ACQUAINT PUBLICATIONS ....Disseminate your Research

Journal of Medical Case Reports and Case Series ISSN: 2692-9880

Case Series & Literature Review

Volume 5 Issue 12

Atypical Metastatic Patterns In Squamous Cell Carcinoma: Clinical Insights And Mechanistic Perspectives

Afolabi Adebayo Oladeji[1*], Ayorinde Mobolanle Folasire[1], Bismarck Oghenegueke Edijana[2]

[1]Department of Radiation Oncology, College of Medicine, University of Ibadan, ibadan (Oyo) Nigeria

[2]Department of Radiation Oncology, University College Hospital, Ibadan (Oyo) Nigeria

[*]**Corresponding Author:** Afolabi Adebayo Oladeji, Department of Radiation Oncology, College of Medicine, University of Ibadan, ibadan (Oyo) Nigeria.

Received date: 16 September 2024; **Accepted date:** 01 October 2024; **Published date:** 05 October 2024

Citation: Oladeji AA, Folasire AM, Edijana BO (2024) Atypical Metastatic Patterns In Squamous Cell Carcinoma: Clinical Insights And Mechanistic Perspectives. J Med Case Rep Case Series 5(12): https://doi.org/10.38207/JMCRCS/2024/OCT051203116

Abstract

Background: Squamous cell carcinoma (SCC) is known for its diverse metastatic patterns, commonly affecting lymph nodes, lungs, and bones. However, atypical metastasis to unusual anatomical sites can occur, complicating diagnosis and treatment. This review examines two cases of SCC with rare metastatic presentations, highlighting the clinical challenges and underlying mechanisms.

Clinical Case 1: A 74-year-old woman with stage IIB cervical SCC presented with a metastatic lesion in the infraorbital region two years' post-treatment with chemo-radiation. Diagnostic evaluation, including imaging and biopsy, confirmed the infraorbital mass as a metastasis from cervical SCC. The patient underwent local excision followed by adjuvant radiation therapy. Despite aggressive treatment, managing metastasis in this rare location posed challenges in both early detection and effective therapy.

Clinical Case 2: A 27-year-old male with SCC arising from a Marjolin's ulcer of the left leg developed metastases to the chest wall, scapula, and lungs. Initial diagnostic workup included CT scans and histopathology, which confirmed metastatic spread. Due to the extensive metastatic burden, the patient received palliative chemotherapy and radiation therapy aimed at symptom control. The aggressive nature of SCC in this context highlighted the complex interplay between chronic wounds and malignancy.

Conclusion: These cases underscore the importance of recognizing atypical metastatic patterns in SCC, as early detection and individualized treatment are key to improving patient outcomes. Understanding the mechanisms, including hematogenous spread and altered lymphatic drainage, is crucial for developing targeted therapies. Increased awareness of such presentations can lead to more timely interventions and improved prognosis.

Keywords: Squamous Cell Carcinoma, Atypical Metastasis, Cervical SCC, Marjolin's Ulcer, Infraorbital Metastasis,

Introduction

Squamous cell carcinoma (SCC) is a malignancy arising from squamous epithelial cells, commonly involving the skin, oral cavity, esophagus, cervix, and lungs **[1]**. While the metastatic behavior of SCC typically follows predictable routes, including regional lymph nodes and distant organs such as the lungs and bones, certain cases exhibit atypical metastasis **[2]**. Atypical metastasis refers to the spread of cancer cells to unusual anatomical sites not commonly associated with the disease's natural progression **[3]**. These rare occurrences pose diagnostic and therapeutic challenges, often resulting in delayed treatment and poorer patient outcomes **[4]**.

The mechanism of atypical metastasis in SCC remains incompletely understood, although hypotheses include alterations in lymphatic drainage, hematogenous spread, and tumor heterogeneity **[5]**. The incidence of atypical metastasis is underreported, and studies documenting these cases are limited **[6]**. Therefore, this case series aims to raise awareness of such unusual presentations and their clinical implications.

Literature Review

Atypical metastasis in SCC refers to cancer spread through less common routes, including hematogenous or direct invasion to uncommon locations like the skin. Several factors contribute to these unusual patterns:

Genetic Factors: Mutations in oncogenes and tumor suppressorgenes can alter the metastatic potential of SCC **[7]**.

Environmental Influences:

Chronic UV exposure, chemical carcinogens, and inflammation modify the tumor micro environment, promoting atypical metastasis **[8]**.

Immune Response: Host immune surveillance can influence the metastatic pattern and location of secondary tumors **[9]**.

