Scalp Metastasis From Esophageal Adenocarcinoma

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There are few reported cases of cutaneous metastases of esophageal carcinoma, especially of esophageal adenocarcinoma, but reports may become more common as the incidence of esophageal cancer increases. We present a case of a 67-year-old man with metastatic esophageal cancer in the scalp. Clinical and histologic findings are discussed, and recommendations for clinicians are suggested.

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Esophageal carcinoma has one of the highest mortality rates of all cancers. Less than half of patients survive one year after diagnosis,[1] and the 5-year survival rate is less than 10%.[2] The 2 most common types of carcinomas arising in the esophagus are squamous cell carcinoma and esophageal adenocarcinoma. Squamous cell carcinoma accounted for 90% of esophageal carcinoma before 1970.[2] However, the incidence of esophageal adenocarcinoma has been rapidly rising. Today, at least half of esophageal carcinomas are found to be esophageal adenocarcinoma.[3,4] Cutaneous metastases of esophageal adenocarcinoma are extremely rare, and case reports of their spread to the scalp are exceedingly rare. However, with both the increasing incidence of esophageal carcinoma (particularly adenocarcinoma) and the expansion of therapeutic options, metastatic esophageal adenocarcinoma has become more common; and skin metastases also may become more frequent. We report a patient with a history of treated esophageal adenocarcinoma who was diagnosed with metastatic esophageal adenocarcinoma in the scalp. We also discuss the clinical and histopathologic differential diagnoses of our patient's scalp tumors.

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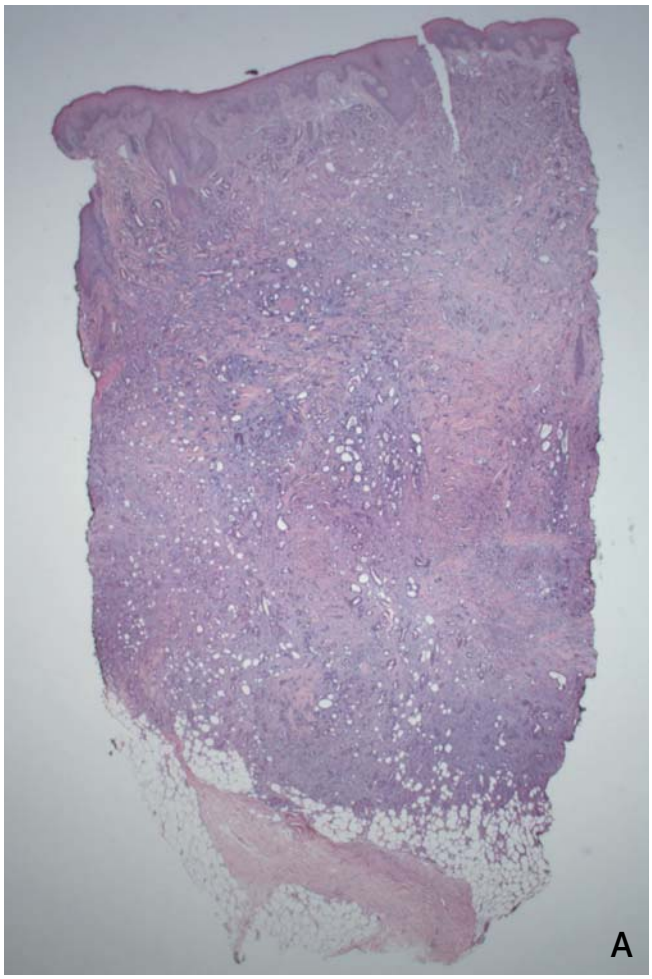
Case Report

A 67-year-old man presented with symptoms of fatigue, anorexia, and weight loss and was admitted for the evaluation and treatment of profound hyponatremia. His medical and surgical histories were significant for primary adrenal insufficiency; esophageal adenocarcinoma treated 2 years earlier with a combination of surgery, chemotherapy, and radiation (with negative surgical margins and lymph node status at that time); status post splanchnicectomy for chronic abdominal pain; a left bundle branch block revealed by an electrocardiogram; and hyperlipidemia. The patient was a former smoker but reported no alcohol or drug use.

Pertinent findings from the patient's physical examination included a 2×3-cm, erythematous, indurated, firm nodule on his left occiput and a similar 0.5-cm nodule on his right parietal region, as well as a 4.5×4-cm abdominal mass just below the xiphoid process. Neurologic and cardiovascular test results were unremarkable, and there was no palpable adenopathy.

Laboratory test results revealed a complete adrenal insufficiency and hyponatremia (serum sodium level, 118 mmol/L). Results of the computed tomography scan revealed bilateral renal masses, an abdominal wall mass slightly inferior to the xiphoid process, and bilateral adrenal masses. Although the results of magnetic resonance imaging of the patient's head showed no pathologic findings, scalp and abdominal biopsies were performed. Differential clinical diagnoses for these nodules included pilar cyst, metastasis of a nonspecified primary eccrine adenocarcinoma, epidermoid cyst, steatocystoma, lipoma, dermoid cyst, glioma, encephalocele, and hemangioma. The patient's blood pressure was normalized with demeclocycline, and then he was discharged.

