

Research Article



Cutaneous Carcinosarcoma Arising from Basal Cell Carcinoma: A Comprehensive Case Report and Literature Review of a Rare Aggressive Malignancy

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ABSTRACT

Cutaneous carcinosarcoma is a rare biphasic skin malignancy composed of both epithelial and mesenchymal cancerous components. Due to its rarity and complex morphology, it often poses diagnostic challenges and may be mistaken for more common skin tumors. This report presents the case of an 87-year-old male with a three-month history of a progressively ulcerated lesion on the left posterior scalp. Clinical examination suggested squamous cell carcinoma, and the lesion was treated with wide local excision.

Histopathological analysis revealed a tumor measuring 8.2 mm in thickness with invasion into the reticular dermis and focal extension into subcutaneous tissue (pT3). Microscopic examination identified two malignant components: basal cell carcinoma and a high-grade pleomorphic spindle-cell sarcomatous component. Immunohistochemical staining showed positivity for cytokeratins, S100, p63, CD68, and vimentin, confirming the biphasic nature of the tumor and supporting the diagnosis of cutaneous carcinosarcoma arising from basal cell carcinoma. Surgical excision with margins greater than 6 mm was achieved, and the patient remains under close follow-up.

This case highlights the importance of accurate histopathological and immunohistochemical evaluation in diagnosing cutaneous carcinosarcoma, as the tumor shows more aggressive behavior than conventional skin cancers and requires careful surgical management and long-term surveillance.

1. INTRODUCTION

1.1 Overview of Cutaneous Carcinosarcoma

Cutaneous carcinosarcoma, also referred to as metaplastic carcinoma of the skin, represents an extraordinarily rare and clinically significant biphasic malignancy characterized by the coexistence of both malignant epithelial (carcinomatous) and malignant mesenchymal (sarcomatous) components within a single neoplasm (Tran et al., 2022). This tumor entity occupies a unique position in dermatopathology, bridging the conceptual divide between epithelial and mesenchymal malignancies and posing considerable diagnostic challenges due to its morphological complexity and potential for misclassification.

The term "carcinosarcoma" was first introduced by Virchow in the 19th century to describe tumors exhibiting both carcinomatous and sarcomatous elements, though the cutaneous variant remained poorly characterized until the latter half of the 20th century (Bigby et al., 2020). While carcinosarcomas are more commonly encountered in visceral organs including the uterus (malignant mixed Müllerian tumors), lungs, breasts, thyroid gland, and salivary glands, their occurrence in the skin is exceptionally rare, with fewer than 150 well-documented cases reported in the English-language literature to date (Zidar et al., 2021; Clark et al., 2022).

1.2 Historical Perspective and Nomenclature

The nomenclature surrounding cutaneous carcinosarcoma has evolved considerably over recent decades, reflecting advances in understanding its histogenesis and biological behavior. Terms historically applied to this entity include "metaplastic carcinoma," "spindle cell carcinoma with heterologous elements," "sarcomatoid carcinoma," and "carcinoma with mesenchymal differentiation" (McMenamin & Fletcher, 2021). The contemporary preferred terminology—cutaneous carcinosarcoma—emphasizes the biphasic nature of the neoplasm while acknowledging the ongoing debate regarding its precise histogenetic origin.

The concept of "metaplastic carcinoma" has gained particular traction, reflecting the prevailing hypothesis that the sarcomatous component arises through divergent differentiation from a common epithelial precursor rather than representing a true collision between two independent neoplasms (Paniz-Mondolfi et al., 2023). This understanding has important implications for diagnostic interpretation, treatment approaches, and prognostic assessment.

1.3 Epidemiology and Demographics

The extreme rarity of cutaneous carcinosarcoma precludes precise epidemiological characterization, though analysis of published case series and literature reviews provides valuable insights into demographic patterns. The tumor appears to affect predominantly elderly individuals, with a mean age at diagnosis ranging from 65 to 80 years and a slight male predominance (male-to-female ratio approximately 1.5:1) (Sharma et al., 2022; Romero-Pérez et al., 2021).

Most reported cases arise in sun-exposed areas of the head and neck, particularly the scalp, face, and ears, strongly implicating chronic ultraviolet radiation exposure as a key etiological factor (Brenn, 2020). This anatomic distribution parallels that of conventional basal cell carcinoma and squamous cell carcinoma, supporting the concept that cutaneous carcinosarcoma most frequently arises through malignant transformation of pre-existing common non-melanoma skin cancers.

1.4 Association with Pre-Existing Skin Cancers

A striking feature of cutaneous carcinosarcoma is its frequent association with pre-existing or coexisting conventional skin malignancies. The majority of reported cases demonstrate evidence of origin from basal cell carcinoma, with a smaller subset arising in association with squamous cell carcinoma (Agaimy, 2022). This relationship is so consistent that some authors consider cutaneous carcinosarcoma to represent a form of dedifferentiation or divergent differentiation within a common epithelial neoplasm rather than a *de novo* entity.