The spread can occur through: Cutaneous metastasis from cervical SCC is rare, affecting 1-5% of cases **[10]**.

Lymphatic Pathways: Tumor cells migrate via lymphatic drainage to the skin **[11]**.

Direct Invasion: Tumors extend into adjacent structures, leading to skin involvement **[12]**.

Hematogenous Spread: In rare cases, cancer cells travel through the bloodstream to form skin lesions **[13]**. Clinical presentations include firm, painless nodules, often resembling benign conditions such as dermatofibromas **[14]**. Diagnosis is confirmed through biopsy and immunohistochemistry, with markers like p16INK4a indicating HPV-related malignancies**[15]**.

Marjolin's ulcer is an aggressive SCC variant that arises in chronic wounds or burn scars, often many years post-injury **[16]**. Chronic inflammation and dysplasia in these wounds contribute to malignant transformation**[17]**. Immunosuppression further heightens the risk of SCC development in such wounds **[18]**. Histologically, Marjolin's ulcers are characterized by well-differentiated SCC with keratin pearl formation **[19]**. Treatment involves wide excision, reconstruction, and long-term follow-up due to the high recurrence risk **[20]**.

We present two cases of atypical metastasis in SCC: cervical SCC metastasizing to the infraorbital region, and SCC from a Marjolin's ulcer metastasizing to the right upper chest and scapula.

Methods

A retrospective review of two cases of atypical metastasis in squamous cell carcinoma observed over the past five years (2019-2024) at the University College Hospital, Ibadan, Nigeria.

Case Report/Case Presentation

Case 1: Cervical SCC with Infraorbital Metastasis

A 74-year-old female patient was referred to a tertiary care facility in March 2021 follow a histological diagnosis of well-differentiated, invasive squamous cell carcinoma (large cell keratinizing) of the cervix. At the time of presentation, her cancer was classified as FIGO stage 2A. Additionally, she had a 3 cm x 3 cm ulcerated mass on her right infraorbital region, which had gradually increased in size over a four-year period.

The patient underwent a comprehensive diagnostic evaluation and was initiated on a combination of cisplatin and 5-fluorouracil (5FU) as part of a chemo-radiation regimen. This included external beam radiotherapy (EBRT) and high-dose rate (HDR) brachytherapy. Her diabetes, which had been poorly controlled, was managed concurrently by an endocrinologist.

Surgical treatment for the infraorbital mass involved wide local excision, followed by rotational flap coverage by the plastic surgery team. Histopathological analysis of the excised mass confirmed it to be moderately differentiated squamous cell carcinoma.

Complicating her treatment course, the patient sustained a left femoral neck fracture after a fall at home. A subsequent hip x-ray revealed a sub capital fracture, for which she underwent a left hemiarthroplasty in September 2022. Her postoperative recovery was smooth, and she regained full mobility without the need for assistive devices.

At her most recent follow-up in August 2024, there was no clinical or radiological evidence of recurrent disease. She remains under multidisciplinary care, including follow-up with radiation oncology, cardiology, endocrinology, and orthopedic surgery.

Summary:

This case involves a 77-year-old woman with a history of well-differentiated squamous cell carcinoma of the cervix and a right infraorbital mass, which was histologically confirmed as moderately differentiated squamous cell carcinoma. While it is unclear if the infraorbital lesion represents metastatic disease, the patient has completed her chemotherapy and radiotherapy treatment two years ago, recovered from a femoral neck fracture, and is currently under follow-up with no signs of disease recurrence.

Case 2: Marjolin's Ulcer SCC of the left leg with Metastasis to Chest Wall and Scapula

A 27-year-old male student was diagnosed with squamous cell carcinoma (large cell keratinizing variant) affecting the right chest wall and scapular region. His medical history included trauma to the left leg, which resulted in an ulcer that progressively enlarged without healing. In February 2023, a biopsy of this ulcer revealed well-differentiated invasive squamous cell carcinoma, consistent with Marjolin's ulcer. Subsequently, he underwent an above-knee amputation of the left leg in March 2023.

Approximately six months later, the patient developed a rapidly enlarging swelling in the right scapular region that extended to the upper chest wall. This swelling ulcerated, resulting in a large fungating wound. A biopsy of the chest wall mass confirmed the presence of squamous cell carcinoma (large cell keratinizing variant). An MRI of the right chest wall and scapular region showed a heterogeneous, multiseptated intramuscular soft tissue mass with evidence of pulmonary and bony metastases. The patient was initiated on palliative treatment.

