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CASE REPORT PEER REVIEWED | OPEN ACCESS

Empyema after radiation therapy for cutaneous squamous cell carcinoma in a patient with scleroderma

Matthew R Barke, Sujata Ojha, Madeline Fitzpatrick, Boone Goodgame

ABSTRACT

Introduction: Cutaneous squamous cell carcinoma (cSCC) is a non-melanomatous neoplasm of the skin that is more likely to develop in immunosuppressed patients or those with autoimmune diseases. Individuals with connective tissue disorders in particular, such as scleroderma, are particularly at an increased risk of developing cancer due to chronic inflammation, tissue damage, genetic susceptibility, and immunosuppressive therapy. Additionally, treatment of cSCC with surgery and radiation therapy, especially in those with autoimmune connective tissue disorders, presents an increased risk of adverse effects, including infection.

Case Report: A 74-year-old woman with a history of systemic scleroderma and cSCC status post Mohs surgical resection and radiation therapy presented with an 8-cm forehead lesion at the site of excised cSCC. One year earlier, she underwent Mohs surgery after biopsy-proven cSCC of the forehead with resulting clear margins. Radiation therapy was recommended as nerve involvement was discovered within the resected tumor. Magnetic resonance imaging of the brain revealed a right parafalcine subdural empyema with peripheral blood and intraoperative cultures positive for *Streptococcus intermedius* and *Candida albicans*. Her hospitalization was complicated by the development of acute hypoxic respiratory failure and septic shock. Ultimately, her family chose to focus on her comfort and she passed peacefully from complications of septic shock.

Conclusion: This case highlights a rare infection after treatment of cSCC which emphasizes that treatment of malignant skin lesions in patients with scleroderma can be challenging. Shared decision-making with a thorough assessment of risks should be emphasized with every patient before proceeding with treatment.

Keywords: Cutaneous squamous cell carcinoma, Empyema, Radiation therapy, Scleroderma

Matthew R Barke[1], MD, Sujata Ojha[1], MD, Madeline Fitzpatrick[1], MD, Boone Goodgame[1], MD

Affiliations: [1]Department of Internal Medicine, Dell Medical School, The University of Texas at Austin, Health Discovery Building, 1601 Trinity St, Room 7700B, Austin, TX 78712, USA.

Corresponding Author: Matthew R Barke, MD, Dell Medical School, The University of Texas at Austin, Health Discovery Building, 1601 Trinity St, Room 7700B, Austin, TX 78712, USA; Email: Matthew.r.barke@gmail.com

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INTRODUCTION

Cutaneous squamous cell carcinoma (cSCC) represents approximately 20% of skin malignancies and has the potential for local destruction and permanent disfigurement [1, 2]. The head and neck are the most common sites of cSCC which presents with cosmetic and functional concerns [2]. However, patients diagnosed with cSCC generally have a favorable prognosis with a 5-year survival rate >90% and a low risk of metastasis [1]. Patients with autoimmune disease and/or immunosuppression have a 65 to 100 times greater likelihood of developing cSCC and are considered high risk when receiving treatment [1, 2]. Additionally, treatment of cSCC with surgery and radiation therapy, especially in those with autoimmune connective tissue disorders, presents with an increased risk of adverse effects, including infection. The authors present a case of cSCC treated with surgical resection plus adjuvant radiation therapy with resulting subdural empyema, bacteremia, and fungemia in a patient with underlying scleroderma.

CASE REPORT

A 74-year-old woman with a history of systemic scleroderma and cSCC status post Mohs surgical resection and adjuvant radiation therapy was admitted to the hospital with two weeks of lethargy, confusion, and headaches. She had been taking prednisone 5 milligrams (mg) and mycophenolate mofetil 500 mg twice a day (BID) for her scleroderma. One year prior to admission, the patient underwent Mohs surgery for a biopsy-proven cSCC forehead lesion with resulting clear margins. Adjuvant radiation therapy was recommended after nerve involvement was discovered on pathologic examination of the resected tumor. She proceeded with 30 radiation treatments; however, midway through the treatment course her forehead was brightly erythematous and raw resulting in a brief suspension of treatment (Figure 1A). Three months after completion of radiation therapy, the site on her forehead began to scab and an infection was suspected but wound cultures did not reveal a bacterial or fungal pathogen (Figure 1B). Over the next month, there was no improvement thus mycophenolate was suspended and she was referred to wound care for weekly wound debridements and dressing changes (Figure 1C). At this time, magnetic resonance imaging (MRI) of the brain revealed early osteonecrotic changes and a defect in the right anterior vertex scalp (Figure 2A and B). Physical exam on admission was significant for an 8-centimeter (cm) honey-crusted forehead lesion with areas of black tissue with no discharge or purulence (Figure 1D). She had just received one week of intravenous (IV) ceftriaxone for *Streptococcus intermedius* bacteremia at an outside hospital. Magnetic resonance imaging of the brain revealed vasogenic edema in the right frontal lobe with a 24 × 22 millimeter (mm) area of rim enhancement representing an early brain abscess with right parafalcine and tentorial subdural empyema (Figure 2C). She underwent craniotomy with abscess incision and drainage followed by craniectomy and reconstruction of the scalp with a free anterolateral thigh flap. Post-surgical MRI of the brain revealed restricted diffusion and persistent edema of the right anterior frontal lobe, frontal lobe herniation through the craniectomy defect, and a left parasagittal frontal lobe focus of hemorrhagic cerebritis (Figure 2D). Intraoperative cultures were positive for *Streptococcus intermedius* and *Candida albicans*; thus, she was prescribed IV ampicillin and fluconazole for a 6-week duration. Her ongoing hospitalization was complicated by multiple deep vein thrombi in the setting of immobilization, acute hypoxic respiratory failure, and septic shock requiring multiple vasopressors. Six weeks after admission, the patient's family decided to transition to focusing on her comfort and the patient passed peacefully.