Results of the initial pathology review suggested a differential diagnosis of microcystic adnexal carcinoma or metastasis. Findings of histologic



An infiltrating gland-forming process replaces the entire dermis without a noticeable epidermal component. There is early involvement of the subcutis (A). The neoplasm is an adenocarcinoma, poorly differentiated with marked gland formation, foci of perineural invasion, and dissection between collagen bundles. The morphology was compatible with the patient's primary adenocarcinoma of the esophagus. The cells were tall and columnar with a few signet-ring foci dispersed throughout (B)(H&E, original magnifications ×2 and ×40, respectively).

staining of tissue sections showed a neoplasm with diffuse infiltration of the dermis by ducts and glandlike structures within a desmoplastic stroma (Figure, A). The neoplastic mass was more prominent in the deep dermis, with no visible continuity of neoplastic islands with the surface epidermis or follicular epithelium. The mitotic rate was brisk. High-power magnification of the specimen revealed that the cells were tall and columnar with a few signet-ring foci dispersed throughout (Figure, B). Pertinent additional histologic results were negative for S100 protein, mucin, and vimentin and showed positivity for focal carcinoembryonic antigen. These results, coupled with the appearance of a neoplasm on hematoxylin-eosin (H&E) staining, indicated a metastatic lesion and not a primary adnexal carcinoma. Furthermore, the abdominal mass was reported to be a clinically metastatic adenocarcinoma infiltrating fibroconnective tissue.

Comment

Esophageal adenocarcinoma chiefly occurs in middle-aged and elderly white men, with a male-female ratio of 7:1 and a white-black ratio of 4:1; the disease is now in the top 15 cancer types affecting white men in the United States.[5] Almost all cases of esophageal adenocarcinoma appear to arise from Barrett esophagus,[6] a premalignant noninvasive condition that is the most significant risk factor for esophageal adenocarcinoma. Barrett esophagus is a complication of chronic gastroesophageal reflux whereby the normal stratified squamous epithelium at the esophageal squamocolumnar junction is displaced by columnar epithelium of gastric or intestinal type. The disorder is found in about 10% of patients who undergo endoscopy for gastroesophageal reflux symptoms.[7] The development of esophageal adenocarcinoma from Barrett esophagus results from a progression of changes within the epithelium known as the metaplasia-dysplasia-adenocarcinoma sequence.[8] The estimated incidence of esophageal adenocarcinoma in patients with Barrett esophagus is 0.2% to 2.1% per year.[9] In addition to Barrett esophagus, other risk factors for esophageal adenocarcinoma are obesity,[10] smoking,[11] increased esophageal acid exposure, use of drugs that decrease the lower esophageal sphincter pressure[10] (eg, nitroglycerin, benzodiazepines, anticholinergics, aminophylline), and status post cholecystectomy.[12]

Because of its close association with Barrett esophagus, esophageal adenocarcinoma usually arises in the distal esophagus, with metastases

first appearing in the celiac and perihepatic lymph nodes.[13] Additionally, although the pathogenesis of esophageal adenocarcinoma is unclear, as is the case with many cancers, there also are genetic changes. p53 abnormalities are found in more than half of esophageal adenocarcinoma cases,[14] and approximately 20% of cases involve amplification of the c-erbB-2 oncogene.[15]

Early esophageal adenocarcinoma can be asymptomatic or a reflection of gastroesophageal reflux disease and its complications. Patients with more advanced cases can experience progressive solid food dysphagia, retrosternal discomfort, and iron deficiency anemia from chronic gastrointestinal blood loss. Patients may even develop tracheobronchial fistulas. Progressive weight loss, bleeding, chest pain, and vomiting are often the presenting symptoms.

The mainstay of diagnosis is endoscopy, with confirmation by histopathologic examination. There are no immunohistochemical features that are diagnostic for esophageal adenocarcinoma, but there are patterns that are suggestive. In addition to epithelial markers AE1/AE3 and epithelial membrane antigen, which are expressed by a large number of malignant epithelial neoplasms, esophageal adenocarcinoma also expresses cytokeratin (CK) 20 and CK7.[14] CK20 is expressed by general gastrointestinal tract tumors; however, unlike most other gastrointestinal tract tumors, CK7 also is expressed in Barrett esophagus and esophageal adenocarcinoma.

Physicians consider treatment of esophageal cancer a palliative practice and cure a chance occurrence. However, when patients with esophageal adenocarcinoma are treated successfully with chemotherapy and radiation therapy followed by surgical excision, esophageal adenocarcinoma usually does not recur locally but presents with metastatic disease, as in our patient.[6] Therefore, we recommend that metastasis be considered a differential diagnosis of any unusual cutaneous mass or nodule in patients with a history of esophageal adenocarcinoma, even those persons in long-term remission.

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