

# Cutaneous Metastasis of a Pulmonary Carcinoid Tumor

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## PRACTICE POINTS

- Cutaneous metastases of carcinoid tumors are extremely rare, and clinical presentation can vary. They can present as firm papules ranging in color from pink to brown, can be painful, and could occur at any site.
- It is imperative to obtain an accurate clinical history and use the appropriate immunohistochemical panel to correctly diagnose cutaneous metastases of carcinoid tumors.
- Neoplasms within the gastrointestinal tract commonly present with carcinoid syndrome, but it also has been observed with bronchial carcinoid tumors and with metastatic disease.

*Carcinoid tumors are uncommon neoplasms of neuroendocrine origin that generally arise in the gastrointestinal or bronchopulmonary tracts and typically are characterized by an indolent clinical course. Metastases from these primary neoplasms more commonly affect the viscera, with rare reports of cutaneous metastases to the skin. We report the case of a patient with a cutaneous carcinoid metastasis that was incidentally brought to our attention because of the exquisite tenderness of the lesion. A brief review of the literature also is provided.*

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## Case Report

A 72-year-old white man with a history of pancreatic adenocarcinoma presented for Mohs micrographic surgery of a basal cell carcinoma on the right helix. On the day of the surgery, the patient reported a new, rapidly growing, exquisitely painful lesion on the

cheek of 3 to 4 weeks' duration. Physical examination revealed a 0.8×0.8×0.8-cm, extremely tender, firm, pink papule on the right preauricular cheek. A horizontal deep shave excision was done and the histopathology was remarkable for neoplastic cells with necrosis in the dermis. We observed dermal cellular infiltrates in the form of sheets and nodules, some showing central necrosis (Figure 1). At higher magnification, a trabecular arrangement of cells was seen. These cells had a moderate amount of cytoplasm with eccentric nuclei and rare nucleoli (Figure 2). Mitotic figures were seen at higher magnification (Figure 3). Immunohistochemistry of the neoplastic cells exhibited similar positive staining for the neuroendocrine markers chromogranin A and synaptophysin (Figure 4). Staining of the neoplastic cells also was positive for thyroid transcription factor 1 (TTF-1) and cancer antigen 19-9. Villin and caudal type homeobox 2 stains were negative. These results were consistent with cutaneous metastasis from a known pulmonary carcinoid tumor.

On further review of the patient's medical history, it was discovered that he had undergone a Whipple procedure with adjuvant chemotherapy and radiation for pancreatic adenocarcinoma approximately 4 years prior to the current presentation. He was then followed by oncology, and 3 years later a chest computed tomography suggested possible disease

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progression with a new pulmonary metastasis. This pulmonary lesion was biopsied and immunologic staining was consistent with a primary neuroendocrine neoplasm of the lung, a new carcinoid tumor. The tissue was positive for cytokeratin (CK) 7, TTF-1, cancer antigen 19-9, CD56, synaptophysin, and chromogranin A, and was negative for villin and CK20. By the time he was seen in our clinic, several trials of chemotherapy had failed. Serial computed tomography subsequently demonstrated progression of the lung disease and he later developed malignant pleural effusions. Approximately 6 months after the cutaneous carcinoid metastasis was diagnosed, the patient died of respiratory failure.

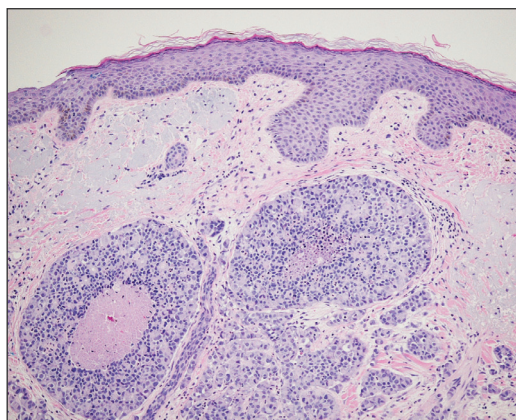
### Comment

Carcinoid tumors are uncommon neoplasms of neuroendocrine origin that generally arise in the gastrointestinal or bronchopulmonary tracts. Metastases from

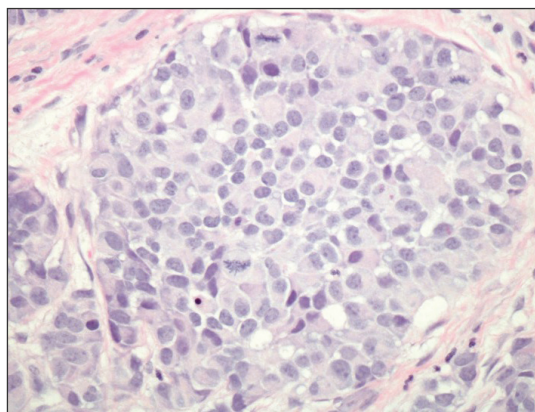
these primary neoplasms more commonly affect the regional lymph nodes or viscera, with rare reports of cutaneous metastases to the skin. The true incidence of carcinoid tumors with metastasis to the skin is unknown because it is limited to single case reports in the literature.