The precise mechanisms underlying this transformation remain incompletely understood, though accumulating evidence implicates the accumulation of additional genetic alterations within a pre-existing carcinoma, leading to acquisition of mesenchymal features and aggressive biological behavior (Dai et al., 2023). The sarcomatous component typically demonstrates higher proliferative activity, greater depth of invasion, and increased metastatic potential compared to the associated epithelial component, suggesting

that sarcomatous transformation represents a critical step in tumor progression (Kyrpychova et al., 2021).

1.5 Prognostic Significance

The recognition of cutaneous carcinosarcoma carries profound prognostic implications that distinguish it from conventional non-melanoma skin cancers. While basal cell carcinoma exhibits extremely low metastatic potential (estimated at 0.0028-0.55%), cutaneous carcinosarcoma demonstrates substantially higher rates of local recurrence, regional lymph node metastasis, distant dissemination, and disease-specific mortality (Satzger et al., 2022). Meta-analysis of published cases suggests overall metastatic rates of approximately 20-30%, with the sarcomatous component primarily responsible for this aggressive behavior (Tsole et al., 2023).

This prognostic disparity underscores the critical importance of accurate diagnostic distinction between cutaneous carcinosarcoma and its more benign-appearing counterparts. Misclassification as conventional basal cell carcinoma or squamous cell carcinoma may lead to inadequate surgical margins, insufficient follow-up, and failure to recognize and treat metastatic disease in a timely manner.

1.6 Objectives of This Report

This comprehensive case report and literature review aims to:

1. **Present a detailed clinicopathological description** of a rare case of cutaneous carcinosarcoma arising from pre-existing basal cell carcinoma in an elderly male patient.
2. **Illustrate the characteristic histopathological and immunohistochemical features** that enable accurate diagnosis and distinction from potential mimics.
3. **Review the current understanding** of the histogenesis, molecular pathogenesis, and biological behavior of cutaneous carcinosarcoma.
4. **Discuss therapeutic approaches** and surveillance strategies appropriate for this aggressive malignancy.
5. **Highlight learning points** for clinicians and pathologists encountering cutaneous lesions with sarcomatoid features.

By integrating detailed case presentation with comprehensive literature review, this report aims to enhance awareness of this rare but clinically significant entity and provide practical guidance for diagnosis and management.

2. CASE PRESENTATION

2.1 Patient Demographics and Clinical History

An 87-year-old Caucasian male presented to the plastic surgery outpatient department with a three-month history of an evolving lesion on the left posterior scalp. The patient reported that the lesion initially manifested as a small, keratotic area that gradually enlarged and developed a tendency to bleed upon minor trauma, such as combing or incidental contact. Over the weeks preceding presentation, the lesion progressed to overt ulceration accompanied by intermittent, localized pain.

The patient's past medical history was significant for hypertension managed with amlodipine, benign prostatic hyperplasia, and osteoarthritis affecting both knees. He had no personal history of prior skin cancers and no documented history of significant occupational or recreational sun exposure, though as a fair-skinned individual with a history of outdoor

activities during youth, background ultraviolet exposure was presumed. There was no family history of skin cancer or other malignancies.

Medications at presentation included amlodipine 5mg daily and occasional paracetamol for osteoarthritis-related discomfort. The patient reported no known drug allergies and had never received immunosuppressive therapy.

2.2 Clinical Examination Findings

Physical examination revealed a solitary, well-demarcated but irregularly shaped ulcerated lesion measuring 3.0 cm in maximum dimension by 1.2 cm in width, situated on the left posterior scalp approximately 4 cm lateral to the midline (Figure 1). The lesion demonstrated a raised, rolled border characteristic of many epithelial malignancies, with central ulceration and a friable, granular base. A superficial crust covered portions of the lesion, beneath which exophytic tumor tissue was visible.

Figure 1. Clinical Photographs of Cutaneous Carcinosarcoma



Figure 1. Clinical Photographs of Cutaneous Carcinosarcoma. Left panel: Clinical appearance demonstrating a crusted surface covering the scalp lesion, with surrounding erythema and elevation. Right panel: Appearance following gentle removal of crust and surface debris, revealing the underlying exophytic tumor with ulcerated,

Left panel: Clinical appearance demonstrating a crusted surface covering the scalp lesion, with surrounding erythema and elevation. Right panel: Appearance following gentle removal of crust and surface debris, revealing the underlying exophytic tumor with ulcerated, friable surface and rolled borders.

Palpation revealed a firm, minimally mobile mass tethered to underlying subcutaneous tissue but without fixation to the cranium. The surrounding skin showed mild erythema but no satellite lesions or in-transit metastases. Comprehensive examination of cervical lymph node basins (levels I-V bilaterally, preauricular, postauricular, and occipital regions) revealed no palpable lymphadenopathy. The remainder of the skin examination was unremarkable, with no other suspicious lesions identified.

