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Review

Clinicopathologic characteristics of metastatic esophageal carcinoma isolated to the pineal region: A case report and review of the literature

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ABSTRACT

Metastasis to the pineal region is a rare event, and esophageal adenocarcinoma metastatic to the pineal region is exceptionally rare, with only two cases reported in the current literature. Here, we characterize a third case of metastatic esophageal adenocarcinoma to the pineal region, and compare clinicopathological characteristics among all three cases. The three patients were men, with ages at neurological presentation ranging from 48 to 65 years. Time from initial esophageal adenocarcinoma diagnosis to development of neurologic symptoms ranged from 12 to 23 months. Neuroimaging in all cases showed an isolated enhancing pineal region mass with sizes ranging from 1.8 to 2.2 cm. All cases were believed to have local control of esophageal disease prior to metastatic sequela, with initial treatment including esophageal resection with or without chemoradiation therapy. No cases had evidence of primary site disease progression at time of metastatic presentation, nor were there signs of other sites of metastasis. All patients underwent tumor excision and were referred for subsequent radiotherapy. Overall, all three cases demonstrate similar demographics, histology, and clinical presentations. In the appropriate clinical setting it is important to keep esophageal metastasis in the differential diagnosis, particularly in the setting of isolated pineal lesions.

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Contents

1. Introduction

The pineal gland is a unique structure, which lacks a blood brain barrier and is located on the posterior wall of the third ventricle (Dahiya and Perry, 2010). Primary pineal tumors are rare, comprising less than 1% of all primary central nervous system (CNS) tumors (Fauchon et al., 2000) and metastasis to the pineal region is a very rare event estimated to account for only 0.4% of all intracranial metastatic tumors (Nemoto et al., 2013). The most common site of primary origin of a pineal metastasis is lung and the most common histological phenotype seen is small cell carcinoma of the lung, followed by squamous cell carcinoma and adenocarcinoma (Kakita et al., 2003). The next most common sites of primary origin of pineal metastasis are breast, malignant melanoma and less frequently kidneys and rectum (Kakita et al., 2003). Clinical characteristics, treatment approaches and diagnostic approaches for metastatic pineal gland tumors are not extensively characterized in the literature due to rarity. Due to the anatomic and histologic complexity and high vascularity of the pineal region, approximately 11% of biopsies are either non-diagnostic or misdiagnosed (Konovalov and Pitskhelauri,

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2003), which highlights the complexity of both obtaining tissue from this region and making an accurate histologic diagnosis.

Esophageal carcinoma is relatively uncommon in the United States but is a fatal disease in the majority of cases affecting men four times more than women (Hur et al., 2013). The overall 5-year survival rate for patients with esophageal adenocarcinoma in the United States is approximately 17%, which is slightly higher than the rate for patients with squamous cell carcinoma (Rustgi and El-Serag, 2015). Adenocarcinoma is the most common histologic variant in the United States followed by squamous cell carcinoma and over the past three decades, the rates of esophageal squamous cell carcinoma have declined, while those of esophageal adenocarcinoma have been progressively increasing (Hur et al., 2013). The most common metastatic sites are retroperitoneal or celiac lymph nodes, liver and lung with brain metastasis only very rarely reported in the literature (Irie et al., 1978).

Metastasis to the pineal region is a clinically significant event, as potential sequelae include hydrocephalus and brainstem compression, and prognosis is generally poor with milder manifestations including headache, encephalopathy or Parinaud syndrome (Lassman et al., 2006). When pineal metastases do occur, it tends to be when the primary pathology is either in remission or unidentified. An extensive review of the English speaking literature revealed only three cases of esophageal cancer (two adenocarcinoma and one neuroendocrine carcinoma) metastatic to the pineal region (Matsuda et al., 2014; Schuster et al., 1998), confirming that esophageal adenocarcinoma metastases to the pineal region are a rare subset of an infrequent entity. Here we describe a patient with a history of esophageal adenocarcinoma presenting with a newly diagnosed pineal gland mass, ultimately determined to be metastatic disease. This case highlights the importance of keeping a metastatic process in the differential diagnosis for pineal masses, even if the primary cancer is historically unlikely to present there.

2. Case presentation

The patient was a 65-year-old man with a history of esophageal adenocarcinoma diagnosed 12 months prior to neurological presentation, status-post-neoadjuvant chemoradiation with a clinically noted marked treatment response. The patient developed a progressive change in mental status over a course of approximately 5 weeks prior to presentation, which started with jaw clenching followed by right upper extremity, gait unsteadiness and confusion. He was found down and taken to an outside hospital where imaging showed obstructive hydrocephalus due to a pineal mass and the patient was transferred to our institution for further management.

