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CASE REPORT | ESOPHAGUS

Metachronous Squamous Cell Carcinoma of the Esophagus After Resolution of Previous Adenocarcinoma

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ABSTRACT

Esophageal cancer is the sixth leading cause of cancer-related death worldwide. Metachronous malignancies refer to multiple independent primary cancers diagnosed at least 6 months apart. The incidence of metachronous esophageal cancers with different histologic subtypes is extremely rare. This case presents an unprecedented occurrence of esophageal adenocarcinoma, followed by metachronous squamous cell carcinoma.

KEYWORDS: metachronous malignancies; metachronous esophageal malignancies; esophageal squamous cell carcinoma; esophageal adenocarcinoma

INTRODUCTION

Esophageal cancer ranks as the sixth leading cause of cancer-related death worldwide.[1] It primarily manifests in 2 forms: adenocarcinoma and squamous cell carcinoma.[1] This disease is characterized by rapid metastasis and nonspecific symptoms, such as difficulty in swallowing, weight loss, and occasional regurgitation.[1]

In oncology, metachronous refers to the occurrence of 2 or more independent primary malignancies, where the subsequent malignancies arise more than 6 months after the diagnosis of the first malignancy.[2] The incidence of metachronous esophageal cancers with different histologic subtypes in a single patient is exceedingly rare. The literature contains scant documentation of cases involving esophageal adenocarcinoma (EAC), followed by metachronous squamous cell carcinoma. We present a unique case illustrating this sequence, which has not been previously reported in the literature.

CASE REPORT

A 67-year-old man with a history of smoking and previously treated T2N0Mx EAC presented with worsening dysphagia and a single episode of hematemesis. The patient remained hemodynamically stable and maintained adequate oxygen saturation on room air. Three years earlier, the patient presented with similar symptoms and underwent an endoscopic esophageal biopsy, revealing Barrett's mucosa (intestinal metaplasia) with high-grade dysplasia affecting the muscularis mucosa (Figure 1). Further imaging studies, including endoscopic ultrasound, computed tomography, and positron emission tomography, detected no lymph node or distant organ involvement. As a result, the patient's esophageal cancer was classified as T2N0M0. Fearing potential surgical complications, the patient declined to undergo an esophagectomy. After an extensive discussion about the risks and benefits with the healthcare team, the patient opted for chemoradiation treatment. They received 61.2-Gy units in 34 fractions, supplemented with carboplatin and taxol. A follow-up esophagogastroduodenoscopy with biopsy performed 1 year later showed no signs of active disease.

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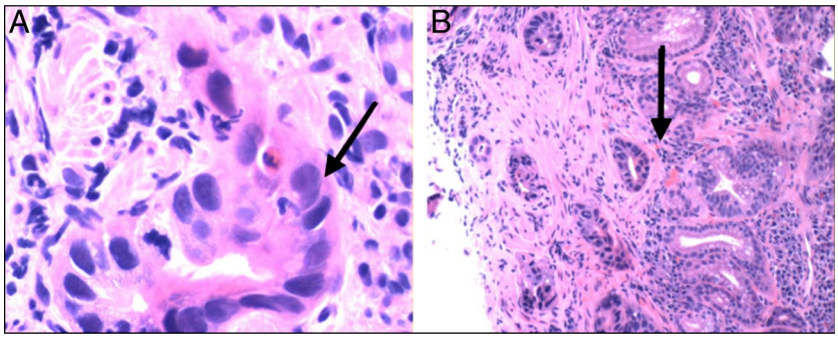

Figure 1. (A) (Photomicrograph magnified at 100×) The black arrow is pointing at high-grade dysplasia. (B) (Photomicrograph magnified at 40×) The black arrow is pointing at esophageal adenocarcinoma involving the muscularis mucosa.

Unfortunately, the patient was lost to follow-up until this visit, when he presented again with recurring dysphagia symptoms. Based on his presentation, chest, abdominal, and pelvic computed tomography angiography were performed, which revealed no active gastrointestinal bleeding but mild diffuse esophageal dilation and mid-distal esophageal wall thickening. An esophagogastroduodenoscopy was conducted, showing a medium-sized, fungating, nonbleeding, partially obstructing, and ulcerating mass in the lower third of the esophagus at the exact location as the previously treated EAC (Figure 2). Biopsies revealed a moderately differentiated squamous cell carcinoma (Figure 3). Photomicrographs exhibited nests of moderately differentiated squamous carcinoma infiltrating desmoplastic fibrous tissue, with pleomorphic tumor nuclei varying in size, shape, and focal keratinization. The patient underwent an open gastrostomy tube placement and was scheduled for outpatient chemotherapy, with the possibility of radiation therapy depending on clinical progression.

DISCUSSION

In reviewing the literature, multiple primary malignant tumors are characterized as several malignancies originating from different tissues with distinct morphologies.[3] Malignancies that develop within 6 months are classified as synchronous, whereas those appearing after 6 months are considered metachronous.[3,4] Although squamous cell carcinoma and adenocarcinoma are the 2 most common types of esophageal cancer globally, the presence of different histologic types of dual cancers in the same organ is an intriguing and rare clinical finding.[5]

In our case report, a patient previously treated for EAC with only chemoradiation therapy later presented with signs and symptoms of esophageal cancer once more. On further examination, the diagnosis was squamous cell carcinoma (SCC). Interestingly, the second primary malignant tumor was located in the same organ, the esophagus, and more specifically, in the exact same location: the lower third of the esophagus.

