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Metastatic neuroendocrine carcinoma in the skin

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Abstract

Cutaneous metastases secondary to neuroendocrine tumors are rare. Herein we report a case of a 75-year-old woman who presented with a rare cutaneous metastatic disease. She was previously diagnosed with metastatic neuroendocrine carcinoma of unknown primary, with metastases to liver, lung, and bone. Biopsy of the skin lesion demonstrated archetypical pathology and positive immunohistochemical staining for chromogranin A and synaptophysin. The patient started palliative chemo-radiation therapy and passed away soon after.

Keywords: neuroendocrine tumor, cutaneous neoplasm, cutaneous metastasis

Introduction

Neuroendocrine tumors arise from neuroendocrine cells, and are relatively uncommon. These tumors are grouped into a relatively broad class of malignancies related to their inherent ability to synthesize and secrete peptide hormones. Cutaneous metastases secondary to neuroendocrine tumors are rare.

Case Synopsis

The patient is a 75-year-old woman with no personal history of skin cancer. She presented to our clinic with a 1-year history of an enlarging asymptomatic nodule on her left anterior shoulder. Four years previously she had been diagnosed with metastatic low-grade neuroendocrine carcinoma of unknown primary, with metastases to liver, lung, and bone. Her diagnosis of neuroendocrine tumor was based on the biopsy of her liver mass. The primary team suspected GI origin based on the finding of several tumors in the

abdomen. At the time this diagnosis was made, she presented with abdominal pain, flushing, diarrhea, and markedly elevated serotonin levels; there were no cutaneous lesions.

Physical examination revealed an 8-mm, well-demarcated, dome shaped, erythematous nodule with a smooth surface and speckled black pigmentation at its center (**Figure 1**).

Histology demonstrated multiple nodular dermal aggregates of cells with atypical small round nuclei and scant cytoplasm (**Figure 2**).

Immunohistochemical studies showed that the tumor cells stained strongly positive for chromogranin A and synaptophysin, but stained negative for cytokeratin 20. (Figures 3, 4)

In the setting of a patient with known metastatic neuroendocrine carcinoma, these histologic findings were consistent with the diagnosis of cutaneous metastatic neuroendocrine carcinoma. The patient started palliative chemotherapy and radiation therapy, but died four months later.

Discussion

Neuroendocrine tumors (NETs) belong to a heterogenous family of malignant neoplasms with varied biologic behaviors. The incidence rate of NETs is 2-5 per 100,000 patients, with a significant recent increase in reported worldwide cases [1]. NETs arise from neuroendocrine cells throughout the body and most commonly from pancreatic and gastrointestinal tissue [2]. NETs may also arise from thymus, thyroid glands, parathyroid glands, adrenal glands, pituitary gland, lungs, heart, ovaries, ear, and skin [2, 3]. Some of these tumors may secrete excessive levels of the



Figure 1. An 8.0 mm well-demarcated purplish red nodule with dark speckles.

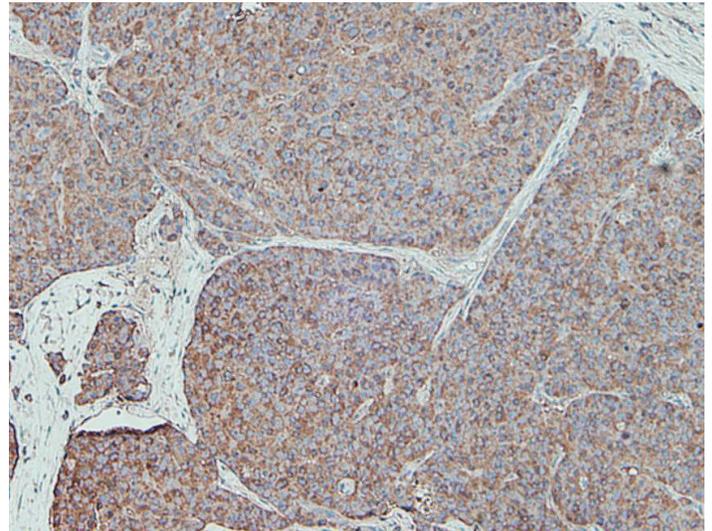


Figure 3. Tumor cells label positive for chromogranin: original magnification X10.

