

Symptomatic iron deficiency anemia from neglected giant basal cell carcinoma



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Key words: anemia; basal cell carcinoma; female; giant; iron deficiency; neglect.

INTRODUCTION

Basal cell carcinomas (BCCs) comprise the largest portion of malignant neoplasm globally and predominantly affect white men between the fourth and sixth decade of life.¹ In cases of giant BCCs (>5 cm), approximately one-third arise from neglect in the setting of psychosocial factors: denial, poor access to care, cultural practices, etc. Secondary influences, such as localized bleeding or pain, generalized fatigue, or familial encouragement, typically serve as the impetus for seeking medical care.² Although pinpoint bleeding is often associated with giant BCCs, a review of literature identified few reports of anemia subsequent to nonmelanoma skin cancer. We present an unusual case of chronic iron deficiency anemia correlating with neglect of a giant, infiltrating BCC in an otherwise healthy woman. Because of increased tumor size and malignancy potential, associated symptoms, or psychosocial components, treatment of these cancers requires an exhaustive, multimodal approach, as outlined later.

CASE REPORT

A 56-year-old woman with a history of migraines, cholelithiasis, and no tobacco or alcohol use presented to urgent care by primary care physician referral for fatigue, dyspnea, and lightheadedness progressively worsening during several weeks. Apart from negative cervical and breast cancer screening results 8 years before, the patient had not received a medical evaluation for greater than 10 years. Vital signs demonstrated mild hypertension (139/77 mm Hg), tachycardia (106/min), and fever (100.9°F; 38.2°C) and complete physical exam was negative apart from

Abbreviation used:

BCC: basal cell carcinoma

head, eyes, ears, nose, throat and skin. Significant pallor of the oral mucosa and conjunctiva was appreciated, in addition to fungating lesions on the right lateral aspect of the shoulder (11.0 × 20.0 × 2.5 cm), anterior mid portion of the chest (4.5 × 4.5 × 0.5 cm), and left lateral side of the neck (1.0 × 3.0 × 0.5 cm) (Figs 1 and 2). Dressing removal at the shoulder elicited copious serosanguinous drainage, bleeding, mild odor, and tenderness to palpation, although no symptoms were associated with neck and chest sites. The lesions had slowly grown during 3 to 4 years, with oozing blood at the shoulder for several months. Despite twice-daily dressing changes with “surgical pads,” and her husband’s encouragement, she had not sought care because of generalized anxiety and fear regarding possible diagnosis of malignancy.

The patient was admitted for further evaluation by internal medicine, oncology, and plastic surgery, with laboratory studies revealing chronic iron deficiency anemia, characterized by a low hemoglobin level (4.4 g/dL; reference 12.0-16.0 g/dL), low mean corpuscular volume (61.6 μM; reference 80-100 μM), decreased ferritin level (10 ng/mL; reference 12-150 ng/mL), and decreased iron (transferrin) saturation (2%; reference 15%-50%). Blood smear testing showed severe microcytic anemia with anisopoikilocytosis suggestive of regenerating marrow. Hemoglobin level stabilized to 7.9 g/dL after the

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Fig 1. Preoperative images of the lateral aspect of the right shoulder lesion.

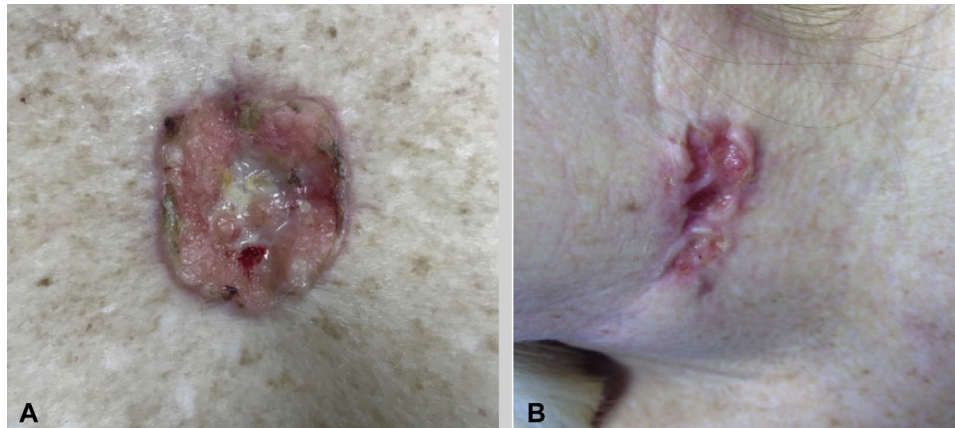


Fig 2. Preoperative images of lesions of the mid portion of the chest, anterior aspect of the chest (**A**), and left lateral aspect of the neck (**B**).