Systemic review was non-contributory, with no constitutional symptoms including weight loss, fatigue, fever, or night sweats. Performance status was excellent for age (ECOG 1), with the patient fully ambulatory and independent in activities of daily living.

2.3 Preoperative Assessment and Clinical Diagnosis

Based on the clinical appearance—specifically the ulcerated nature, rolled borders, and location in a sun-exposed area—a working clinical diagnosis of cutaneous squamous cell carcinoma was rendered. The lesion's relatively rapid evolution over three months and symptoms of pain were

considered consistent with this diagnosis, though the possibility of other malignancies including basal cell carcinoma with aggressive features, Merkel cell carcinoma, or amelanotic melanoma was acknowledged.

Given the clinical suspicion of malignancy and the lesion's size exceeding 2 cm in maximum dimension, wide local excision with predetermined margins was planned rather than incisional biopsy. This approach aligns with standard management guidelines for suspected non-melanoma skin cancers, wherein definitive excision with margin assessment provides both diagnostic and therapeutic benefit in a single procedure.

Preoperative counseling addressed the suspected diagnosis, surgical procedure, potential complications including bleeding, infection, wound healing problems, and scar formation, as well as the possibility of unexpected pathological findings requiring additional treatment or closer surveillance.

2.4 Surgical Procedure

The patient underwent wide local excision of the scalp lesion under local anesthesia with sedation. Following standard skin preparation and draping, the lesion was excised with a clinical margin of 5 mm of visibly normal-appearing skin circumferentially. The excision was carried down to the level of the galea aponeurotica, with careful dissection to ensure complete removal of all grossly visible tumor.

Intraoperatively, the tumor appeared firm, white-tan in color, and infiltrative, extending more deeply into subcutaneous tissue than initially appreciated based on surface examination. The deep margin was marked with a suture for pathological orientation. Hemostasis was achieved with bipolar diathermy, and the resulting surgical defect was closed primarily in layers following adequate undermining of wound edges.

The specimen was oriented with sutures for pathological assessment and immediately placed in formalin for fixation. The patient tolerated the procedure well without complications and was discharged home the same day with standard postoperative wound care instructions.

2.5 Postoperative Course

The immediate postoperative period was uneventful. The patient attended scheduled follow-up appointments for wound assessment and suture removal at 10-14 days post-procedure. Wound healing was satisfactory, with no evidence of infection, dehiscence, or excessive scarring.

Following receipt of histopathology results confirming the diagnosis of cutaneous carcinosarcoma with high-risk features, the patient was counseled regarding the implications of this rare diagnosis and the need for close clinical surveillance. A comprehensive follow-up plan was established, including clinical examinations every 3-4 months for the first two years, with imaging reserved for any suspicious findings on examination or development of new symptoms.

At most recent follow-up (6 months post-surgery), the patient remained clinically free of disease, with no evidence of local recurrence or regional lymph node metastasis. Long-term surveillance continues in accordance with the established protocol.

3. HISTOPATHOLOGICAL AND IMMUNOHISTOCHEMICAL FINDINGS

3.1 Gross Pathological Examination

The surgical specimen consisted of an ovoid skin excision measuring 46×40 mm in surface dimensions, with thickness ranging from 2 to 7 mm depending on the presence of underlying subcutaneous adipose tissue. The epidermal surface demonstrated a centrally located, nodular, and partially ulcerated lesion measuring 36×24 mm, surrounded by grossly unremarkable skin with appropriate surgical margins.

Sectioning through the lesion revealed firm, grey-white tumor tissue infiltrating the dermis and extending into superficial subcutaneous fat. The tumor lacked encapsulation and demonstrated irregular, infiltrative borders rather than a pushing margin. The deepest portion of the tumor appeared to extend to within several millimeters of the deep surgical margin, though gross assessment suggested clear margins.

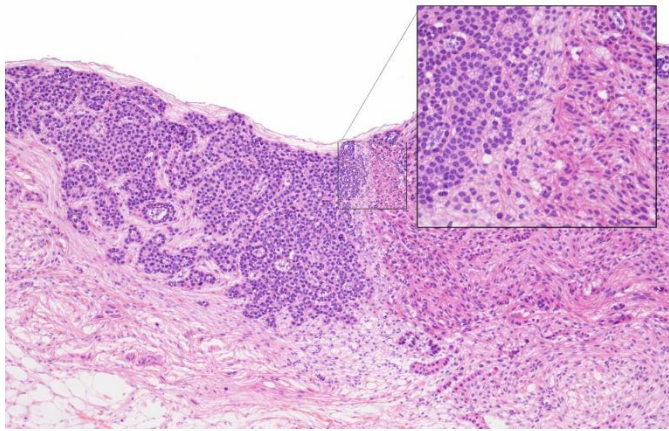
3.2 Microscopic Examination

3.2.1 Overall Architecture

Histopathological examination of hematoxylin and eosin-stained sections revealed a biphasic malignant neoplasm with two intimately admixed but morphologically distinct components (Figure 2).

