

# A Rare Case of Metastatic Esophageal Adenocarcinoma Presenting as an Isolated Cerebellar Lesion 5 Years After Treatment

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## Abstract

*Isolated brain metastasis (IBM) as a recurrence of primary esophageal adenocarcinoma (AC) has rarely been reported in the literature and typically manifests within a short period of time after diagnosing the primary lesion. We present here an unusual case of an IBM presenting nearly 5 years after neoadjuvant chemoradiation therapy and surgical resection of a primary distal esophageal tumor with no interval evidence of recurrence. A 53-year-old man presented to our gastroenterology clinic with progressive dysphagia and weight loss. On upper endoscopy, the patient was found to have a large obstructing distal esophageal mass with biopsies reported as moderately differentiated AC. Subsequent computed tomography (CT) chest/abdomen/pelvis (C/A/P) and magnetic resonance imaging (MRI) brain were negative for any distant metastases. The patient received preoperative chemotherapy and radiation therapy, followed by distal esophagectomy with findings of stage IIIB disease. He did well after surgery and was monitored closely by his oncologist with no evidence of recurrence on interval imaging or follow-up endoscopy. Several years after his diagnosis, however, the patient developed new neurologic symptoms, and an MRI brain revealed a solitary cerebellar lesion with surrounding edema concerning for metastatic disease. Positron emission tomography and CT C/A/P were negative for any other new lesions. The tumor was resected, and pathology was confirmed as metastatic AC of esophageal origin. To our knowledge, this is the first case of recurrent esophageal AC presenting as an isolated cerebellar lesion 5 years after treatment of the primary tumor.*

## Keywords

*Esophageal adenocarcinoma, neoadjuvant chemoradiation therapy, isolated brain metastasis*

## Abbreviations and Acronyms

AC = adenocarcinoma  
CT C/A/P = computed tomography scan chest/abdomen/pelvis  
GEJ = gastroesophageal junction  
IBM = isolated brain metastasis  
MRI = magnetic resonance imaging  
SCC = squamous cell carcinoma

## Introduction

Esophageal cancer is the eighth-most common cancer and the sixth-most common cause of cancer death worldwide.<sup>1</sup> The majority of esophageal cancers worldwide are squamous cell (SCC), but the incidence of adenocarcinoma (AC) arising out of Barrett's esophagus has risen dramatically, particularly among white males.<sup>2-3</sup> AC is now more prevalent than SCC in the United States and Western Europe. There are several known risk factors for esophageal AC, but a history of smoking, higher body

mass index, gastroesophageal reflux disease, and a low fiber diet carry the highest attributable risk, accounting for almost 80% of cases in the United States.<sup>4</sup>

According to the National Cancer Institute's Surveillance, Epidemiology, and End Results Program database, approximately 18% of patients with esophageal cancer are found to have localized disease on presentation, 33% have spread to regional lymph nodes, and 39% have distant metastases, with the remaining 10% not being staged.<sup>5</sup> AC most frequently metastasize to intrabdominal sites (liver, peritoneum), while metastases from SCCs are usually intrathoracic.<sup>6</sup> From most to least common, the sites of distant metastases in patients with esophageal cancer are reported to be liver, distant lymph nodes, lungs, bones, adrenal glands, and brain.<sup>7</sup>

Survival in patients with esophageal cancer depends on the stage of the disease; patients with metastases detected in lymph node and solid organs have the lowest survival rates. The overall 5-year survival rate is approximately 19.9%.<sup>5</sup> The 5-year survival rate for patients with localized disease is 47.1%, for those with regional metastases, survival is 25.2%, and for those with distant metastases, survival is 4.9%.<sup>5</sup> The median survival of a patient with distant metastasis is only 6 to 12 months. SCC and AC, stage-by-stage, appear to have equivalent survival rates. Neoadjuvant chemoradiotherapy followed by surgical resection has become the standard of care for non-metastatic esophageal cancer, with the highest survival among those who have achieved a complete pathologic response (absence of viable residual tumor) at the time of surgery.<sup>8</sup>

Brain metastases have been considered uncommon in patients with esophageal cancer, with a published incidence of less than 5%.<sup>9-10</sup> The median time to diagnosis of brain metastasis is approximately 12 months, and the majority of these are supratentorial.<sup>11-12</sup> We present here an unusual case of an isolated brain metastasis (IBM) presenting nearly 5 years after treatment of a primary distal esophageal tumor with no interval evidence of recurrence.

