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Scalp Metastasis as the First Presentation of an Underlying Aggressive Pancreatic Cancer

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Abstract

Pancreatic ductal adenocarcinoma, an extremely aggressive cancer, has high metastatic potential. Cutaneous metastasis is very uncommon, representing only <10% of all cases, presenting mostly around the umbilical region. Non-umbilical metastasis is even rarer, and the significance remains unknown. In this article, we describe a case of a 76-year-old gentleman who initially presented with an asymptomatic scalp lesion, which on biopsy revealed metastatic adenocarcinoma of pancreatic origin. Detailed workup revealed extremely high tumor burden with metastases involving muscles, subcutaneous tissues, bone, lung, spleen, liver, and colon. Cutaneous involvement in pancreatic cancer represents poor survival with widespread dissemination of the disease. The involvement of some sites and not others and the extreme degree of aggressiveness might reflect subgroups of this cancer with different molecular biology. Identifying these groups may have utility in determining prognosis and stratifying treatment for patients. This will hopefully translate into better diagnostic tests and therapies in the near future.

Keywords

pancreatic cancer, metastatic, PDL1 cancer, scalp metastasis

Introduction

Pancreatic cancers are highly lethal malignancies ranking fourth in cancer-related mortality in the United States.[1] As per the American Cancer Society, for all stages of pancreatic cancer combined, the 1-year relative survival rate is 20% and the 5-year rate is 5%. Late presentation, advanced stage, and lack of effective therapies confer a poor prognosis.[2] The most frequent sites of distant metastasis include liver (76% to 94%), followed by peritoneum (41% to 56%), abdominal lymph nodes (41%), and lung (45% to 48%).[3] Metastatic spread to other organs like skin, bone, brain, lung, and muscles is rare. Non-umbilical cutaneous metastasis may reflect wide dissemination of disease translating to poor overall survival. Involvement of multiple unusual sites of metastases is uncommon and may reflect subgroups of these cancers with a different molecular signature. Herein we present an aggressive PDL-1 upregulated pancreatic cancer presenting with multiple unusual sites of metastasis.

Case Presentation

A 76-year-old gentleman with a past medical history of hypertension, alcohol abuse, and ex-smoker presented initially to the dermatology clinic with a progressively enlarging lump over his frontal scalp for 4 to 6 weeks (Figure 1). He was hemodynamically stable, and his physical examination was unremarkable except for a 2 × 2 cm lump over the frontal scalp. His complete blood count, renal and liver functions were within normal limits. Skin biopsy revealed dermal involvement of irregularly shaped aggregates of epithelium arranged as glandular structures lined by cells characterized by enlarged vesicular and hyperchromatic nuclei with conspicuous nucleoli, which was consistent with metastatic adenocarcinoma favoring primary gastrointestinal origin as illustrated in Figure 2. Further workup with esophagogastroduodenoscopy and colonoscopy did not reveal any abnormal findings. Positron emission tomography computed tomography scan revealed a hypermetabolic 3 × 2 cm lesion

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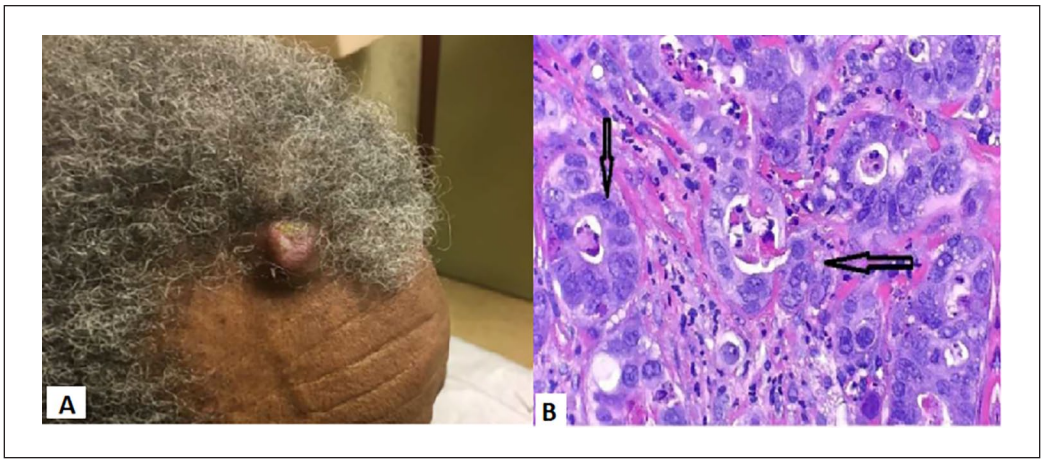