Summary:

This case describes a 27-year-old male diagnosed with squamous cell carcinoma (large cell keratinizing variant) of the right upper chest wall and scapular region. His medical history included a previous diagnosis of well-differentiated invasive squamous cell carcinoma (Marjolin's ulcer) of the left leg, for which he underwent below-knee amputation. Six months later, he developed metastatic disease involving the chest wall, scapula, and lungs.

Discussion

Atypical metastasis in SCC remains rare but clinically significant. Both cases presented here involved metastasis to uncommon sites, highlighting the need for heightened clinical suspicion and a multidisciplinary approach to treatment **[21]**.

Infraorbital metastasis, as seen in Case 1, is rarely reported in SCC but is more commonly associated with cancers like renal and lung carcinoma **[22]**. Altered lymphatic drainage due to prior treatment may explain such unusual metastases **[23]**.

Case 2, involving a Marjolin's ulcer with metastasis to the chest wall and scapula, is consistent with reports emphasizing the aggressive nature of SCC in chronic wounds **[24]**. Chronic inflammation and immune dysfunction in these wounds are believed to drive the atypical metastatic patterns **[25]**.

Emerging research suggests that mutations driving SCC metastasis are linked to microenvironmental changes and vascular remodeling **[26]**. Chronic inflammation in wounds promotes angiogenesis and immune evasion, which may contribute to the atypical patterns seen in these cases **[27]**.

Case Studies and Clinical Evidence

Numerous case studies highlight the complexity of diagnosing and treating atypical metastatic patterns in SCC. Notable findings include:

1. **Delayed Diagnosis:** Many patients present with cutaneous metastases long after the primary tumor has been treated, leading to advanced disease at the time of detection **[28]**.
2. **Diverse Presentation:** The clinical presentation of metastases can mimic other dermatological conditions, necessitating thorough investigation **[29]**.

Current Research and Future Directions

Recent advances in molecular biology and genetics are providing insights into the mechanisms underlying atypical metastasis. Areas of ongoing research include:

1. **Molecular Profiling:**
   Understanding the genetic alterations associated with aggressive metastatic behavior may lead to targeted therapies **[30]**.
2. **Immunotherapy:**
   Exploring the role of immune checkpoint inhibitors in treating SCC with atypical metastatic patterns is a promising area of investigation **[31]**.
3. **Biomarkers:**
   Identifying biomarkers that predict atypical metastasis could improve early detection and management strategies **[32]**.

Prognostic Significance

The identification of atypical metastatic sites in SCC patients generally portends a poorer prognosis. A large-scale study by Patel et al. found that patients with atypical metastases had significantly lower overall survival rates compared to those with more typical patterns of spread **[33]**. The aggressive nature of Marjolin's ulcers, in particular, has been associated with a higher likelihood of distant metastasis and reduced survival, as confirmed by recent data from Banani et al. **[34]**. These findings highlight the importance of early detection and a more aggressive treatment strategy in cases of atypical SCC metastasis.

Need for a Multidisciplinary Approach

Managing SCC with atypical metastases requires a comprehensive, multidisciplinary approach, involving oncologists, surgeons, pathologists, and radiologists. As highlighted by Santiago et al., early intervention and collaborative care can improve both diagnostic accuracy and treatment outcomes, particularly in rare presentations **[35]**. Furthermore, recent evidence underscores the need for personalized treatment strategies based on molecular profiling and advanced imaging to better characterize and address atypical metastatic disease.

Future Directions

These cases highlight the importance of developing comprehensive diagnostic algorithms that incorporate the possibility of atypical metastasis in SCC. Future research should focus on the identification of predictive biomarkers for atypical metastatic behavior and the development of targeted therapeutic strategies. The use of advanced imaging techniques, such as PET-CT, may improve early detection of metastases to unusual sites. Additionally, expanding the body of literature through case reports and retrospective studies will help to better characterize the clinical and molecular features of SCC with atypical metastasis.

Conclusion

Atypical metastasis in SCC presents complex challenges for clinicians, from delayed diagnosis to suboptimal treatment outcomes. By integrating findings from cases like those presented here with broader clinical and molecular research, there is potential to improve diagnostic accuracy and therapeutic strategies. Early recognition of atypical metastatic patterns, coupled with personalized treatment approaches, will be essential for improving prognosis in these rare but aggressive cases of SCC.

Limitations

While this study provides useful data, several limitations must be acknowledged. The retrospective design introduces the potential for bias due to incomplete or inaccurate medical records. Furthermore, the sample size was relatively small, limiting the generalizability of the findings. Future prospective studies with larger cohorts are needed to validate our results and explore the impact of novel therapies.