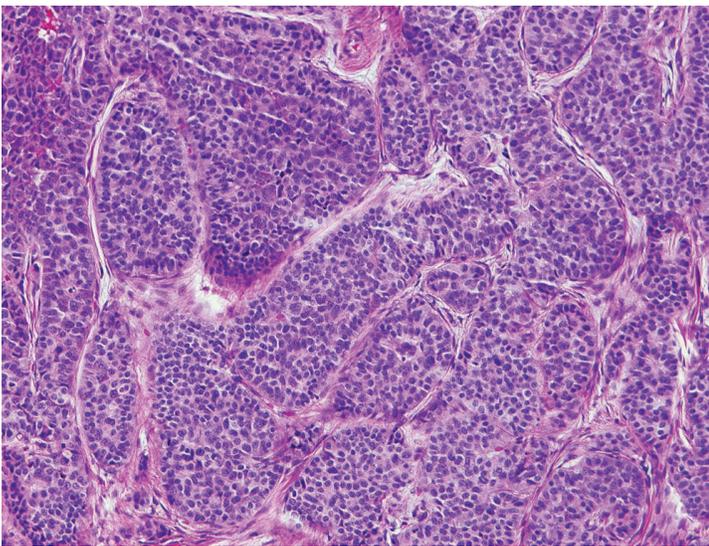


Figure 2. Diffuse dermal infiltration by nodule of cells with atypical small round nuclei and scant cytoplasm. Hematoxylin-eosin stain, original magnification x10.

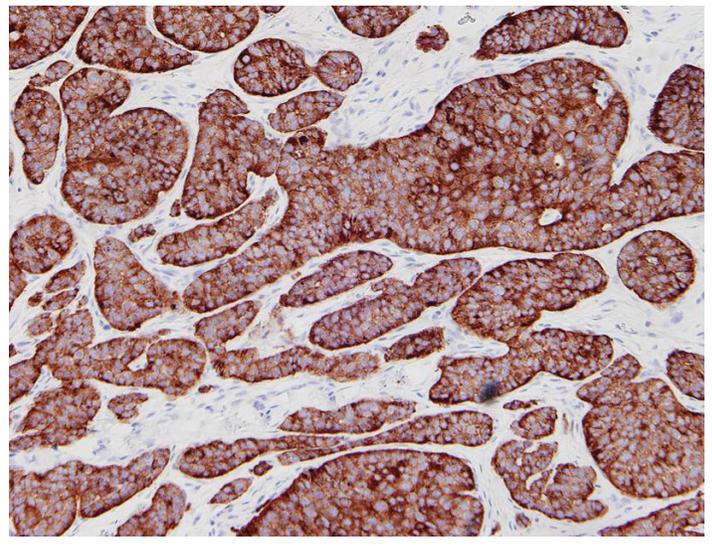


Figure 4. Tumor cells showed positive staining with synaptophysin: original magnification X10.

hormone associated with the relevant tissue and the patient may become symptomatic. NETs that arise in the gastrointestinal tract, for example, may cause over-secretion of serotonin, which often causes abdominal pain, flushing, and diarrhea, as seen in our patient.

The vast majority of NETs are caused by sporadic mutations. NETs may, however, also occur in the setting of multiple endocrine neoplasia types 1 and 2, von Hippel-Lindau disease, tuberous sclerosis complex, and neurofibromatosis [3]. Patients with primary NETs often experience long delays before diagnosis; this is because their symptoms may be

nonspecific and early detection may be difficult. Approximately 30% of patients with primary NETs develop metastatic disease; common sites include the lymph nodes, liver, and lungs. Chromogranin A and synaptophysin are reliable markers for the diagnostic of NETs [4]. In the evaluation of metastatic disease, other markers may be helpful. Homeobox transcription factor CSX-2 correlates well with tumors derived from the intestines, whereas TTF-1 correlates with tumors derived from the lungs [5]. Cutaneous metastatic neuroendocrine carcinoma is rare and has, to the best of our knowledge, been reported in only 42 cases [5-8].

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