patient received 3 units of packed red blood cells, intravenous iron sucrose, folate, and vitamin B12. Noninfectious systemic inflammatory response syndrome criteria were also met with leukocytosis ($13.1/\text{mm}^3$; reference $4500\text{--}11,000/\text{mm}^3$) and tachycardia, thought secondary to anemia and blood transfusion, with negative methicillin-resistant staphylococcus aureus polymerase chain reaction and blood culture results. Biopsy with immunohistochemical staining showed infiltrative BCC diffusely positive for GATA3 and focal staining for EMA (Fig 3). No imaging studies were pursued because of lack of regional lymphadenopathy or systemic involvement. Skin examination result was otherwise unremarkable. Subsequent outpatient dermatologic and plastic surgery evaluations resulted in vismodegib initiation, external beam radiotherapy, and reconstruction of the right lateral aspect of the shoulder with a split-thickness graft from the right thigh, with no obvious

extension to deeper tissues such as bone. The lesions of the left lateral aspect of the neck and chest were excised via Mohs micrographic surgery, with clear margins but with evidence of a BCC (chest) and basosquamous carcinoma with perineural invasion (neck). In accordance with the discretion of these outside providers, no additional oncologic evaluation or treatments were pursued; however, the patient has remained compliant with recommended dermatologic follow-up visits. Three months of iron supplementation were, however, completed, with a most recent hemoglobin level of 11.7 g/dL and no recurrence of dyspnea, lightheadedness, or fatigue at 1-, 3-, and 6-month follow-up.

DISCUSSION

Although BCCs are typically indolent, slow-growing skin cancers, untreated lesions may become aggressive, symptomatic, or locally invasive. Although

Table I. Literature review: cases of anemia in the setting of basal cell carcinomas and subtypes

Authors	Sex and age, years	Site(s) and sizes, cm	Malignancy diagnosis	Laboratory evaluation
Al-Hadithy et al ¹	F (77)	Left posterior aspect of neck (20 cm)	Mixed basaloid adenocarcinoma	"Low" iron and ferritin "High" TIBC
Bisgaard et al ⁴	F (86)	Right shoulder (7.0 × 6.5)	Basosquamous carcinoma	Hgb: 7.0 Hct: 23.9
Higgins and Hull ⁵	F (79)	Right side of neck and face Left side of neck and face Mid upper back: (9.3 × 4.5)	BCC	Hgb: 4.4 MCV: 57.7
Breglia and Oliva ⁶	M (58)	Vertex of scalp (12 × 9)	BCC	Hgb: 5.8 MCV: 65.5 Ferritin: 5
Clements et al ⁸	M (50)	Left anterolateral side of chest (15 × 15)	BCC	Hgb: 7.0 MCV: 64.4
Fresini et al ⁷	M (72)	Back (30 × 20)	BCC (adenoid type)	Hypochromic microcytic anemia
Laudenschlager et al ¹¹	M (66)	Back (15 × 12)	BCC	Symptomatic anemia
Torok et al ⁹	M (33)	Several lesions on face, neck, and trunk (largest 9 × 8 × 4)	Nevoid BCC syndrome	Hgb: 6.0 Hct: 19 MCV: 56.0 TIBC: 229.0 Iron saturation: 12.0
Andersen and Lei ¹²	NA	Forehead and scalp	BCC	Severe anemia

Units were recorded as follows: ferritin (nanogram per milliliter; reference range 15-200 ng/mL [men] and 12-150 ng/mL [women]); Hgb (grams per deciliter; reference range 13.5-17.5 g/dL [men] and 12.0-16.0 g/dL [women]); Hct (reference range 41%-53% [men] and 36%-46% [women]); serum iron (reference range 20%-50% [men] and 15%-50% [women]); mean corpuscular volume (cubic micrometers; reference range 80-100 μm^3); and TIBC (micrograms per deciliter; reference range 250-425 $\mu\text{g}/\text{dL}$).

BCC, Basal cell carcinoma; F, women; Hct, hematocrit; Hgb, hemoglobin; M, men; MCV, mean corpuscular volume; TIBC, total iron-binding capacity.

metastasis is rare, morbidity largely results from deep tissue invasion, including infiltration of the dermis or extradermal structures: bone, muscle, or cartilage. In a 51-case review of giant BCCs (>5 cm) by Archontaki et al,³ the estimated risk of metastasis was approximately 6%, with a 17.07% and 37.5% risk of mortality in patients with negative lymph node results and metastasis, respectively. Because of the biological nature of giant BCCs, including their characteristic tissue friability, ulceration, and possible necrosis, pinpoint bleeding is not uncommon. Iron deficiency anemia is also prevalent in the general population, with estimates of 2% to 5% in adults and postmenopausal women.¹ In contrast, reports of acute or chronic anemia correlated with nonmetastatic, giant BCC are rare, with only 10 identified by review of the literature (Table I). Al-Hadithy et al,¹ Bisgaard et al,⁴ and Higgins and Hull⁵ outlined 3 cases of giant BCC resulting in chronic iron deficiency anemia without an otherwise identified source in women aged 77 to 86 years. Six additional cases were identified in men aged 33 to 72 years (Table I).