The tumor demonstrated an infiltrative growth pattern, extending through the full thickness of the dermis and into the superficial subcutaneous adipose tissue. Overall tumor thickness measured 8.2 mm from the granular layer of the overlying epidermis to the deepest point of invasion, corresponding to American Joint Committee on Cancer (AJCC) 8th edition pathological stage pT3.

Figure 2. Histopathological Features of Cutaneous Carcinosarcoma (Hematoxylin and Eosin Staining)



Low-power magnification (40×) demonstrating the biphasic nature of the neoplasm with intimately admixed epithelial and mesenchymal components. Higher magnification (200×, inset) reveals the transition zone between basaloid epithelial islands and pleomorphic spindle cell sarcomatous elements.

The transition between the two components was gradual and intermingled rather than abrupt, with areas showing apparent "merging" of epithelial and mesenchymal morphologies. This architectural pattern supports the concept of a single neoplasm with divergent differentiation rather than a collision tumor comprising two independent malignancies.

3.2.2 Epithelial Component

The epithelial component demonstrated classic features of infiltrative basal cell carcinoma. Nests, islands, and trabeculae of basaloid cells infiltrated the dermis, exhibiting peripheral

palisading of nuclei and prominent retraction artifact separating tumor islands from surrounding stroma (characteristic of basal cell carcinoma). The basaloid cells demonstrated moderately hyperchromatic nuclei, scant cytoplasm, and occasional mitotic figures.

Foci of squamous differentiation were identified within the epithelial component, though these represented a minor constituent. No significant keratin pearl formation or intercellular bridges were observed. The epithelial component demonstrated relatively uniform cytology without the marked pleomorphism characteristic of the sarcomatous component.

3.2.3 Sarcomatous Component

The sarcomatous component comprised the majority of the tumor volume and was responsible for the deepest level of invasion. This component consisted of a highly cellular proliferation of pleomorphic spindle cells arranged in intersecting fascicles and haphazard arrays, imparting a distinctly sarcomatous appearance (Figure 3).

Figure 3. Sarcomatous Component of Cutaneous Carcinosarcoma (Hematoxylin and Eosin, 400×)

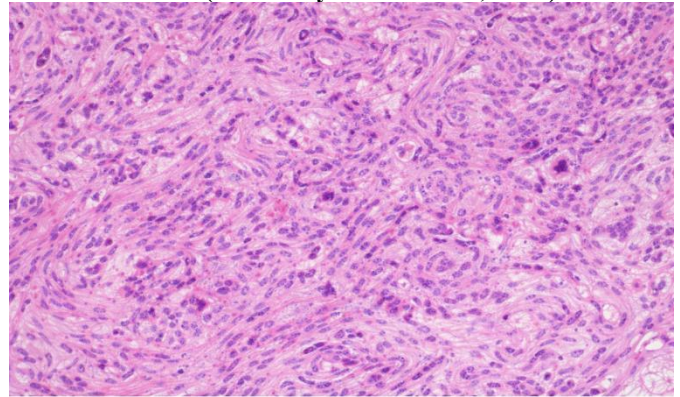


Figure 3. Sarcomatous component of cutaneous carcinosarcoma (hematoxylin and eosin, 400×) demonstrating pleomorphic spindle cells, with marked nuclear atypia, hyperchromasia and abundant mitotic figures including atypical.

High-power magnification demonstrating pleomorphic spindle cells with marked nuclear atypia, hyperchromasia, and abundant mitotic figures including atypical forms. The cells are arranged in fascicles with a storiform pattern in some areas.

The spindle cells demonstrated marked nuclear pleomorphism, hyperchromasia, prominent nucleoli, and abundant eosinophilic cytoplasm. Mitotic activity was brisk, with up to 15-20 mitotic figures per 10 high-power fields, including numerous atypical mitotic forms. Foci of tumor necrosis were identified within the sarcomatous component, reflecting rapid tumor growth and high-grade biological behavior.

No specific mesenchymal differentiation (such as osteosarcomatous, chondrosarcomatous, or rhabdomyosarcomatous elements) was identified in this case, classifying it as cutaneous carcinosarcoma with "non-heterologous" sarcomatous component (also termed "homologous" type).

3.2.4 Depth of Invasion and Margins

The deepest point of invasion, located within the subcutaneous adipose tissue, consisted exclusively of sarcomatous elements. This observation supports the concept that the mesenchymal component drives the aggressive infiltrative behavior of these neoplasms.

All surgical margins (peripheral and deep) were clear of tumor by a minimum distance of 6 mm, satisfying standard criteria for

complete excision of high-risk cutaneous malignancies. No lymphovascular invasion was identified, and perineural invasion was absent.

3.3 Immunohistochemical Findings

Immunohistochemical analysis was performed to characterize the immunophenotype of both tumor components and to exclude potential diagnostic mimics (Table 1, Figure 4).