Figure 1. (A) Cutaneous metastatic scalp lump at presentation. (B) Skin biopsy showing pancreatic adenocarcinoma (dermal involvement of irregularly shaped aggregates of epithelium arranged as glandular structures lined by cells characterized by enlarged vesicular and hyperchromatic nuclei with conspicuous nucleoli).

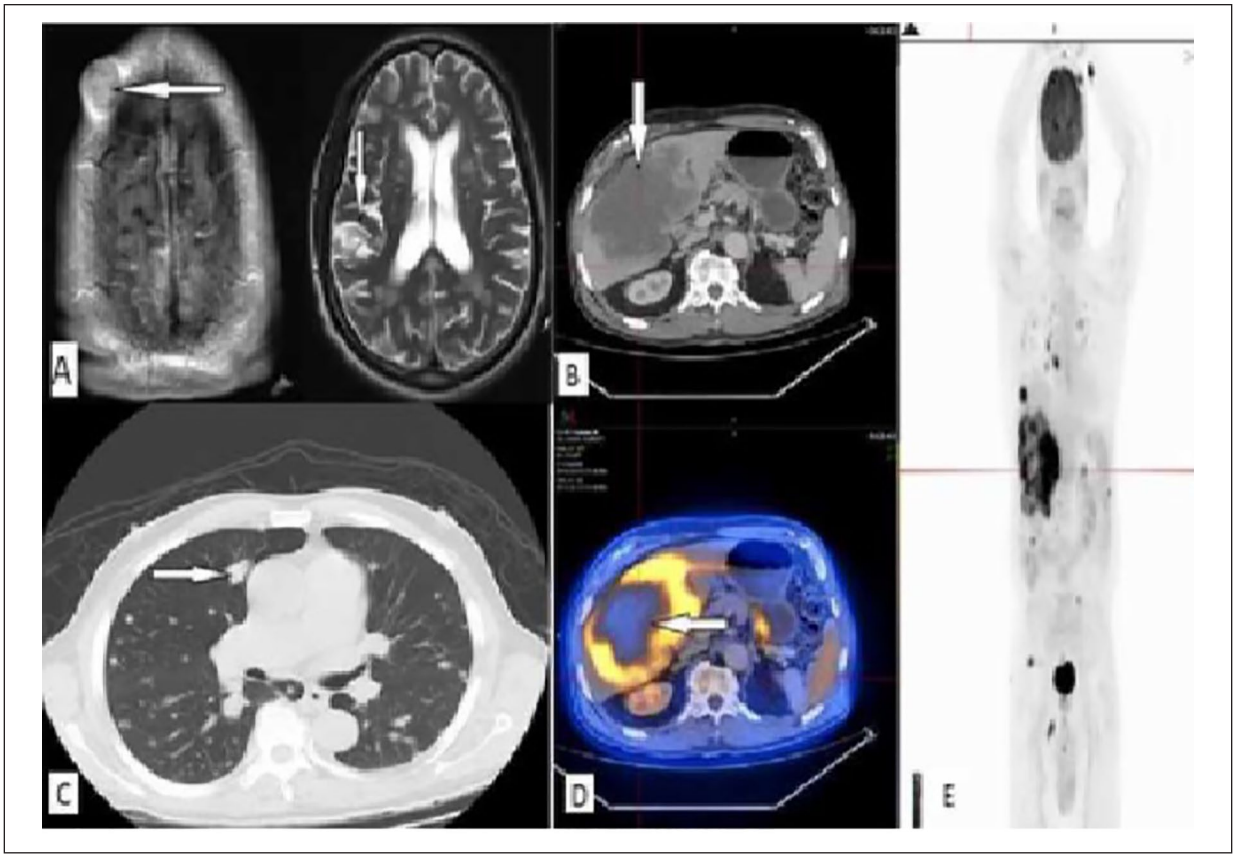

Figure 2. Extensive metastatic lesions of unusual sites in computed tomography (CT) scans—skull, brain (A), liver (B, D), and lung (C). Positron emission tomography CT showing extensive metastatic spread throughout the whole body (E).