EAC and SCC share common risk factors, such as old age, smoking, and male sex, which may account for the metachronous occurrence of SCC after EAC under the concept of field cancerization.[1,6] After an extensive review, studies suggest that the metachronous changes observed in our patient are more likely attributable to thermal injury from radiofrequency ablation because the epithelial origins of columnar and squamous epithelium share common progenitors.[7] Consequently, eradicating adenocarcinoma with radiofrequency ablation could have predisposed the tissue to squamous cell proliferation. Another potential explanation is damage caused by radiation

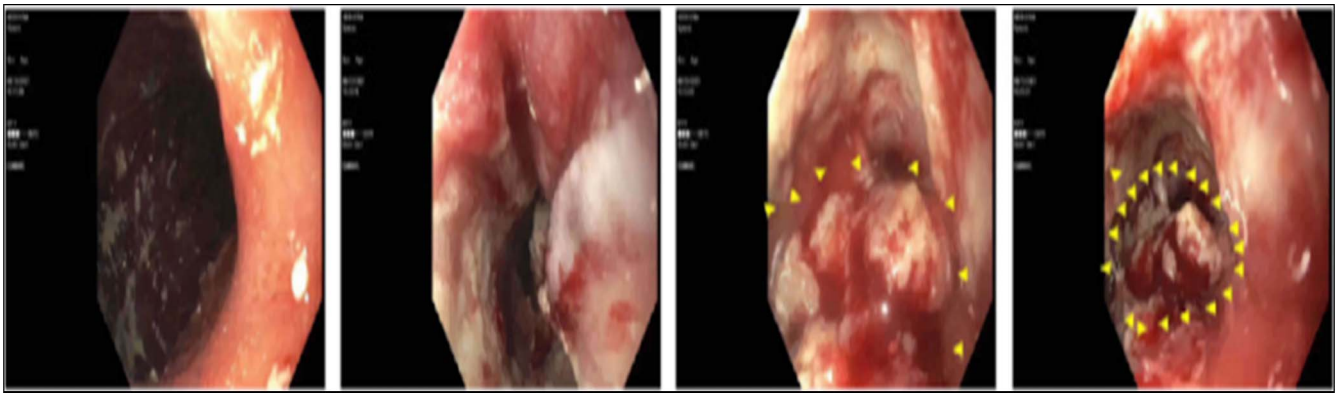

Figure 2. EGD from the second visit showing a hemorrhagic and ulcerating mass found at the lower third of the esophagus.

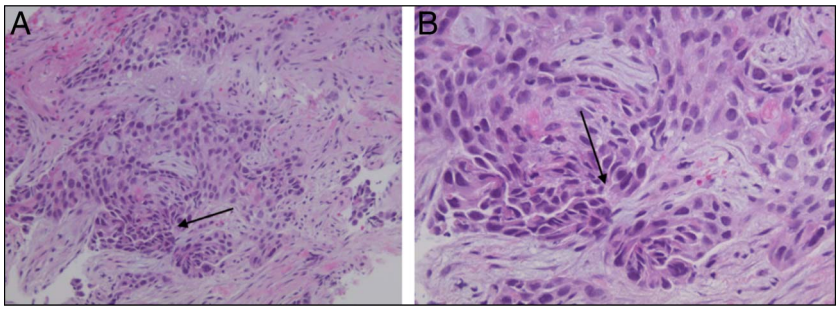

Figure 3. (A) (Photomicrographs magnified at 40×) and (B) (Photomicrographs magnified at 100×) display nests of moderately differentiated squamous carcinoma infiltrating desmoplastic fibrous tissue. The pleomorphic tumor nuclei vary in both size and shape, with focal keratinization being observed. Additionally, occasional mitotic figures (1-2) are also visible.

therapy for previous cancers (EAC in our case), which is a leading risk factor for SCC.[8]

Managing T2N0M0 EAC is challenging because of preoperative staging discrepancies and a lack of definitive guidelines, compounded by a dearth of randomized trials.[9] The National Comprehensive Cancer Network advises upfront surgery for low-risk lesions but recommends chemotherapy or chemoradiation for other cases.[9] Patient preferences also influence treatment choice, with some opting for nonsurgical methods, as in our case.

Contrarily, esophageal SCC (ESCC) is more chemoradiation therapy–sensitive.[10,11] Because esophagectomy often leads to significant postoperative issues, chemoradiation therapy is widely used for ESCC, despite the availability of other viable treatments.[12] For advanced ESCC, the typical approach is neoadjuvant therapy followed by esophagectomy.[12]

Multiple primary malignant tumors have an incidence rate ranging from 0.52% to 11.7%, highlighting the importance for healthcare providers to screen for recurrence and the development of second primary malignancies.[2] Clinicians and endoscopists should be made aware of this risk. Follow-up and appropriate screening are essential for patients during and after treatment to ensure the timely diagnosis and management of metachronous lesions of the esophagus.

DISCLOSURES

Author contributions: All authors mentioned earlier contributed to the conception, design, drafting, finalizing, and approval of the final manuscript in order of appearance and meet the ICJME criteria for authorship. All authors are willing to accept accountabilities for all aspects of the manuscript. S. Taj is the article guarantor.

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