Table 1. Immunohistochemical Profile of Cutaneous Carcinosarcoma

Antibody	Epithelial Component	Sarcomatous Component	Interpretation
Pan-cytokeratin (AE1/AE3)	Strong positive	Focal positive	Confirms epithelial differentiation; divergent origin
Epithelial membrane antigen (EMA)	Positive	Negative	Epithelial-specific marker
p63	Strong nuclear positive	Focal nuclear positive	Supports basaloid epithelial origin
Vimentin	Negative	Strong diffuse positive	Confirms mesenchymal differentiation
S100	Focal positive	Focal positive	Melanocytic marker; excludes melanoma when combined with other markers
CD68	Negative	Focal positive	Histiocytic marker; may reflect reactive changes
Smooth muscle actin (SMA)	Negative	Negative	Excludes leiomyosarcomatous differentiation
Desmin	Negative	Negative	Excludes rhabdomyosarcomatous differentiation
SOX10	Negative	Negative	Supports exclusion of melanoma
Melan-A	Negative	Negative	Excludes melanocytic differentiation
CD34	Negative	Negative	Excludes vascular differentiation

Figure 4. Immunohistochemical Profile of Cutaneous Carcinosarcoma

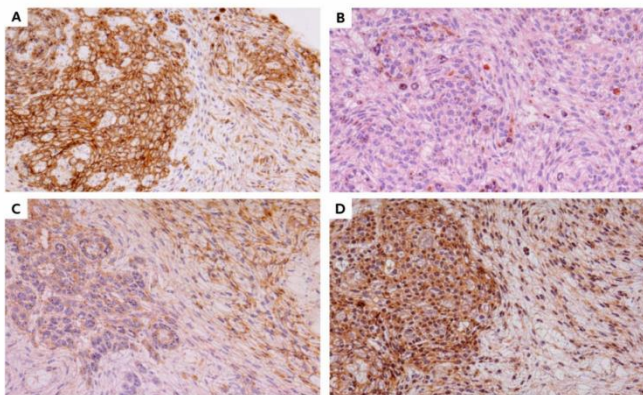


Figure 4. Immunohistochemical profile of cutaneous carcinosarcoma. Panel A: Strong pan-cytokeratin expression in epithelial component (brown chromogen, 200 $\times$). Panel B: Focal cytokeratin expression in sarcomatous component

*Panel A: Strong pan-cytokeratin expression in epithelial component (brown chromogen, 200 $\times$). Panel B: Focal cytokeratin expression in sarcomatous component confirming

epithelial derivation (200 $\times$). Panel C: Diffuse vimentin expression in sarcomatous component (200 $\times$). Panel D: p63 nuclear staining in both components supporting basal cell origin (200 $\times$).*

3.3.1 Epithelial Marker Expression

The epithelial component demonstrated strong, diffuse immunoreactivity for pan-cytokeratin (AE1/AE3) and epithelial membrane antigen (EMA), confirming its carcinomatous nature. Strong nuclear expression of p63 was observed throughout the epithelial component, supporting basaloid differentiation consistent with basal cell carcinoma.

Importantly, the sarcomatous component showed at least focal positivity for cytokeratin in approximately 30-40% of tumor cells, with patchy, weak to moderate staining intensity. This finding is critical for diagnosis, as it demonstrates the epithelial derivation of the sarcomatous elements and distinguishes true carcinosarcoma from pure sarcomas or sarcomatoid carcinomas lacking true mesenchymal differentiation.

3.3.2 Mesenchymal Marker Expression

The sarcomatous component exhibited strong, diffuse cytoplasmic positivity for vimentin, confirming its mesenchymal immunophenotype. This contrasted sharply with the epithelial component, which was uniformly vimentin-negative except for rare scattered cells at the interface between components.

3.3.3 Exclusion of Diagnostic Mimics

A panel of additional markers was employed to exclude potential mimics:

- **S100 protein** demonstrated focal positivity in both components but lacked the diffuse, strong staining pattern characteristic of melanoma. Combined with negative SOX10 and Melan-A, melanoma was effectively excluded.
- **Smooth muscle actin (SMA)** and **desmin** were negative in both components, excluding leiomyosarcomatous or rhabdomyosarcomatous differentiation.
- **CD34** negativity excluded vascular differentiation and argued against diagnoses including angiosarcoma or dermatofibrosarcoma protuberans.
- **CD68** showed focal positivity in the sarcomatous component, interpreted as representing reactive histiocytic infiltration rather than true histiocytic differentiation.

3.4 Final Pathological Diagnosis

The constellation of histopathological and immunohistochemical findings supported the final diagnosis of: **Cutaneous carcinosarcoma (metaplastic carcinoma) arising in association with basal cell carcinoma**

- Biphasic malignant neoplasm with intimately admixed basal cell carcinoma and high-grade pleomorphic spindle cell sarcoma components
- Tumor thickness: 8.2 mm
- Pathological stage: pT3 (AJCC 8th edition)
- Depth of invasion: Through reticular dermis into subcutaneous adipose tissue
- Surgical margins: Clear by >6 mm
- No lymphovascular or perineural invasion identified

4. LITERATURE REVIEW

4.1 Historical Context and Evolving Concepts

The recognition of cutaneous carcinosarcoma as a distinct diagnostic entity has evolved considerably over the past century. Early descriptions of biphasic skin tumors were hampered by limited understanding of immunohistochemical techniques and reliance on morphological assessment alone, leading to inconsistent terminology and diagnostic criteria (Tran et al., 2022).