Among these 9 patients, medical history was significant only for well-controlled hypertension, hyperlipidemia, ischemic cardiomyopathy status post coronary artery bypass graft surgery, and atrial fibrillation.^{1,4,6,7} Lesions predominantly arose in sun-exposed areas, including the head or neck, apart from 2 reports of lesions arising on the upper back and anterolateral aspect of the chest wall.^{4,8} Regional lymphedema was identified in only 1 case, with no reports of systemic dissemination.¹ All cases were attributed to neglect or denial, with a 9.6-year average growth time, an average hemoglobin level of 6.1 g/dL, and an average mean corpuscular volume of 60.8 μm^3 .^{1,4-6,8,9} In addition to anemia-related symptoms such as fatigue, palpitations, and dyspnea on exertion, BCC-related comorbid conditions included chronic sepsis.⁸ Patients achieved negative margin results with full recovery after reconstructive surgery, blood transfusions, and close follow-up. Although surgical management was the treatment focus of these studies, adjuncts or alternatives to surgery may be

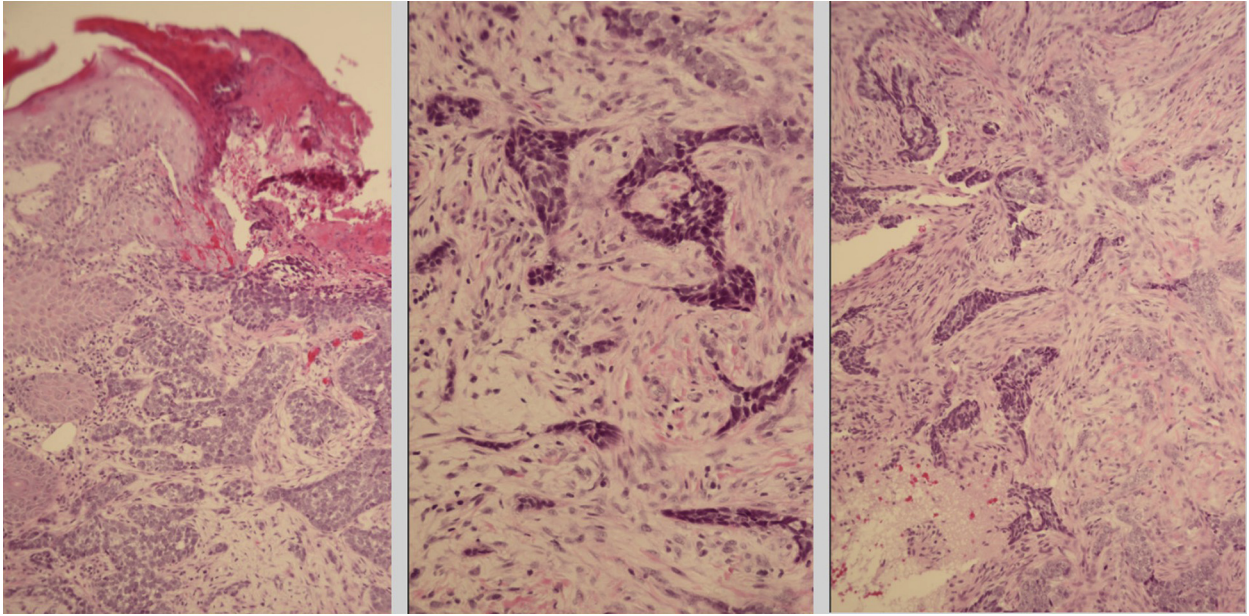


Fig 3. Histopathology showing infiltrative basal cell carcinoma. Section shows a basaloid lesion with some squamous areas, tumor cells positive for GATA3, and focal staining for EMA. Immunostains were performed with appropriate controls.

appropriate in some patients, including hedgehog pathway inhibitors (vismodegib, sonidegib), local radiation, and photo- or chemotherapies.²

We present a case of iron deficiency anemia with the lowest published hemoglobin level (4.4 g/dL) to date, to our knowledge, that was correlated with a giant BCC and subsequently treated with combination vismodegib and reconstructive surgery. Because of a benign medical and social history and an otherwise negative laboratory evaluation result, the patient's chronic iron deficiency anemia was attributed to her nonmelanoma skin cancer. The case is also significant for BCC presentation on the right shoulder in a relatively young woman compared with individuals in previous reports with negative medical history and diagnostic evaluation results. This case highlights the importance of skin examinations in clinical practice, particularly in healthy individuals and patients with unexplained diagnostic findings, because data estimate that one-third of BCCs occur in sun-protected areas. One must always be wary of the positive "Band-Aid sign," covering a large fungating mass. It demonstrates the dire consequences of neglected giant BCCs, resulting in significant deformity, several comorbid conditions, and extensive treatment courses.¹⁰ It also highlights the importance of integrating specialists and therapies, when appropriate, for prognostic benefit.

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