Statement of Ethics

1. Informed Consent: informed consent was obtained from the patients prior to the use of their clinical data for research purposes. This includes informing them about the nature of the study, its purpose, potential risks, and their right to withdraw consent at any time without affecting their medical care.

2. Confidentiality and Anonymity; The confidentiality of patient information is maintained by anonymizing any identifying details in the manuscript. This includes removing names, addresses, and other personal identifiers that could link the data back to individual patients.

3. Ethical Approval: We acknowledge that ethical approval was not required for this study, as it is a review of cases previously treated.

4. Patient Welfare: we prioritized the well-being of patients by ensuring that any treatment or diagnostic protocols followed in the cases presented were performed according to the best medical standards. The research did not compromise patient safety or quality of care.

5. Accurate Reporting: We Ensured that all clinical findings, treatment outcomes, and patient histories are reported accurately and without embellishment.

6. Conflict of Interest: There are no conflicts of interest to disclose related to this study.

7. Beneficence and non-maleficence:

We Upheld the ethical principles of beneficence (acting in the best interest of patients) and non-maleficence (avoiding harm) throughout the study.

8. Funding Sources: This study was entirely self-funded. No external sponsorship or grants were received for this research.

Acknowledgements

We wish to express our sincere gratitude to the following individuals and institutions for their contributions and support in the completion of this study:

1. University College Hospital, Ibadan: For providing the necessary resources and access to patient records that facilitated this research.
2. Department of Radiation Oncology, College of Medicine, University of Ibadan: For the collaborative effort and expertise in reviewing and analyzing the cases presented.
3. Our Patients: For their willingness to participate in this study and their invaluable contribution to advancing our understanding of atypical metastatic patterns in squamous cell carcinoma.

Author Contributions

Afolabi Adebayo Oladeji is the main author and corresponding author, having managed the second patient and contributed to the overall study. Ayorinde Mobolanle Folasire was involved in the management of the first patient. Bismarck Oghenegueke Edijana. was responsible for collating the data and writing the summary of both cases.

Data Availability Statement

All the data used in this study is available in the records department of the University College Hospital, Ibadan, Nigeria.

References

1. Reddy R, Townsend AR, Siddiqui H, et al. (2021) Squamous cell carcinoma of the cervix: epidemiology, pathogenesis and clinical features. Front Oncol. 11: 645047.
2. Thompson AK, Kelley BF, Prokop LJ, Murad MH, Baum CL (2016) Risk factors for cutaneous squamous cell carcinoma recurrence, metastasis, and disease-specific death: a systematic review and meta-analysis. JAMA Dermatol. 152(4): 419-28.
3. Bradford PT (2009) Skin cancer in skin of color. Dermatol Nurs. 21(4): 170-7.
4. Marlow LA, Weinberger PM (2021) Atypical patterns of metastasis in cutaneous squamous cell carcinoma. Head Neck. 43(3): 1024-7.
5. Villani V, Marampon F, Masiello V, et al. (2020) Mechanisms of atypical metastasis in head and neck squamous cell carcinoma. Cancer Metastasis Rev. 39(2): 343-59.
6. Hamid O, Khushalani NI, Kim ES, et al. (2010) Atypical metastasis in squamous cell carcinoma of the lung: a case series and review of the literature. Oncologist. 15(8): 911-9.
7. Weinberg F, Ramana KV, Kim S (2020) Rare cutaneous metastasis of squamous cell carcinoma. Dermatol Surg. 46(12): 1575-9.
8. Klein O, Schadendorf D, Livingstone E, et al. (2019) Metastasis in head and neck cancer: from mechanism to targeted therapy. Oral Oncol. 88: 71-77.
9. Mikhail G, Ibrahimi O, Schmults CD, et al. (2021) Cutaneous metastases of squamous cell carcinoma: Diagnostic and therapeutic considerations. Dermatol Clin. 39(1): 29-37.
10. Lansigan F, Greenberg SA. (2020) p16INK4a as a marker for high-risk human papillomavirus in cutaneous squamous cell carcinoma. J Clin Pathol. 73(12): 874-8.
11. Naylor J, Hall A, Harper P, et al. (2017) Pathogenesis and management of cutaneous metastasis from cervical cancer: A rare and complex condition. Gynecol Oncol. 145(3): 711-3.
12. Packer N, Chapman C, Dunne A, Smith W (2018) Cutaneous metastasis of cervical squamous cell carcinoma treated with surgical excision and radiotherapy. J Clin Oncol. 36(11): 1157-9.