## Case Report

A 53-year-old Japanese man presented to our outpatient gastroenterology clinic in Honolulu, Hawai'i, with progressive dysphagia to solids and liquids. He also reported a weight loss of 10 pounds over the past month. He denied any history

of gastroesophageal reflux disease, smoking, or heavy alcohol use. Upper endoscopy revealed a large friable, ulcerated, fungating mass at 38 cm, causing near complete obstruction of the esophageal lumen (Figure 1). The scope could not be advanced beyond the mass. Multiple biopsies were taken, and pathology revealed moderately differentiated AC.

A staging work-up by oncology including computed tomography (CT) chest/abdomen/pelvis (C/A/P), positron emission tomography scan, and magnetic resonance imaging (MRI) brain was negative for any obvious lymphadenopathy or distant metastases. After receiving pre-operative chemotherapy and radiation therapy, the patient underwent laparoscopic Ivor-Lewis esophagectomy with creation of a neo-esophagus. He was found to have a 4.8-cm tumor at the gastroesophageal junction (GEJ) with lymph-node positive disease, and his final pathologic diagnosis was reported as Siewert II, stage G3T3N2M0 (IIIB) poorly differentiated esophageal adenocarcinoma. The patient did well after surgery without any dysphagia, and he began to

gain weight steadily. He was followed closely by oncology, and CT C/A/P done every 6 months after surgery showed no evidence of metastasis. A follow-up upper endoscopy performed 2 years later was also normal, and the patient was felt to be in clinical remission.

Approximately 5 years after surgery, the patient developed persistent nausea, dizziness, and vertigo and was noted to be losing weight again. He was found on MRI brain to have a new  $4.0 \times 2.9 \times 3.5$ -cm well-circumscribed cerebellar lesion with surrounding edema and mass effect concerning for metastasis (Figure 2). Positron emission tomography scan/CT C/A/P was negative for any other new lesions. The patient underwent surgical resection of the lesion with findings confirming metastatic AC of esophageal origin with features similar to the GEJ tumor (Figure 3). He is now awaiting post-operative stereotactic radiosurgery and will continue to be followed closely by the oncology and neurosurgery services.



Figure 1. Image of Mass in Esophageal Lumen taken by Endoscopy

Large friable, ulcerated, fungating mass at 38 cm causing near complete obstruction of the esophageal lumen.

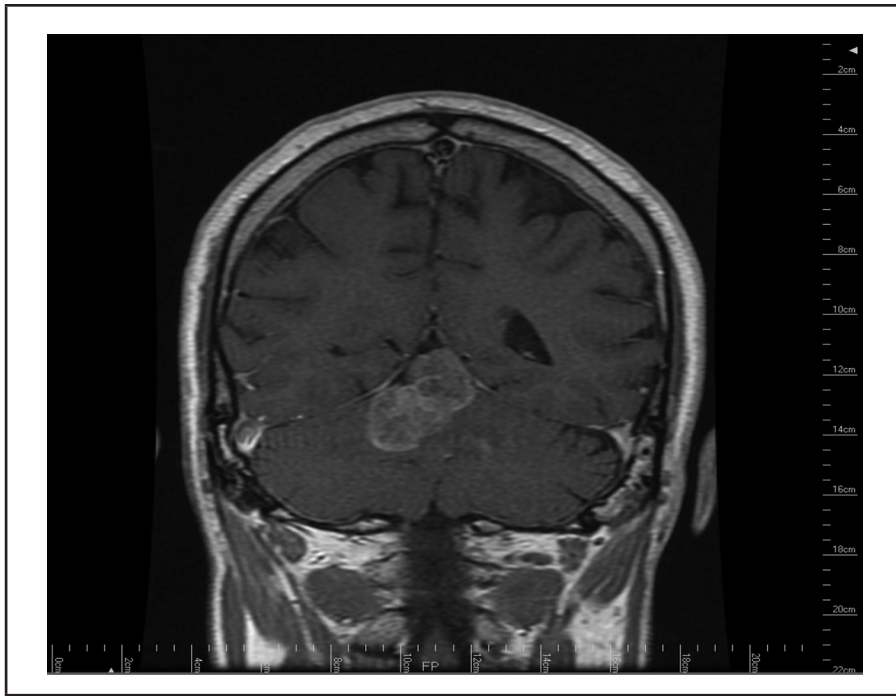


Figure 2. Magnetic Resonance Imaging of Brain with Mass in Cerebellum

Coronal view of cerebellar tumor with dimensions of  $4.0 \times 2.9 \times 3.5$  cm-enhancing lobulated well-circumscribed mass of central right cerebellum and cerebellar vermis containing hemorrhagic products with moderate surrounding edema and mass effect greater on the right.