The term "carcinosarcoma" was initially applied to any tumor exhibiting both epithelial-like and spindle-cell morphology, often without definitive proof of the malignant nature of both components or exclusion of reactive stromal changes. The advent of immunohistochemistry in the late 20th century revolutionized the classification of these neoplasms by enabling precise characterization of cellular differentiation through antigen expression patterns (Bigby et al., 2020).

Contemporary understanding recognizes cutaneous carcinosarcoma as a true biphasic malignancy requiring demonstration of malignant epithelial and malignant mesenchymal components, with immunohistochemical confirmation of appropriate differentiation in each component. This refined definition has enabled more accurate diagnosis, improved understanding of biological behavior, and more meaningful comparison of cases across institutions.

4.2 Epidemiology and Risk Factors

4.2.1 Incidence and Prevalence

Cutaneous carcinosarcoma remains exceptionally rare, with fewer than 150 well-documented cases reported in the English-language literature (Zidar et al., 2021). The true incidence is difficult to estimate due to historical under-recognition, diagnostic variability, and the tendency for cases to be reported individually or in small series rather than aggregated in large databases.

Analysis of large institutional databases suggests that cutaneous carcinosarcoma accounts for less than 0.1% of all cutaneous malignancies, though this figure may underestimate true prevalence due to misclassification (Clark et al., 2022). The tumor is substantially less common than conventional basal cell carcinoma (which constitutes approximately 75-80% of non-melanoma skin cancers) or squamous cell carcinoma (15-20%).

4.2.2 Demographic Characteristics

Review of published cases reveals consistent demographic patterns (Sharma et al., 2022):

- **Age:** Mean age at diagnosis ranges from 65 to 80 years, with a broad distribution from the fifth to tenth decades. The tumor is exceptionally rare in individuals under 50 years of age, suggesting that cumulative environmental exposures and age-related biological changes contribute to pathogenesis.
- **Gender:** A consistent male predominance is observed across most series, with male-to-female ratios ranging from 1.3:1 to 2:1. This gender disparity may reflect differences in occupational and recreational sun exposure patterns, though hormonal influences cannot be excluded.
- **Ethnicity:** The overwhelming majority of reported cases have occurred in fair-skinned individuals of

European descent, consistent with the importance of ultraviolet radiation in pathogenesis. Cases in darker-skinned individuals are exceptionally rare.

4.2.3 Anatomic Distribution

Cutaneous carcinosarcoma exhibits a striking predilection for chronically sun-exposed skin, with the head and neck region accounting for approximately 70-80% of reported cases (Brenn, 2020). Within this region, the scalp (particularly in bald or thinning-haired males), face (especially nose, cheeks, and forehead), and ears are most commonly involved.

Less common sites include the extremities (approximately 15-20% of cases) and trunk (<10%). This anatomic distribution closely parallels that of conventional basal cell carcinoma and squamous cell carcinoma, supporting the concept that chronic ultraviolet exposure is the primary environmental risk factor.

4.2.4 Ultraviolet Radiation and Other Risk Factors

The preponderance of cases in sun-exposed skin strongly implicates chronic ultraviolet (UV) radiation exposure as the principal etiological factor. UV radiation induces characteristic DNA damage patterns (including cyclobutane pyrimidine dimers and 6-4 photoproducts) that, when inadequately repaired, lead to accumulation of mutations in key tumor suppressor genes and oncogenes (Romero-Pérez et al., 2021).

Additional risk factors may include:

- **Immunosuppression:** Several cases have been reported in organ transplant recipients and other immunocompromised individuals, suggesting that immune surveillance plays a role in preventing carcinosarcoma development or progression.
- **Ionizing radiation:** Rare cases have been described in previously irradiated skin fields, analogous to radiation-induced sarcomas in other contexts.
- **Genetic predisposition:** The role of heritable factors remains poorly characterized, though the absence of familial clustering suggests that germline mutations are not major determinants.

4.3 Histogenesis and Molecular Pathogenesis

4.3.1 Theories of Origin

The precise histogenesis of cutaneous carcinosarcoma has been the subject of considerable debate, with three main theories proposed (Agaimy, 2022; Dai et al., 2023):

1. Monoclonal Origin with Divergent Differentiation: The prevailing hypothesis posits that both tumor components arise from a single pluripotent stem cell or from a common epithelial precursor that subsequently undergoes divergent differentiation. Under this model, the sarcomatous component represents epithelial-mesenchymal transition (EMT) within a pre-existing carcinoma, wherein epithelial cells acquire mesenchymal features including spindle cell morphology, loss of cell-cell adhesion, increased motility, and expression of mesenchymal markers.