The clinical presentation of cutaneous carcinoid metastases has been reported most commonly as firm papules of varying sizes with no specific site predilection.<sup>1</sup> The color of these lesions has ranged from erythematous to violaceous to brown.<sup>2</sup> Several of the reported cases were noted to be extremely tender and painful, while other reports of lesions were noted to be asymptomatic or only mildly pruritic.<sup>3-7</sup>

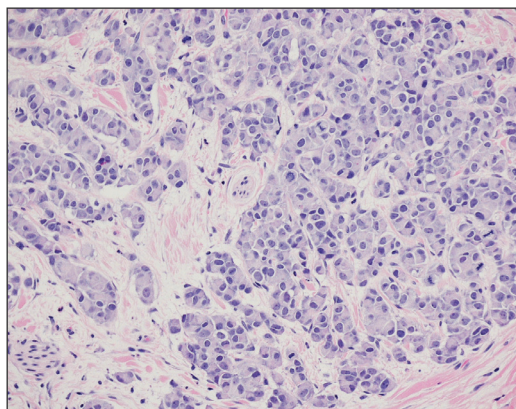
Carcinoid syndrome is more common with neoplasms present within the gastrointestinal tract, but it also has been reported with large bronchial carcinoid tumors and with metastatic disease.<sup>8,9</sup> Paroxysmal flushing is the most prominent cutaneous



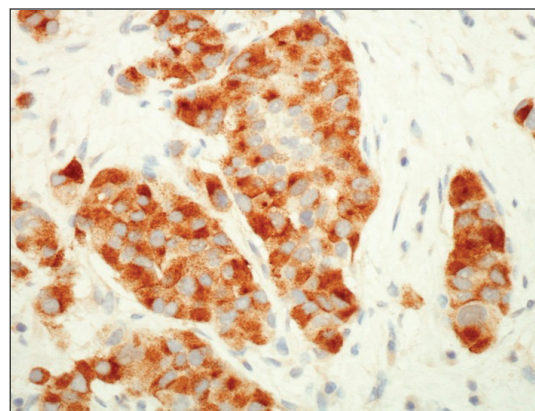
**Figure 1.** Cutaneous metastasis of a pulmonary carcinoid tumor. A dermal cellular infiltrate of sheets and nodules, some showing central necrosis (H&E, original magnification  $\times 40$ ).



**Figure 3.** Cutaneous metastasis of a pulmonary carcinoid tumor. Mitotic figures can be seen (H&E, original magnification  $\times 400$ ).



**Figure 2.** Cutaneous metastasis of a pulmonary carcinoid tumor. A trabecular arrangement of cells with a moderate amount of cytoplasm with eccentric nuclei and rare nucleoli (H&E, original magnification  $\times 400$ ).



**Figure 4.** Cutaneous metastasis of a pulmonary carcinoid tumor. Immunohistochemistry was positive for chromogranin A (original magnification  $\times 400$ ).

manifestation of this syndrome, occurring in 75% of patients.<sup>10,11</sup> Other common symptoms include patchy cyanosis, telangiectasia, and pellagra-like skin lesions.<sup>3</sup> Carcinoid syndrome secondary to bronchial adenomas is thought to differ from gastrointestinal carcinoid neoplasms in that it has prolonged flushing (hours to days instead of minutes) and is characterized by marked anxiety, fever, disorientation, sweating, and lacrimation.<sup>8,9</sup>

Many cases of cutaneous carcinoid metastases have been accompanied by reports of exquisite tenderness,<sup>7</sup> similar to our patient. The pathogenesis of the pain in these lesions is still unclear, but several hypotheses have been established. It has been postulated that perineural invasion by the tumor is responsible for the pain; however, this finding has been inconsistent, as neural involvement also has been present in nonpainful lesions.<sup>2,5,7,12</sup> Another theory for the pain is that it is secondary to the release of vasoactive substances and peptide hormones from the carcinoid cells, such as kallikrein and serotonin. Lastly, local tissue necrosis and fibrosis also have been suggested as possible etiologies.<sup>7</sup>

The histology of cutaneous carcinoid metastases typically resembles the primary lesion and may demonstrate fascicles of spindle cells with focal areas of necrosis, mild atypia, and a relatively low mitotic rate.<sup>10</sup> Other neoplasms such as Merkel cell carcinoma and carcinoidlike sebaceous carcinoma should be considered in the differential diagnosis. A primary malignant peripheral primitive neuroectodermal tumor or a primary cutaneous carcinoid tumor is less common but should be considered. Differing from carcinoid tumors, Merkel cell carcinomas usually have a higher mitotic rate and positive staining for CK20. The sebaceous neoplasms with a carcinoidlike pattern may appear histologically similar, requiring immunohistochemical evaluation with monoclonal antibodies such as D2-40.<sup>13</sup> A diffuse granular cytoplasmic reaction to chromogranin A is characteristic of carcinoid tumors. Synaptophysin and TTF-1 also are positive in carcinoid tumors, with TTF-1 being highly specific for neuroendocrine tumors of the lung.<sup>10</sup>

Cutaneous metastases of internal malignancies are more common from carcinomas of the lungs, gastrointestinal tract, and breasts.<sup>5</sup> Occasionally, the cutaneous metastasis will develop directly over

the underlying malignancy. Our case of cutaneous metastasis of a carcinoid tumor presented as an exquisitely tender and painful papule on the cheek. The histology of the lesion was consistent with the known carcinoid tumor of the lung. Because these lesions are extremely uncommon, it is imperative to obtain an accurate clinical history and use the appropriate immunohistochemical panel to correctly diagnose these metastases.

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