

Alopecia areata and myasthenia gravis presenting as paraneoplastic phenomena of breast cancer



Charles Dunn, MD,^a Rajiv Nathoo, MD,^a Aaron Tauer, MD,^b and Layne Green, MD^c
Oviedo, Florida and Anchorage, Alaska

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INTRODUCTION

Alopecia areata (AA) is an organ-specific autoimmune phenomenon characterized by the acute onset of patterned nonscarring hair loss. Its association with other autoimmune conditions is well-documented.¹ It also has been linked with the increased risk of certain types of malignancy.² However, AA as a paraneoplastic syndrome is extremely uncommon and limited in the literature to sparse case reports almost exclusively related to hematologic cancers.³⁻⁶ We present the unique case of a 60-year-old woman seen in a dermatology clinic with acute-onset hair loss and diplopia discovered to be secondary to AA and myasthenia gravis (MG) respectively. During secondary evaluation of MG, the woman was diagnosed with invasive ductal carcinoma of her right breast. Therapeutics targeted toward treatment of her breast cancer resulted in improvement of her presenting AA and MG features.

CASE REPORT

A 60-year-old woman presented to the dermatology clinic through the request of a neurologist for evaluation of nonscarring scalp alopecia temporally related to the onset of diplopia. The patient reports that she woke up one morning with acute onset of double vision and concomitant patchy hair loss. She reported that her double vision seemed to worsen toward the end of the day. Her hair loss was limited to the scalp and was not associated with pruritus or pain. Both diplopia and hair loss worsened over the next 6 months prompting her to seek medical care.

Abbreviations used:

AA: alopecia areata
 MG: myasthenia gravis

She was first seen by Ophthalmology with no structural ocular issues identified and was subsequently referred to Neurology. Neurologic exam showed prominent 3rd and 4th cranial nerve deficits with right eyelid ptosis. Cutaneous evaluation showed well-circumscribed oval patches of scalp hair loss sparing eyebrows, lashes, and other hair bearing surfaces (Fig 1). Screening brain magnetic resonance imaging showed normal anatomy without evidence of vascular abnormality or space occupying lesion. Laboratory evaluation demonstrated unremarkable androgen profile, vasculitis screening, nutritional/thyroid studies, serum electrolytes, and rheumatic serum studies. Trichoscopy showed few anagen/catagen hairs. The majority of follicles had no sheath and were tapered at one end with abrupt termination at the opposite end consistent with AA (Fig 2). Second-tier laboratory evaluation showed elevated levels of anti-acetylcholine receptor antibodies consistent with a diagnosis of MG. She was started on pyridostigmine, intralesional triamcinolone, and clobetasol scalp solution with limited symptomatic improvement over the course of 2 months. Chest computed tomography as part of the MG work-up looking for mediastinal mass showed evidence of concerning calcifications within her right breast (Fig 3). Mammography and biopsy

From the Kansas City University/Graduate Medical Education Consortium—Advanced Dermatology and Cosmetic Surgery, Oviedo^a; Department of Neurology^b and Department of Dermatology^c, United States Air Force Medicine Corps, Joint Base Elmendorf, Anchorage.

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Correspondence to: Charles Dunn, MD, Kansas City University of Medicine and Biosciences, 151 Southhall Lane, Ste 300, Maitland, FL 32751. E-mail: CDunn@KansasCity.edu.

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Fig 1. **A**, Alopecia before mastectomy after 3 rounds of intralesional triamcinolone. **B**, Alopecia 6 weeks after mastectomy.

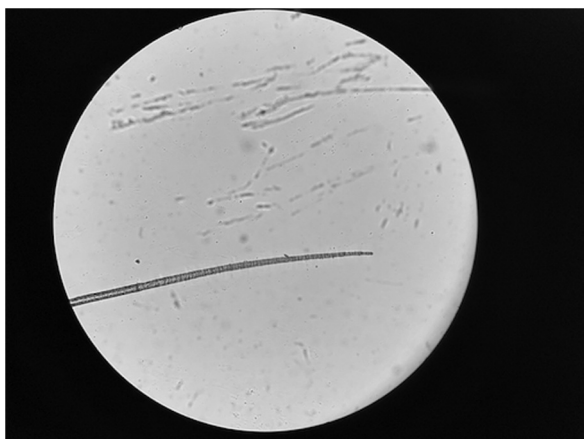


Fig 2. Trichoscopy showing short broken-off hairs more narrow near the point of scalp entry, suggestive of alopecia areata.