over the pancreatic head with multiple metastatic lesions involving the skull bones, frontal scalp tissue, occipital lobe of the brain, subcutaneous tissue of the neck as well as multiple lesions in lung, ribs, paraspinal muscles, liver, colon, spleen, psoas, and gluteus maximus muscle. His CA 19-9 was >9000 U/mL, consistent with the extensive metastatic disease. Next-generation sequence analysis of the tumor revealed >10 different mutations including PDL-1/PDL-2

amplification; CDKN2A/2B loss; JAK2 amplification; PIK3CA amplification; SMAD4, SOX2, TET2, and TERC amplification; and TP53 and PAX5 mutations.

Even though he was asymptomatic at presentation, he very rapidly deteriorated and was not a good candidate for systemic chemotherapy. He subsequently died within 6 weeks of presentation. This case represents a subgroup of an aggressive pancreatic cancer with a unique molecular signature presenting with multiple unusual metastatic sites.

Discussion

Cutaneous metastasis in pancreatic cancer is rare with <25 cases reported in the literature. Non-umbilical cutaneous metastasis as an initial presentation is a rare presentation of pancreatic cancer. Cutaneous metastasis presents later during the disease and rare to be a first presentation, as in our case.[4]

Even though pancreatic cancer commonly metastasizes to liver, peritoneum, abdominal lymph nodes, and lung, it is still not uncommon to find the metastatic disease in virtually every organ site, including the brain, gallbladder, heart, colon, kidneys, ovaries, uterus, urinary bladder diaphragm, pericardium, seminal vesicles, skin, thyroid, testis, spleen stomach, spleen, and testis. Small pancreatic lesions even as small as 2 cm can present with metastasis. Studies conducted by Kamisawa et al indicated certain features to be more commonly found in pancreatic cancers with high metastatic potential including high-grade anaplastic features and absence of E-cadherin expression.[5] Next-generation sequencing analysis of our patient revealed amplification of PDL-1, PDL-2, and JAK2 genes. Ikeda et al previously described PDL-1 upregulation in solid cancers through JAK-STAT signaling when there is a simultaneous amplification of PDL1 and JAK2.[6] The upregulated PDL1 expression remains to be a poor prognostic marker as per studies done by Mu et al.[7] PDL-1 (CD274) amplification is very rare in pancreatic malignancy and has been reported in <1% of all cases. It is associated with advanced stage, poor differentiation, and poor prognosis. JAK2 mutations are usually common in myeloproliferative disorders rather than solid tumors.

Various clinical studies have reported improved survival with PDL-1 antibodies as well as JAK2 inhibitors in patients presenting with amplification of these genes.[8-10] However, they are still being studied only in preclinical models of pancreatic cancer, due to the rarity of its occurrence.

Current treatment options for metastatic and locally advanced pancreatic cancers representing 80% of all cases have not shown increased survival for more than a year.[11] Despite significant progress in diagnostic imaging techniques, early diagnosis of pancreatic cancers always remains a challenge. The role of PDL-1 inhibitors and its effectiveness in pancreatic cancers is yet to be studied. The unique presentation of multiple unusual sites of metastasis seen in our patient could be attributed to the unique molecular signature of his tumor, which is rarely seen in pancreatic cancers. This case was presented as a poster in the ACG Annual Scientific Meeting in Philadelphia in 2018.[12]

Author Contributions

PR collected data and wrote the manuscript. GJ supervised the writing of the manuscript. LB collected the data and discussed the content of manuscript. All authors read and approved the final manuscript.

Declaration of Conflicting Interests

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Written informed consent was obtained from a legally authorized representative for anonymized patient information to be published in this article.

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