Multidisciplinary Management of a Rare Case of Esophageal Adenocarcinoma with Cardiac, Pulmonary, Liver, Adrenal Gland and Brain Metastasis

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Abstract

We report the case of a 48-year-old gentleman affected by diffuse metastatic gastroesophageal junction (GEJ). Positron emission tomography (PET) scan demonstrated diffuse metastatic disease involving brain, heart, lungs, liver and adrenal glands. Transthoracic echocardiogram showed a mass in the left ventricular apex measuring 2.46 cm × 1.32 cm. Cardiac Magnetic resonance imaging (MRI) showed 2.3 cm mass in the apex of the left ventricle. Peripheral blood circulating tumor DNA (ctDNA) analysis confirmed dissemination of cancer and showed mutations in TP53, AR, PIK3CA, and Erbb2 amplification. Combination chemotherapy consisting of trastuzumab, capecitabine and oxaliplatin was initiated with a significant reduction of tumor markers: CEA from 60.7 to 19.7 ng/mL (67.5%) and CA19-9 from 2104 to 139 Units/mL (93.4%). A repeated PET scan demonstrated resolution of FDG avidity of left ventricle/pericardium, decreased avidity and size of adrenal gland masses, lung nodules and primary esophageal mass. We reviewed and summarized the recent literatures regarding the clinical presentations, diagnostic tools, tumor histology, treatment modalities and clinical prognosis of cardiac metastases from esophageal cancer. This report also highlights the potential role of ctDNA as a cost effective marker in the management of metastatic esophageal cancer.

Keywords: Esophageal adenocarcinoma; Adenocarcinoma of the gastroesophageal junction (GEJ); Multidisciplinary team; Cardiac metastasis; Circulating tumor DNA (ctDNA)

Introduction

Esophageal cancer is relatively uncommon in the United States, with 16,910 new cases and 15,690 deaths anticipated in 2016 [1]. The major risk factors for esophageal adenocarcinoma include Barrett’s esophagus, gastroesophageal reflux, tobacco use and obesity [2]. The overall 5-year survival rate of patients diagnosed with esophageal cancer ranges from 15% to 25% [3]. Cases of cardiac metastasis from esophageal cancer are rare, but the incidence of cardiac metastases has risen over the last 30 years, perhaps attributable to increased life expectancy in oncologic patients benefitting from advances in cancer diagnosis and management. We herein report the diagnostic challenge and multidisciplinary management of a rare case of gastroesophageal junction (GEJ) adenocarcinoma, with diffused metastatic disease involving the brain, heart, lungs, liver and adrenal glands.

Case Presentation

A 48-year-old gentleman with a history of Hepatitis C and cirrhosis was referred to oncology for a consultation. He underwent right liver lobe radiofrequency ablation for a liver mass, which was demonstrated by an abdominal CT scan two years ago (Figure 1). Initial differential diagnosis included hepatocellular carcinoma but AFP was within normal range and CA19-9 and CEA were elevated. An impression of metastasis from the gastrointestinal tract was investigated. A PET scan showed focal increased FDG avidity of the esophagus, the left ventricle/pericardium, multiple bilateral pulmonary nodules, and bilateral adrenal gland (Figure 2A and B). An Esophagogastroduodenoscopy was performed, which showed a GEJ mass; and biopsy showed esophageal adenocarcinoma. HER2/neu amplification was demonstrated by fluorescence in situ hybridization (FISH). Adrenal mass biopsy showed metastatic adenocarcinoma, immunohistochemically positive for CDX-2, CK 20, CK7 (focal) and negative for TTF-1.

An Electrocardiogram showed sinus tachycardia with frequent ventricular premature complexes, right bundle branch block with marked T-wave abnormality. A Transthoracic echocardiogram showed a mass in the apical region of the left ventricle measuring 2.46 cm × 1.32 cm (Figure 3A). The estimated ejection fraction was 60-65%. Cardiac MRI showed a 2.3 cm mass in the apex of the left ventricle (Figure 3B). A CT scan of the head revealed a mass in the third ventricle, a left frontal lobe mass and obstructive hydrocephalus (Figure 4A and 4B).