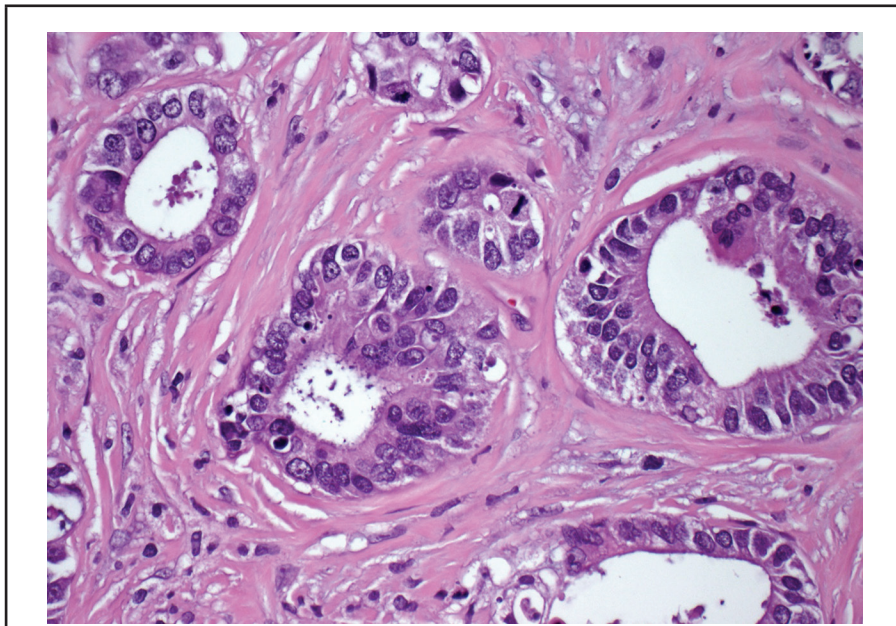


Figure 3. Imaging of Metastatic Adenocarcinoma Cells in the Brain

Cerebellar tumor (20x magnification) - metastatic adenocarcinoma with features similar to the gastroesophageal junction tumor.

## Discussion

### Epidemiology

Current consensus-based guidelines for staging, such as those published by the National Cancer Comprehensive Network and European Society for Medical Oncology, do not recommend routine pretreatment brain imaging for patients with esophageal or esophagogastric junctional cancers since brain metastasis is considered uncommon in these patients.<sup>13-14</sup> It is not considered to be cost-effective or necessary as part of the initial staging evaluation or subsequent surveillance unless symptoms or signs raise suspicion for brain metastases. Brain metastases are now being encountered more commonly than previously appreciated however, perhaps due to improved survival in patients with esophageal cancer as well as advanced neuroimaging techniques.<sup>15</sup>

In more contemporary esophageal cancer cohorts with higher percentages of AC, the incidence of brain metastases has been reported to be as high as 13%.<sup>16</sup> In a large retrospective study by Harada and others, the rate of brain metastases in upper gastrointestinal cancer was highest among patients with proximal esophageal AC. Siewert type I lesions (epicenter of lesion 1 to 5 cm above GEJ) and presence of lymph node metastases were independent risk factors for brain metastases in these patients.<sup>17</sup> Our patient initially presented with a distal esophageal AC (Siewert type II, epicenter of lesion up to 1 cm above and 2 cm below GEJ) but was found to have lymph node metastases at the time of surgery which likely increased his risk of brain metastases.

Nobel and her colleagues defined IBMs as truly isolated recurrences of esophageal cancer in patients who have achieved complete pathologic response after neoadjuvant therapy or the first observed site of widespread distant metastases in those with residual nodal disease.<sup>18</sup> They further suggested that patients who receive neoadjuvant therapy and achieve a complete pathologic response would benefit most from brain imaging, both preoperatively and with routine surveillance, due to the increased likelihood of IBM.<sup>18</sup> Our patient was found to have lymph node-positive disease after neoadjuvant therapy, but a CT C/A/P at the time of his brain metastasis did not reveal any evidence of concurrent systemic metastases. This finding supports the suggestion that these patients should receive brain imaging, both preoperatively and with routine surveillance.