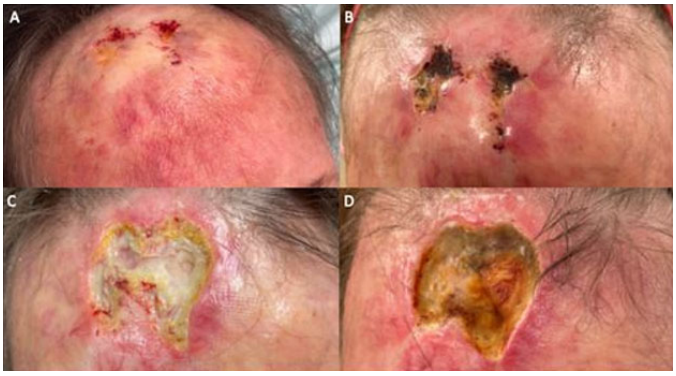

Figure 1: Evolution of the forehead lesion. (A) Erythematous skin with honey-colored lesion midway through scheduled radiation treatments resulting in brief suspension of radiation. (B) Scabbed forehead lesion after completion of radiation with suspicion for bacterial infection. (C) Forehead lesion with weekly sessions of wound debridement and dressing changes. (D) 8-centimeter (cm) honey-crusted forehead lesion with areas of black tissue with no discharge or purulence.

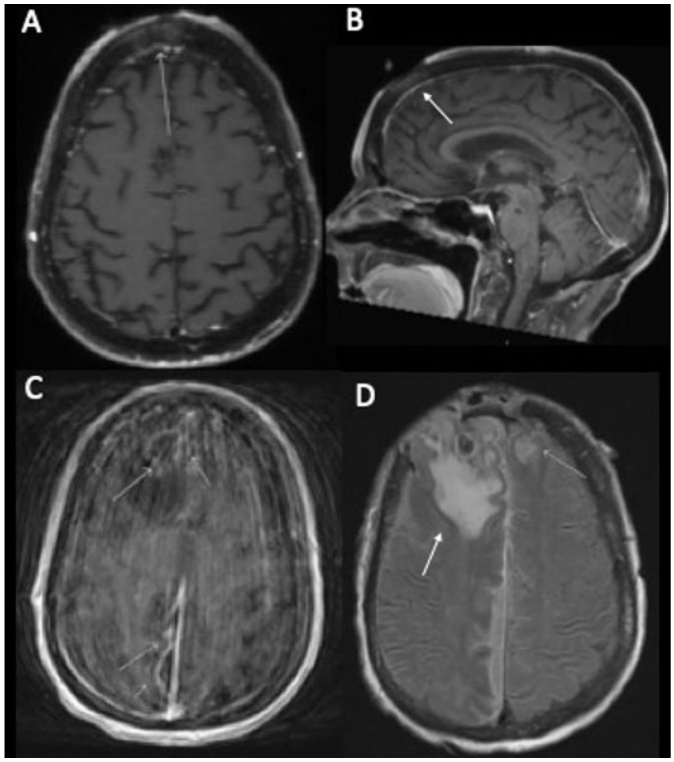

Figure 2: Evolution of the forehead lesion on magnetic resonance imaging (MRI) of the brain. (A) T1 axial image completed one month prior to presentation with a roughly 2 cm area reflecting early osteonecrotic changes. (B) T1 sagittal image completed one month prior to presentation with a 2.5 cm defect in the right anterior vertex scalp. (C) Upon presentation, T1 axial image revealed a faint ring enhancement in the right frontal lobe concerning for early brain abscess along with right parafalcine and tentorial subdural empyema. (D) Post-operative T2 coronal image with persistent surrounding vasogenic idea with frontal lobe herniation and left parasagittal frontal lobe focus of hemorrhagic cerebritis.

