Case Report

Cutaneous Metastases of Ampullary Adenocarcinoma: Case report and literature review

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Abstract
Cutaneous metastases occur in 1% to 10% of patients with metastatic disease. Their recognition is important due to prognostic implications. The most frequently observed cutaneous metastatic cancers are breast, lung, colon, and melanoma with a wide variation in morphology of lesions, and generally they imply a poor prognosis. We present a rare case of a 64-year-old woman with cutaneous metastases on the scalp from ampullary carcinoma and long-term follow-up.

Key words: Cutaneous metastasis, cancer, ampullary carcinoma.

Case report
A 64-year-old woman known for stage IIA (pT3 pN0 M0) ampullary adenocarcinoma with pancreatobiliary phenotype, underwent Whipple procedure in September 2014 and received gemcitabine as adjuvant chemotherapy. In July 2018, she developed systemic recurrence with mediastinal disease and superior vena cava syndrome and received first-line palliative chemotherapy with cisplatin/5-fluorouracil (5FU), the best response was stable disease. In October 2020 she presented with a 2-month history of rapidly growing scalp lesions on the occipital and left parietal region. Two erythematous nodules, with mélècere crust and firm consistency on palpation were found, the largest one measured 2 cm. (Image1a, b) Dermoscopy revealed a central ulcer, white and pink areas some structureless areas, serpentine, comma-shaped, and arborizing vessels (Image1c). A skin biopsy showed nests of moderately differentiated neoplastic cells arranged in a glandular pattern (Image1d,e). Immunohistochemical analysis was positive for CK2, CK19, CDX2, but negative for CK20, compatible with pancreatobiliary carcinoma (Image1f,g,h). After skin involvement was confirmed, she started second-line chemotherapy with irinotecan.

Discussion
Ampullary carcinoma represents less than 1% of gastrointestinal cancers. Curative surgery is possible for those with localized disease, however, most of the patients will eventually develop recurrent disease. Palliative chemotherapy has variable response rates ranging from 10-40% and an overall survival of 8.1-20.4 months1.

Incidence depends upon the particular malignancy. The highest incidence is observed in metastatic melanoma in which up to 45% of patients can develop skin metastases2. They may appear as multiple or single nodules, plaques, ulcers, inflammatory or sclerodermoid lesions, it may be the first sign of recurrent disease, with 75% of patients also having visceral metastases.3 Schulman et al4 recently reported the variation in the local immunologic environment. They demonstrated that regulatory T cell (Treg) density and CD4:CD8 ratio vary across regions. Since Tregs are localized in hair follicles, areas with relatively high Treg density and increased CD4:CD8 ratio include the head and neck. These areas may be permissive to tumor growth, making them sites most frequently affected per surface area unit. Dissemination may occur hematogenously or through the lymphatics, it has been suggested that the vascularity of the scalp and possible dissemination through the vertebral venous system may be contributing factors.3

On dermoscopy skin metastases show a high prevalence of a vascular pattern composed mainly by serpentine or linear irregular vessels, followed by arborizing vessels, and polymorphous pattern, consistent with the ability of a tumor to produce and recruit new capillaries.3

There are only a few cases of cutaneous metastases of ampullary carcinoma, most of them involved the head and neck except for the case reported by Cho et al5, in which the thumb and middle finger were affected. Recently, Fernandez-Flores6 described the case of a 57-year-old woman with a scalp metastasis diagnosed 4 years before, she died 2 years after the diagnosis from widespread disease.

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Figure 1a: Image on the occipital region with erythematous nodule diameter of 2 cm, well defined borders with meliceric and hematic crust and firm consistency and irregular on palpation.

Figure 1b: Dermatoscopy, central ulcer, white and pink areas some structureless areas, as well as serpentine, comma-shaped, and arborizing vessels.

Figure 1c: Biopsy, nests of moderately differentiated neoplastic cells arranged in a glandular pattern.

Figure 1d: Close up of nests of moderately differentiated neoplastic cells.

Figure 1e: CD20 positive

Figure 1f: CK7 positive

Figure 1g: CDX2 positive

Table 1: Cases reported by the literature review.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/Sex</th>
<th>Location</th>
<th>Immunohistochemistry</th>
<th>Time from initial diagnosis</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cho et al⁸</td>
<td>71/M</td>
<td>Left thumb and right middle finger</td>
<td>TTF-12, PSA2, MUC22, CK202, MUC1+, CK7+</td>
<td>27 months</td>
<td>Death 8 months after cutaneous metastasis</td>
</tr>
<tr>
<td>Liu et al¹¹</td>
<td>55/M</td>
<td>Neck (surgical scar), chest wall, flank, and back</td>
<td>CK7+, CK202</td>
<td>12 months</td>
<td>Death 8 months after cutaneous metastasis.</td>
</tr>
<tr>
<td>Bansal et al¹²</td>
<td>45/F</td>
<td>Forehead</td>
<td>-</td>
<td>12 months</td>
<td>Lost to follow-up after 6 months</td>
</tr>
<tr>
<td>Current case</td>
<td>64/F</td>
<td>Occipital and parietal scalp</td>
<td>CK2+, CK19+, CDX2+, CK20-</td>
<td>50 months</td>
<td>Alive in palliative radiotherapy, 22 months after cutaneous metastasis</td>
</tr>
</tbody>
</table>

Cutaneous metastasis can cause considerable morbidity secondary to infection, bleeding, disfigurement and pain. Systemic therapy alone often has limited efficacy but skin directed therapy may be potentially useful for symptom palliation, although it will not change the prognosis.

In our case, cutaneous metastases were seen 50 months after initial diagnosis. It suggests that skin involvement could see more frequently in long-term survivors. This emphasizes the importance of dermatological examination in these patients in order to identify and treat appropriately.
In conclusion, we presented a case with unusual metastatic spread in a patient with ampullary carcinoma. Despite the rarity, it is relevant.

Reference