trial participation if appropriate. Early integration of palliative and supportive care is essential to address the multifaceted needs of patients with advanced esophageal cancer and enhance their quality of life.

4. Conclusion

The case of this 43-year-old male, who presented with symptoms mimicking achalasia and was subsequently diagnosed with Stage IVA esophageal squamous cell carcinoma, poignantly illustrates the deceptive nature of this malignancy and the critical importance of a high index of suspicion in patients with progressive dysphagia. The diagnostic journey, from initial nonspecific complaints to definitive histopathological confirmation and comprehensive staging, underscores the necessity for prompt and thorough endoscopic and imaging evaluations. Misattributing such symptoms to benign motility disorders without adequate exclusion of malignancy can lead to unacceptable delays in oncological management and poorer patient outcomes. The management of locally advanced esophageal SCC, as exemplified by this T4N1M0 case, is inherently complex and necessitates a robust multidisciplinary approach. Systemic therapy, incorporating cytotoxic agents and potentially targeted drugs like cetuximab, tailored to the individual patient's clinical status and tumor characteristics, forms a cornerstone of treatment for unresectable disease. Integral to this is aggressive nutritional support, often requiring procedures like gastrostomy, to combat malnutrition and improve treatment tolerance. While the prognosis

for Stage IVA esophageal SCC remains challenging, ongoing advancements in systemic therapies, including the integration of immunotherapy and novel targeted agents, offer hope for improved disease control and survival. This case reinforces several key clinical tenets: the imperative for early and accurate diagnosis of esophageal cancer through meticulous investigation of suspicious symptoms; the need for comprehensive staging to guide therapeutic decisions; and the value of individualized, multidisciplinary care that addresses not only the oncological aspects but also the nutritional and palliative needs of the patient. Continued research into biomarkers, innovative treatment strategies, and early detection methods is crucial to make meaningful progress against this formidable disease.

5. References

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