revealed stage I invasive ductal carcinoma of her right breast (pT1cN0M0) which was HER2/Neu+ and ER/PR-with pagetoid spread (Fig 4). She underwent partial mastectomy with central breast excision and subsequent radiation therapy without systemic corticosteroids. The patient recovered well from oncologic therapy and subsequently demonstrated rapid improvement in her presenting autoimmune symptoms.

DISCUSSION

AA is a benign condition that typically presents with oval or round, well-circumscribed bald patches overlying a smooth surface. Incidence estimates suggest 2% of the US population will develop AA during their lifetime.² Etiologically, AA is considered a predominately T cell-mediated autoimmune process, characterized by the infiltration of a cytotoxic subset of CD8⁺, NKG2D⁺ T cells into hair follicles.⁷⁻⁹ AA is commonly linked with several autoimmune conditions, including vitiligo, thyroid disease, rheumatoid arthritis, and systemic lupus erythematosus.¹



Fig 3. Chest computed tomography demonstrating concerning calcified mass within the tissue of the right breast.

Moreover, AA has known associations with malignancy—most notably lymphoma, breast cancer, kidney, and urinary bladder cancer² with the belief that this association is related to the nuanced interplay between defects of the immune system and oncogenesis.³ Despite this association, AA as a paraneoplastic phenomenon, or harbinger of active malignancy, is extremely uncommon, with data limited to case reports. Almost all of these reports show a primary association with lymphoma variants and not solid organ malignancy.³⁻⁶ In all but one of these cases, manifestations of AA occurred simultaneously with the onset of systemic symptoms, suggestive of malignancy.³ All of these cases also showed advanced oncologic disease burden at the time of diagnosis and demonstrated resolution of AA as early as after 1 cycle of chemotherapy to as late as 12 months after completing therapy.³⁻⁶ The AA



Fig 4. Mammogram showing calcifications consistent with ductal carcinoma of the patient's right breast.

represented was also clinically severe, with at least 2 cases presenting with AA totalis.^{3,4}

In comparison, MG is also an organ-specific autoimmune disorder characterized by weakness and fatigability of skeletal muscles due to dysfunction of the neuromuscular junction. While T lymphocytes play an important role, MG is largely considered a B cell-mediated autoimmune process, with 80% to 90% of patients possessing detectable autoantibodies against the acetylcholine receptor which leads to acetylcholine receptor blockade, internalization, and complement mediated destruction.¹⁰ Unlike AA, MG represents a paraneoplastic effect of thymoma in up to 10% to 15% of patients.¹⁰

The patient in this case report represents a unique manifestation of illness in that there was acute and temporal correlation with the onset and resolution of AA and MG after treatment of breast cancer. This timing suggests linked pathology, supporting the paraneoplastic hypothesis. In 2015, a similar presentation was reported by Kamada et al,¹⁰ where a 57-year-old woman with AA and MG associated with thymoma responded well to thymectomy and high doses of glucocorticosteroid. Outside of this, PubMed-based literature reviews reveal no reports linking AA and MG as a paraneoplastic syndrome to breast cancer. Our patient, conversely, did not receive systemic glucocorticoids.

While not fully elucidated, studies of AA as a paraneoplastic process suggest a mechanism linked

to impaired cellular immune responses down-regulating CD8⁺ suppressor T lymphocytes and up-regulating CD4⁺ T lymphocytes targeting hair follicle melanocytes. It is interesting to note that MG and AA represent primary pathologic mechanisms involving 2 separate arms of the adaptive immune system. This presentation thus could highlight the need for a heightened suspicion of malignancy if copresentation occurs.

In summary, this case serves to underscore the rare but significant potential of AA to represent a herald for possible underlying malignancy, especially if associated with acute onset of other autoimmune phenomena. It also emphasizes the need for increased awareness of AA and its implications on the prognosis and diagnosis of breast cancer.

Conflicts of interest

None disclosed.

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