Figure 1: (A) Abdominal CT showing ill-defined arterial enhancing lesion within the right lobe of the liver measuring approximately 3.2 × 2.6 × 2.4 cm. (B) No definitive residual tumor identified after right lobe liver ablation.

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MRI of the brain showed a heterogeneously enhancing T1 hyperintense pineal region mass measuring 1.9 cm × 2.2 cm × 2.0 cm (Figure 4C). Peripheral blood ctDNA analysis showed mutations in TP53, AR, PIK3CA, and Erbb2 amplification. The patient was subsequently seen by a multidisciplinary team that included medical oncologists, radiation oncologists, interventional radiologists, cardiologists, thoracic surgeons and neurosurgeons. After a full recovery from left ventriculoperitoneal shunt for obstructive hydrocephalus, the patient was started on a combination regimen of trastuzumab, capecitabine and oxaliplatin. After the three cycles of chemotherapy, repeated PET-CT scan demonstrated complete resolution of FDG avidity of left ventricle/pericardium, significant decreased avidity and size of adrenal gland masses, esophageal mass (Figure 2C and D) and lung nodules. He also had a significant tumor marker reduction: CEA from 60.7 to 19.7 ng/mL (67.5%) and CA 19-9 from 2104 to 139 Units/mL (93.4%) (Figure 5). Currently, the patient remains active and his treatment is ongoing.

Discussion

The two major subtypes of esophageal cancers are squamous cell carcinoma and adenocarcinoma. Barrett’s esophagus, tobacco use, obesity and gastroesophageal reflux disease (GERD) are associated with an increased risk of esophageal adenocarcinoma. Myocardial metastasis from esophageal cancer is rare [4]. Pericardium and epicardium (53%) are the most common sites of cardiac metastases, followed by myocardium (41%) and endocardium (6%). 33% of metastases invade the left ventricle & left atrium, 22% the right ventricle & right atrium and 7% invade the ventricular septum [5]. The routes of cardiac metastasis include the hematogenous route to the myocardium and endocardium, which is the most common route, the lymphatic route to the pericardium and direct invasion from adjacent tumors [6]. After an extensive literature search, we identified nine reported cases of cardiac metastasis from esophageal cancer (Table 1). All of these reported cases showed a poor prognosis. Surgical resection was performed in two patients (cases 5 and 8) to avoid sudden death due to complete obstruction of the right ventricular outflow tract by the tumor. All previously published cases involved squamous cell carcinoma, but our case involves adenocarcinoma. It seems that the clinical prognosis is usually disappointing regardless of whatever treatment is selected, and patients usually die within one year on an average from diagnosis with cardiac metastasis. Cardiac metastasis presentations include pericardial effusion, pericardial tamponade and arrhythmia. ECG may mimic acute myocardial infarction with ST elevation. Clinicians may raise concerns regarding cardiac metastasis in patients with a history of cancer who present with cardiac symptoms and ECG changes. CT chest, MRI, echocardiography and FDG/PET scans are efficient in diagnosing cardiac metastases.

A multidisciplinary approach in a tertiary cancer center setting is essential for the optimal management of rare and aggressive cancers. Teams of specialists can balance the therapeutic efficacy, side effects
and quality of life to develop the best individualized treatment plan. Davies et al. study also found that a multidisciplinary team approach significantly improves staging accuracy for gastro-esophageal cancers and leads to better management decisions for individual patients [7].

Circulating tumor DNA (ctDNA) is naked tumor DNA present in the plasma, which originates from tumor cells undergoing lysis, necrosis or apoptosis. ctDNA carries tumor-specific sequence alterations, and sequencing could be performed to detect somatic genomic alterations. It is an emerging noninvasive biomarker to monitor tumor dynamics, and leads to better management decisions for individual patients [7].

Prospective trials will be needed to evaluate the clinical utility and cost effectiveness of ctDNA in the management of metastatic esophageal cancer.

### References

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