Brain magnetic resonance imaging (MRI) demonstrated a 2.2 cm heterogeneously enhancing mass centered within the pineal gland (Fig. 1). There was associated obstructive hydrocephalus. In retrospect, there were two questionable areas of linear enhancing foci (each measuring 3 mm) within the medial and right superior cerebellar folia, the significance of which are unclear.

Excision of the pineal mass, along with placement of an extra-ventricular drain, was performed via right frontal craniotomy with a transcortical and transchoroidal approach to the posterior third ventricle. Intraoperative pathology consultation of the pineal mass demonstrated predominantly necrosis with few clusters of a high-grade epithelial neoplasm (Fig. 2). Permanent section histology of the pineal mass showed a moderately-differentiated metastatic adenocarcinoma, with morphology similar to the primary esophageal site and a consistent immunophenotype with strong cytoplasmic cytokeratin 7 (CK7) immunoreactivity (Fig. 2). The patient underwent further staging post-operatively, and no additional metastatic disease was identified. The patient was subsequently referred for radiotherapy.

3. Discussion

This case represents a rare disease, esophageal adenocarcinoma, metastatic to an exceedingly rare site in the CNS, the pineal region. In our review of the literature, only three other cases of esophageal adenocarcinoma have been described in the literature, and only two of those had a similar adenocarcinoma phenotype. With our case, and the two reported cases in the literature, all three patients with metastatic esophageal adenocarcinoma to the pineal region were men, with the age at time of initial neurological presentation ranging from 48 to 65 years (Table 1) (Schuster et al., 1998). In contrast, the single case of esophageal neuroendocrine metastasis to the pineal region occurred in a 68-year-old woman (Matsuda et al., 2014). The time from initial esophageal adenocarcinoma diagnosis to time of the development of neurologic symptoms in our case was only 12 months, which is shorter than the time intervals reported in the other two metastatic adenocarcinoma cases which were 18 months and 23 months (Schuster et al., 1998). The metastatic neuroendocrine tumor had a similar time interval between diagnosis and neurological presentation, which was also 12 months (Matsuda et al., 2014). Neuroimaging in all cases showed an isolated enhancing pineal region mass and the size of the metastatic adenocarcinoma pineal cases ranged from 1.8 to 2.2 cm (Matsuda et al., 2014; Schuster et al., 1998). The size of the neuroendocrine tumor metastasis was not reported in the literature. All cases were believed to have local control of esophageal disease prior to metastatic sequela, with initial treatment including esophageal resection with or without chemoradiation therapy and none of the cases had evidence of primary site disease progression at the time of metastatic presentation, nor was there evidence of other sites of metastasis (Matsuda et al., 2014; Schuster et al., 1998). All patients underwent pineal tumor resection and were referred for subsequent radiotherapy. It is worth noting that there are no reported cases of esophageal squamous cell carcinoma, the predominant histological subtype of esophageal carcinoma, metastatic to the pineal region (Zhang, 2013).

This is a very rare case of esophageal adenocarcinoma metastatic to the pineal gland. Despite similar neuroradiology characteristics, pineal region tumors are extremely heterogeneous with respect to their histopathology, natural history and response to therapy. The prognosis of

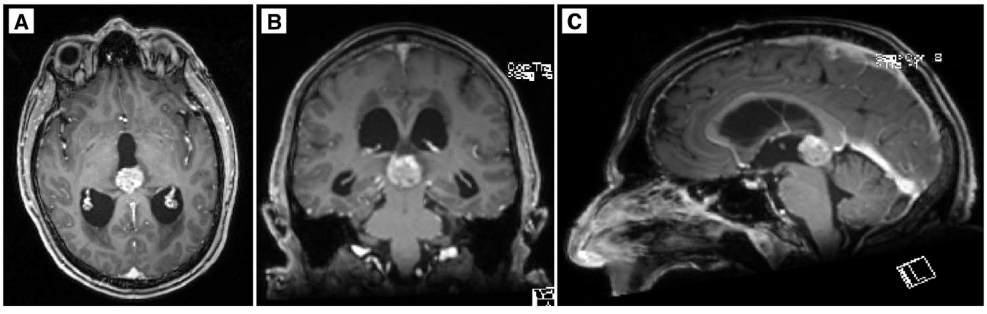

Fig. 1. Radiographic characteristics of the pineal metastasis. A) Axial, B) coronal, and C) sagittal magnetic resonance images of the brain show a 2.2 cm, heterogeneously enhancing mass isolated to the pineal region in the brain.

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