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Case Report

Paraneoplastic Vitiligo Associated With Adrenocortical Carcinoma

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Abstract

Malignancies may induce clinical sequelae distant from the sites of the tumor. Such paraneoplastic phenomena are known to affect many organs, including the skin. Vitiligo is a disorder of patchy depigmentation, appearing as white macules with distinct margins. Rarely, vitiligo has been reported as a paraneoplastic occurrence, in the settings of pituitary adenoma, thymoma, gastric carcinoma, and lymphoma. We now describe a man presenting with the abrupt onset of vitiligo on the hands coinciding with recurrence of adrenocortical carcinoma (ACC) in the abdomen. The vitiligo rapidly dissipated following resection of his cancer. We believe this to be the first report of paraneoplastic vitiligo associated with ACC. Endocrinologists typically manage ACC and should be aware of this link, as the de novo observation of vitiligo may signal the onset or recurrence of underlying tumor. Other practitioners that encounter patients with new vitiligo should add ACC to their differential diagnosis of potential underlying conditions.

Key Words: vitiligo, adrenocortical carcinoma, paraneoplastic syndrome

Abbreviations: ACC, adrenocortical carcinoma; CT, computed tomography.

Introduction

Up to 20% of patients with cancer experience paraneoplastic syndromes: signs and symptoms that occur at locations remote from the sites of the primary malignancy and metastases [1]. Paraneoplastic phenomena may be due to tumoral release of substances such as peptide hormones, cytokines, or growth factors, or due to the cross-reaction of antitumor antibodies with normal tissues, but pathogenesis is often unclear [1, 2]. The syndromes are varied and many different organs may be affected. Diarrhea, electrolyte disturbances, polycythemia, hypertension, and abnormalities of the endocrine or nervous system have commonly been cited. Cutaneous manifestations of paraneoplastic syndromes include itching, flushing, keratoses (eg, Bazex syndrome), pigmented skin growths, pemphigus, migratory necrolytic erythema, florid cutaneous papillomatosis, erythema gyratum repens, malignant acanthosis nigricans, acanthosis palmaris, and, rarely, vitiligo. This case report describes an instance of vitiligo associated with adrenocortical carcinoma (ACC), a phenomenon that has not been described previously.

Case Presentation

A 68-year-old man noted the rapid development of nontender depigmented macules and small patches on both hands. The patient has no history of autoimmune disease. He was not experiencing unusual emotional stress. He had not been exposed to toxic substances and had not been sunburned. The patient has experienced sporadic, mild eczema but has no history of vitiligo or other dermatologic disorders. There was no family history of vitiligo. Three years previously he had been diagnosed with stage 3 ACC and underwent resection of a 27-cm tumor above the right kidney, a 3-cm satellite lesion, the right lobe of the liver, and the right kidney [3]. There were no metastases identified, and 26 lymph nodes were negative for tumor. Endocrine laboratory values revealed elevations of serum cortisol concentration (18.0 µg/dL [496.6 nmol/L]; PM normal <11.3 µg/dL [<311.8 nmol/L]), 24-hour urinary cortisol (73 µg [201 nmol]; normal 3.5-45 µg [9.7-124 nmol]), and serum dehydroepiandrosterone sulfate (734 µg/dL [19.9 µmol/L]; normal 35-212 µg/dL [1.0-5.7 µmol/L]). Corresponding suppressions of serum adrenocorticotropin concentration (<5.0 pg/mL [<1.1 pmol/L]; normal 7.2-63 pg/mL [1.6-14.2 pmol/L]) and serum free testosterone (28 pg/mL [97.1 pmol/L]; normal 30-140 pg/mL [104.0-485.4 pmol/L] were noted. Normal results were attained for plasma metanephrine (<0.20 nmol/L; normal 0.00-0.49 nmol/L), plasma normetanephrine (<0.20 nmol/L; normal 0.00-0.89 nmol/L), plasma renin activity (6.6 ng/mL/h [156.42 pmol/L/h]; normal 2.9-10.8 ng/mL/h [68.7-256.0 pmol/L/h] sodium depleted), serum aldosterone (7.9 ng/dL [219.1 pmol/L]; normal ≤ 21 ng/dL [≤582.5 pmol/L]), serum estradiol (25 pg/mL [91.8 pmol/L]; normal male < 32 pg/mL [<117.5 pmol/L]), and serum thyrotropin (2.5 µU/mL; normal 0.3-4.2 µU/mL).