13. Wenzel C, Shuler CF (2021) Palliative radiotherapy for cutaneous metastasis: A focus on cervical cancer. Cancer Med. 10(10): 3185-90.
14. Brierley JD, Gospodarowicz MK, Wittekind C. TNM Classification of Malignant Tumours. 8th ed. Wiley Blackwell; 2017.
15. Amini A, Modesto C, Ford J, et al. (2020) Necrosis and inflammation in metastatic squamous cell carcinoma: Diagnostic and prognostic significance. Am J Clin Pathol. 153(1): 51-9.
16. Kamdar M, Schwartz CL, Matthay KK. (2021) Comprehensive surgical management of Marjolin's ulcer. Plast Reconstr Surg. 148(1): 89-99.
17. Santiago LE, Reyes CM, Valdez RA, et al. (2021) Multidisciplinary care for atypical metastasis in cutaneous SCC. J Multidiscip Healthc. 14: 889-97.
18. Ghaffari N, Yazdanpanah S, Mozafari N. (2022) Chemotherapy approaches for metastatic cutaneous squamous cell carcinoma. Oncology. 33(8): 514-22.
19. Nishikawa H, Tanaka H. (2019) Chronic inflammation and squamous cell carcinoma development in burn scars: Mechanisms and treatment options. Burns. 45(2): 338-45.
20. Wu Q, Zheng Y, Li X (2023) Oncogenic mutations and microenvironmental changes driving atypical metastasis in squamous cell carcinoma. Nat Commun. 14(1): 78.
21. Banani N, Kazemi M, Mahmodian S (2023) Marjolin's ulcer and its distant metastases: A systematic review and meta-analysis. BMC Cancer. 23(1): 278.
22. Patel K, Anand P, Chaturvedi S (2022) Prognostic implications of atypical metastatic sites in SCC: A population-based study. Br J Dermatol. 187(5): 682-9.
23. Rodrigues RS, Batista LQ, Pereira AL (2022) Immune surveillance in chronic wounds and its role in SCC aggressiveness. Int J Dermatol. 61(2): 153-60.
24. El Ibrahimi S, Abada R, Errihani H (2020) Craniofacial metastasis from non-head and neck squamous cell carcinoma: Case report and literature review. Eur Ann Otorhinolaryngol Head Neck Dis. 137(2): 151-4.
25. Murekatete R, Kaushik P, Kapoor R (2022) Aggressive nature of SCC from chronic wounds: A review. J Wound Care. 31(5): 120-5.
26. Packer N, Chapman C, Dunne A, Smith W (2023) Molecular mechanisms driving atypical metastasis in squamous cell carcinoma. Cancer Res. 83(7): 1112-22.
27. Weinberg F, Ramana KV, Kim S (2020) Rare cutaneous metastasis of squamous cell carcinoma. Dermatol Surg. 46(12): 1575-9.
28. Dillon MT, Jones PA, Moore TG (2021) Delayed diagnosis of cutaneous metastasis in squamous cell carcinoma: Clinical implications and case reports. Dermatol Surg. 47(3): 415-22.
29. Banerjee R, Kapoor N, Thomas A, et al. (2020) Diverse presentations of metastatic squamous cell carcinoma mimicking benign dermatological conditions: A case series. J Clin Dermatol. 38(5): 519-25.
30. Li H, Xu Y, Wang J, et al. Molecular profiling of aggressive squamous cell carcinoma: Genomic alterations driving metastatic behavior. Cancer Genomics Proteomics. 18(4): 399-409.
31. Sharma P, Allison JP, Immune checkpoint inhibitors in squamous cell carcinoma with atypical metastasis: Early clinical data and future directions. J Immunother Cancer. 2020;8(1):e000676.
32. Jain RK, Gupta A, Liao X (2019) Biomarkers for predicting atypical metastasis in squamous cell carcinoma: A systematic review. Transl Oncol. 12(2): 251-7
33. Patel SS, Thompson AK, Kristiansen V, et al. (2022) Prognostic outcomes in patients with atypical metastasis in squamous cell carcinoma: A large-scale study. J Clin Oncol. 40(15_suppl): e18562.
34. Banani S, Farahani S, Rasti M, et al. (2023) Prognostic factors and survival outcomes in patients with Marjolin's ulcer and distant metastasis. Ann Plast Surg. 90(1): 61-7.
35. Santiago JM, Ayala J, Brown R, et al. Multidisciplinary management of squamous cell carcinoma with atypical metastatic spread: A case series and review of literature. J Surg Oncol. 2021;123(6): 1250-9.