2. Collision Tumor Theory: An alternative hypothesis suggests that cutaneous carcinosarcoma represents a collision between two independent neoplasms—one epithelial, one mesenchymal—that arise separately and subsequently merge. This theory is supported by rare cases demonstrating distinct genetic alterations in each component, but is considered less likely for most cases given the intimate admixture and transitional zones observed histologically.

3. Composition Tumor Theory: A third possibility proposes that both components arise from a common stem cell that retains capacity for dual differentiation throughout tumor development, analogous to the concept of "composition tumors" described in other organs.

4.3.2 Evidence Supporting Monoclonal Origin

Accumulating evidence strongly favors the monoclonal origin hypothesis for most cutaneous carcinosarcomas:

- **Genetic studies:** Analysis of allelic loss patterns has demonstrated identical genetic alterations (including loss of heterozygosity at multiple loci) in both epithelial and mesenchymal components of individual tumors, supporting common clonal origin (Singh et al., 2003; Paniz-Mondolfi et al., 2023).
- **Transitional zones:** Histological examination frequently reveals areas of gradual transition between components, with cells exhibiting intermediate morphology and mixed immunophenotype, rather than sharp demarcation between distinct tumor populations.
- **Shared mutations:** Next-generation sequencing studies have identified identical mutations in TP53, PTCH1, and other driver genes in both components of individual tumors (Kyrpychova et al., 2021).
- **Immunohistochemical overlap:** The finding of focal cytokeratin expression in sarcomatous cells, as observed in this case, demonstrates retained epithelial features despite acquisition of mesenchymal morphology and vimentin expression.

4.3.3 Molecular Mechanisms

The molecular pathogenesis of cutaneous carcinosarcoma involves complex interplay of genetic and epigenetic alterations driving tumor initiation, progression, and divergent differentiation (Dai et al., 2023):

- **TP53 mutations:** Mutations in the TP53 tumor suppressor gene are frequently identified and likely represent an early event in tumorigenesis, contributing to genomic instability and enabling accumulation of additional alterations.
- **PTCH1 mutations:** Given the frequent association with basal cell carcinoma, mutations in the PTCH1 gene (part of the Sonic Hedgehog signaling pathway) are commonly observed, particularly in the epithelial component.
- **Epithelial-mesenchymal transition (EMT) :** The process of EMT appears central to development of the sarcomatous component, involving downregulation of epithelial markers (E-cadherin, cytokeratins), upregulation of mesenchymal markers (vimentin, N-cadherin), and activation of EMT-associated transcription factors (Snail, Slug, Twist, ZEB1).
- **Copy number alterations:** Comparative genomic hybridization studies have revealed complex patterns of chromosomal gains and losses, with greater genomic instability typically observed in the sarcomatous component.

4.4 Histopathological Differential Diagnosis

The differential diagnosis of cutaneous carcinosarcoma is broad and includes several entities that may exhibit spindle cell morphology or biphasic appearance (McMenamin & Fletcher, 2021; Kyrpychova et al., 2021).

4.4.1 Sarcomatoid Squamous Cell Carcinoma

Sarcomatoid squamous cell carcinoma (also termed spindle cell squamous carcinoma) represents the most important and challenging differential diagnosis. Like carcinosarcoma, it exhibits spindle cell morphology and may demonstrate focal cytokeratin expression. However, true sarcomatoid squamous carcinoma lacks a distinct malignant mesenchymal component, with the spindle cells representing de-differentiated epithelial elements rather than true sarcoma. Distinction requires careful assessment of whether the spindle cells demonstrate features of malignancy (pleomorphism, mitotic activity, infiltrative growth) sufficient to warrant classification as sarcomatous, a distinction that can be subjective and controversial.

4.4.2 Spindle Cell Melanoma

Spindle cell melanoma may closely mimic the sarcomatous component of carcinosarcoma, particularly in amelanotic variants. Immunohistochemistry is essential for distinction, with melanoma demonstrating diffuse positivity for S100, SOX10, Melan-A, and HMB-45, while carcinosarcoma shows only focal S100 (often in both components) and negativity for more specific melanocytic markers.

4.4.3 Atypical Fibroxanthoma

Atypical fibroxanthoma (AFX) is a pleomorphic spindle cell neoplasm of sun-damaged skin that may closely resemble the sarcomatous component of carcinosarcoma. However, AFX lacks an associated epithelial component and demonstrates a more superficial, less infiltrative growth pattern. Immunohistochemically, AFX is typically negative for cytokeratins, S100, and desmin, while showing variable expression of CD10, CD68, and smooth muscle actin.

4.4.4 Pleomorphic Dermal Sarcoma

Pleomorphic dermal sarcoma (formerly termed undifferentiated pleomorphic sarcoma or malignant fibrous histiocytoma) shares morphological features with the sarcomatous component but, like AFX, lacks an epithelial component. Distinction requires demonstration that the sarcomatous-appearing cells are truly malignant (rather than reactive) and that no cytokeratin-positive epithelial component is present.