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Serum sodium concentration was 136 mmol/L (normal 135-145 mmol/L), potassium 4.1 mmol/L (normal 3.6-5.2 mmol/L), chloride 103 mmol/L (normal 98-108 mmol/L), and total carbon dioxide 26 mmol/L (normal 22-32 mmol/L). Other routine blood and urine studies were also within normal ranges except for a serum alkaline phosphatase concentration of 327 U/L (normal 36-161 U/L).

He then underwent 2 years of daily oral mitotane adjuvant chemotherapy, completing the treatment 9 months before the current event. Serial surveillance computed tomographic (CT) studies of the chest, abdomen, and pelvis detected no tumor recurrence as recently as 3 months prior to the skin findings. He was taking only 2 medications, which he had been receiving for years: rosuvastatin 40 mg daily for well-controlled hypercholesterolemia and hydrocortisone 10 mg daily, being tapered, for resolving, partial adrenal insufficiency secondary to the prior cancer and mitotane medication. Table 1 shows the results of serial cosyntropin stimulation testing to assess recovery of adrenocortical function.

Diagnostic Assessment

The dorsal aspects of all fingers were involved, with vitiligo most prominent on the thumbs and index fingers (Fig 1). No other skin was affected and there was no change in hair color. Physical examination was otherwise unremarkable except for scars at the sites of prior surgical incisions. Skin was not biopsied and no Wood's lamp examination was performed. Four weeks after the onset of vitiligo, CT revealed a 2.6-cm soft tissue nodule in the left upper quadrant of the abdomen, without evidence of malignancy elsewhere in the abdomen or in the chest or pelvis. Positron emission tomography demonstrated intensely avid uptake of radiolabeled fluorodeoxyglucose at the nodule. The original tumor had been hormonally active (discussed earlier), with elevations of serum cortisol and dehydroepiandrosterone sulfate concentrations, but at the time of the ACC recurrence neither serum cortisol (10.8 μg/dL [298.0 nmol/L]; normal <11.3 μg/dL [<311.8 nmol/L]) nor serum dehydroepiandrosterone sulfate concentration (14 μg/dL [0.4 μmol/L]; normal 35-212 μg/dL [1.0-5.7 μmol/L]) was above normal limits. Adrenocorticotropin (26 pg/mL [5.9 pmol/L]; normal 7.2-63 pg/mL [1.6-14.2 pmol/L]) and thyrotropin (3.2 μU/mL; normal 0.3-4.2 μU/mL) levels were within normal limits.

Table 1. Cosyntropin stimulation test results

Date of test	Hydrocortisone dose	Baseline AM serum cortisol concentration	Serum cortisol concentration 1 h post cosyntropin
20 wk pre vitiligo	10 mg AM/7.5 mg 4-6 h after awakening	4.5 μg/dL (124.2 nmol/L)	5.3 μg/dL (146.2 nmol/L)
6 wk pre vitiligo	7.5 mg AM	8.9 μg/dL (245.6 nmol/L)	10.4 μg/dL (286.9 nmol/L)
6 wk after onset vitiligo	10 mg AM	10.8 μg/dL (298.0 nmol/L)	12.8 μg/dL (353.2 nmol/L)
18 wk after onset vitiligo and 5 wk after ACC resection	10 mg AM	9.8 μg/dL (270.4 nmol/L)	12.4 μg/dL (342.1 nmol/L)

Hydrocortisone dose held prior to blood sampling on testing days. A dose of 250 μg cosyntropin administered intramuscularly. Normal AM serum cortisol concentration 5.0 to 22.6 μg/dL (137.9-623.5 nmol/L).
Abbreviation: ACC, adrenocortical carcinoma.