Welch and others reported that the median time to diagnose brain metastasis from the original diagnosis of esophageal cancer was 11 months.<sup>11</sup> In another study by Kothari et al, the median latency after primary diagnosis was 14 months, ranging from 0 to 70 months.<sup>12</sup> The majority of these lesions (60%) were supratentorial, which includes the cerebrum.<sup>12</sup> In a case report by Tuna and others, a patient developed a cerebellar metastasis from esophageal cancer within 2 years of her primary diagnosis.<sup>15</sup> Interestingly, our patient developed neurologic symptoms and a new cerebellar lesion almost 5 years after his original diagnosis.

### Prognosis

Nobel and her colleagues found that the median overall survival of patients with isolated brain metastases was approximately 0.95 years, but was significantly higher for those with a pathologic complete response to neoadjuvant therapy than those without (median, 1.56 vs 0.66 years).<sup>18</sup>

In their study, Harada and others found that the median overall survival of patients with brain metastases was only 1.16 years but was more favorable for patients with a solitary brain lesion with no other distant metastasis and who underwent surgery or stereotactic radiosurgery for treatment of the lesion.<sup>17</sup> Welch and colleagues observed that survival was superior for patients who initially had surgical resection of brain lesions compared to patients treated with whole-brain radiotherapy or stereotactic radiosurgery alone.<sup>11</sup> Song and others also reported that a solitary brain lesion and surgical treatment of the lesion provide a good prognosis.<sup>19</sup>

Although our patient had residual nodal disease after neoadjuvant therapy, he did present with a solitary brain lesion which was surgically treated and had no concurrent systemic metastases, which are all better prognostic indicators.

### Conclusion

This case illustrates the potential for esophageal adenocarcinoma to present as an isolated brain metastasis several years after treatment of the primary lesion and subsequent clinical remission. The overall incidence of esophageal cancer-related brain metastases appears to be rising. Further studies are needed to determine whether MRI brain should now be considered part of routine staging and surveillance protocols for esophageal adenocarcinoma after diagnosis of a primary tumor.

Siewert-Stein Classification Type	Description
Type I	Adenocarcinoma of the distal esophagus (epicenter of lesion 1 to 5 cm above gastroesophageal junction [GEJ])
Type II	Adenocarcinoma of the cardia (epicenter of lesion up to 1 cm above and 2 cm below GEJ)
Type III	Sub-cardial type adenocarcinoma (epicenter of lesion 2 to 5 cm below GEJ)

Source: Siewert JR, Stein HJ. Classification of the adenocarcinoma of the oesophago-gastric junction. *Br J Surg.* 1998;85(11):1457.

TNM Classification	Description
Tumor (T)	Has the tumor grown into the wall of the esophagus?
Node (N)	Has the tumor spread to the lymph nodes?
Metastasis (M)	Has the cancer spread to other parts of the body?

Source: American Cancer Society. Esophageal Cancer Stages. Available at <https://www.cancer.org/cancer/esophagus-cancer/detection-diagnosis-staging/staging.html>.

Esophageal Adenocarcinoma stage	Description
Stage 0	The cancer is only in the epithelium (top layer of cells lining the esophagus)
Stage I	The cancer is growing into the lamina propria or muscularis mucosa (tissue under the epithelium, submucosa, or muscularis propria (thick muscle layer))
Stage II	The cancer is growing into the muscularis propria and is poorly differentiated (high grade), has spread to 1 or 2 nearby lymph nodes, or is growing into the adventitia (outer layer of the esophagus)
Stage III	The cancer has spread to no more than 6 lymph nodes or is growing into the pleura (the thin layer of tissue covering the lungs), the pericardium (the thin sac surrounding the heart), or the diaphragm (the muscle below the lungs that separates the chest from the abdomen) and has spread to no more than 2 nearby lymph nodes.
Stage IV	The cancer is growing into the trachea (windpipe), the aorta (the large blood vessel coming from the heart), the spine, or other crucial structures and has spread to no more than 6 nearby lymph nodes or has spread to 7 or more nearby lymph nodes

Source: American Cancer Society. Esophageal Cancer Stages. Available at <https://www.cancer.org/cancer/esophagus-cancer/detection-diagnosis-staging/staging.html>.

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## Conflict of Interest

None of the authors identify a conflict of interest.

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