DISCUSSION

Connective tissue diseases such as scleroderma, rheumatoid arthritis, and inflammatory myopathies have been shown to contribute to a higher incidence of cancer compared to the general population [3]. Studies have shown that patients diagnosed with systemic scleroderma found a statistically significant increased risk of developing cSCC, lung, liver, hematologic, and bladder cancers compared to the general population [3, 4]. It is postulated that the increased risk of cancer may be due to defects in immune surveillance, impaired clearance of carcinogens, increased malignant transformation due to epithelial hyperplasia or fibrosis, genetic susceptibility, or cytotoxic immunosuppressive therapies used to treat scleroderma [3, 4]. Specifically, immunosuppressive therapies such as tumor necrosis alpha inhibitors, calcineurin inhibitors, and even mycophenolate have been associated with an increased risk of developing cSCC [2, 5]. In this case, the patient's history of scleroderma treated with immunosuppressive therapy may be part of a larger multifactorial reason she developed cSCC.

The National Comprehensive Cancer Network (NCCN) recommends that primary treatment of high-risk cSCC involves surgical excision with either the Mohs or Tubingen technique [1]. High-risk features include size >4 cm, poor differentiation, desmoplastic, 0.6 mm thickness or invasion beyond subcutaneous fat, and perineural, lymphatic, or vascular involvement [1]. Additionally, The NCCN and the American Society for Radiation Oncology (ASTRO) both recommend the use of adjuvant radiation therapy when there is neural involvement within the tumor [1, 6]. With our patient's lesion considered high risk, she underwent Mohs surgery with negative resection margins followed by 30 treatments with radiation therapy due to the neural involvement within the resected tumor. However, for patients with genetic conditions such as ataxia-telangiectasia, Li–Fraumeni syndrome, and basal cell nevus syndrome that predispose to skin cancer and radiosensitivity, radiotherapy would be contraindicated [1, 6]. The NCCN acknowledges that connective tissue disorders such as scleroderma may be relatively contraindicated while ASTRO states that poorly controlled connective tissue disorders are a relative contraindication for radiation treatment [1, 6]. In our case, the patient's scleroderma had been well controlled for the last 20 years. The use of adjuvant radiation therapy was a reasonable choice as the patient had a high risk lesion with neural involvement, the patient had well controlled scleroderma for many years, and the NCCN and ASTRO guidelines do not state an absolute contraindication in patients with scleroderma.

Radiation therapy is not without its risk of adverse effects, especially in patients with scleroderma. There are concerns that the use of radiation therapy could trigger exaggerated skin and visceral fibrosis leading to increased morbidity [7]. A systematic review of patients with scleroderma receiving radiation therapy for various cancers revealed that 75.5% did not develop worsening skin thickening but developed toxicities ranging from dermatitis and erythema to skin fibrosis, lymphedema, telangiectasia, and dysphagia [7]. At the Mayo Clinic, 75% of patients with scleroderma treated with radiation therapy for malignancy developed acute toxic effects and 65% were left with chronic toxic effects [8]. One patient even developed a severe wound infection postoperatively treated with debridement and antibiotics similar to our case. The heterogeneity in reported adverse events between studies may reflect variations in radiation doses, patient characteristics, malignancy type, and concurrent treatments being received by patients. We were not able to identify the dose of radiation used for our patient so we cannot comment on whether the dose of radiation may have contributed to her condition. Nevertheless, our patient developed a forehead wound while undergoing radiation therapy.

The development of the patient's forehead wound and resulting empyema was likely multifactorial. The patient's forehead initially became raw and erythematous while undergoing radiation therapy. However, during radiation therapy she was actively medically immunosuppressed with prednisone and mycophenolate mofetil. It was not until four months after completion of radiation therapy and an infection was suspected that mycophenolate mofetil was suspended. Additionally, her scleroderma likely complicated wound healing from surgery and led to dehiscence. The combination of these factors led to the development of a localized skin infection. This infection then likely spread contiguously into the brain parenchyma and hematogenously into the blood leading to her presentation. This is an extremely rare presentation as Jensen et al. examined 5674 patients with head and neck squamous cell carcinoma undergoing radiation therapy or chemoradiation finding that bloodstream infections only occurred in 4% of patients but carried a 26% 30-day mortality rate [9].

CONCLUSION

Patients with scleroderma are at an increased risk of developing malignancy due to chronic inflammation, tissue damage, shared genetic susceptibility, and immunosuppressive therapy. The guidelines recommend treating high-risk cSCC with neural involvement with surgical resection followed by adjuvant radiation therapy. Treatment of cSCC presents with risk of adverse effects including infection but heterogeneity in reported adverse events suggests the use of radiation therapy would be reasonable in patients with well controlled scleroderma. This case highlights a rare infection after treatment of cSCC which emphasizes that treatment of malignant skin lesions in patients with scleroderma can be challenging. Shared decision-making with a thorough assessment of risks should be emphasized with every patient before proceeding with treatment.

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Author Contributions

Matthew R Barke – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Sujata Ojha – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Madeline Fitzpatrick – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Boone Goodgame – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.