Treatment

At laparoscopy 9 weeks after the CT, the patient was in fact found to have 2 omental tumors. The nodule observed on CT and positron emission tomography had grown to 3.5 cm and was located within the gastrosplenic ligament. A second, 1.5-cm tumor was detected within the gastrocolic ligament. Both were resected and proved to be ACC, similar in histology to the original cancer. No residual, inoperable ACC was evident.

Outcome and Follow-up

The vitiligo regressed following resection of the tumors. Repigmentation was near complete in 2 weeks. No tumor was reported on CT of the lungs, abdomen, and pelvis 6 weeks postoperatively. Fig. 2 shows the hands 12 weeks following ACC resection. Hydrocortisone medication was discontinued 18 weeks following the surgery, after evaluation of the cosyntropin stimulation test results shown in the final row of Table 1.

Discussion

Vitiligo, skin depigmentation due to loss of melanocytes that results in nonscaly, white macules with distinct margins, has an estimated worldwide prevalence up to 2% [4]. The pathophysiology is not well defined, but proposed mechanisms include genetics, autoimmune phenomena, and oxidative stress. Vitiligo has also been observed as a paraneoplastic occurrence in the settings of pituitary adenoma [5], thymoma [6], gastric carcinoma [7], and lymphoma [8].

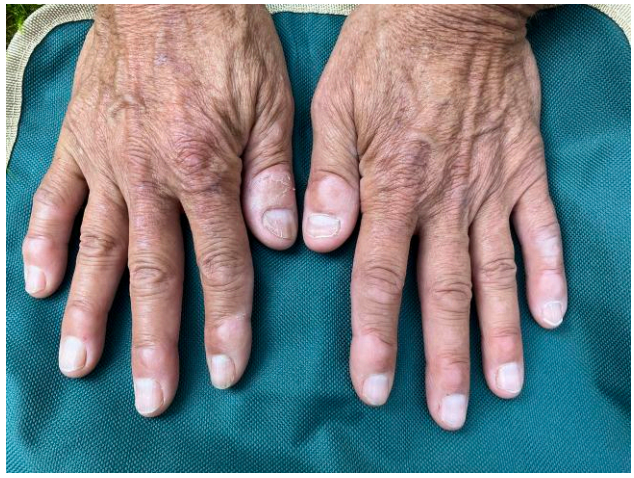

Figure 1. Vitiligo on the dorsal surfaces of the fingers.

Figure 2. Fingers 12 weeks after resection of abdominal adrenocortical carcinoma.

In the present case, the abrupt onset of vitiligo on the fingers of a 68-year-old man coincided with recurrence of ACC and the condition rapidly regressed following cancer resection, strongly suggesting a paraneoplastic etiology. The patient had no known risk factors or predisposing conditions for the development of vitiligo, although eczema has been associated with it. A limit in the evaluation of this case is the lack of a skin biopsy to consider histopathology, but biopsy is not required for the diagnosis of vitiligo. We do not believe the vitiligo was drug induced, as the patient had been taking statin medication for decades and low-dose hydrocortisone would unlikely be related.

To the best of our knowledge, this is the first report of paraneoplastic vitiligo associated with ACC. Endocrinologists typically manage ACC and should be aware of this link, as the de novo observation of vitiligo may signal the onset or recurrence of an underlying tumor. Other practitioners that encounter patients with new vitiligo should add ACC to their differential diagnosis of potential underlying conditions.

Learning Points

- Cancers may cause paraneoplastic phenomena, including dermatoses, due to tumoral release of substances such as peptide hormones, cytokines, or growth factors, or due to the cross-reaction of antitumor antibodies with normal tissues.
- Vitiligo is a depigmentation disorder that results in white skin macules and patches that has, rarely, been reported to complicate malignancies.
- This case report now associates paraneoplastic vitiligo with ACC; endocrinologists should be aware that vitiligo may be a sign of tumor onset or recurrence.

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Contributors

All authors made individual contributions to authorship. D.A.G., R.A.F., and M.A.H. were involved in the diagnosis and management of this patient. D.A.G. wrote the original draft and completed the manuscript submission. All authors reviewed and approved the final manuscript draft.

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Informed Patient Consent for Publication

Signed informed consent obtained directly from the patient.

Data Availability

Data sharing is not applicable to this article as no data sets were generated or analyzed during the current study.

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