4.4.5 Leiomyosarcoma

Cutaneous leiomyosarcoma demonstrates fascicular arrangement of spindle cells with blunt-ended ("cigar-shaped") nuclei and eosinophilic cytoplasm. Immunohistochemical positivity for smooth muscle markers (smooth muscle actin, desmin, h-caldesmon) confirms smooth muscle differentiation and distinguishes it from the non-specific sarcomatous component of carcinosarcoma.

4.4.6 Angiosarcoma

Angiosarcoma may exhibit epithelioid morphology in some cases, potentially mimicking carcinosarcoma. Identification of vasoformative structures, positivity for endothelial markers (CD31, CD34, ERG, FLI1), and absence of cytokeratin expression (except in rare epithelioid angiosarcoma variants) enables distinction.

4.4.7 Dermatofibrosarcoma Protuberans

Dermatofibrosarcoma protuberans (DFSP) is a spindle cell neoplasm with characteristic storiform pattern, CD34 positivity, and presence of COL1A1-PDGFB fusion. It lacks the pleomorphism and high-grade cytology typical of carcinosarcoma's sarcomatous component and does not contain an epithelial component.

4.5 Prognosis and Clinical Behavior

4.5.1 Comparison with Conventional Skin Cancers

The prognostic significance of cutaneous carcinosarcoma diagnosis cannot be overstated. While conventional basal cell carcinoma exhibits metastatic rates of less than 0.1%, cutaneous carcinosarcoma demonstrates substantially more aggressive behavior (Satzger et al., 2022; Tsole et al., 2023):

- **Local recurrence rate:** Approximately 15-25% following standard excision
- **Regional lymph node metastasis:** 15-20% of cases
- **Distant metastasis:** 10-15% of cases
- **Disease-specific mortality:** 15-25% at 5 years

These figures must be interpreted cautiously given the rarity of the entity and potential publication bias toward more aggressive cases, but they consistently demonstrate that cutaneous carcinosarcoma behaves more like a high-grade sarcoma than a conventional carcinoma.

4.5.2 Prognostic Factors

Several factors have been associated with prognosis in cutaneous carcinosarcoma (Sharma et al., 2022; Kyrpychova et al., 2021):

- **Tumor depth:** Deeper invasion correlates with increased risk of metastasis and mortality. Tumors invading beyond subcutaneous fat (into muscle, bone, or beyond) carry particularly poor prognosis.
- **Margins:** Incomplete excision is strongly associated with local recurrence and should prompt re-excision whenever feasible.
- **Sarcomatous component proportion:** Tumors with predominant sarcomatous component (>50%) may exhibit more aggressive behavior, though this relationship requires further study.
- **Heterologous elements:** Some studies suggest that presence of heterologous sarcomatous elements (osteosarcoma, chondrosarcoma, rhabdomyosarcoma) may portend worse prognosis, though data are limited.
- **Lymphovascular invasion:** Identified in a minority of cases and associated with increased metastatic risk.
- **Perineural invasion:** Similarly associated with worse outcomes.

4.5.3 Patterns of Metastasis

When metastasis occurs, regional lymph nodes are the most common initial site, followed by lung, liver, bone, and other distant organs. The sarcomatous component typically predominates in metastatic deposits, though both components may be represented, suggesting that the sarcomatous cells possess greater metastatic capacity.

4.6 Treatment Approaches

4.6.1 Surgical Excision

Complete surgical excision with histologically confirmed clear margins remains the cornerstone of treatment for localized cutaneous carcinosarcoma (Clark et al., 2022; Tran

et al., 2022). Given the tumor's aggressive behavior and infiltrative growth pattern, wider margins than those used for conventional basal cell carcinoma are generally recommended:

- **Low-risk areas:** 1 cm clinical margins
- **High-risk areas (head and neck) :** 1-2 cm margins where anatomically feasible
- **Critical structures:** Margin compromise may be necessary to preserve function, requiring careful risk-benefit assessment and close postoperative surveillance

Mohs micrographic surgery has been employed in selected cases, offering the advantage of complete margin assessment with maximal tissue conservation. However, experience with Mohs for carcinosarcoma is limited, and the technique's efficacy depends on accurate identification of both tumor components, which may be challenging on frozen sections.

4.6.2 Lymph Node Assessment

Given the significant risk of regional lymph node metastasis, consideration should be given to sentinel lymph node biopsy in appropriate candidates (Satzger et al., 2022). Indications may include:

- Tumors >2 cm in diameter
- Deep invasion (>4-6 mm)
- Presence of high-risk features (lymphovascular invasion, high mitotic rate)
- Clinically node-negative patients with otherwise good surgical candidacy

However, the utility of sentinel node biopsy in this rare entity has not been established in prospective studies, and decisions should be individualized.

4.6.3 Adjuvant Therapy

The role of adjuvant therapy in cutaneous carcinosarcoma is poorly defined due to the rarity of the entity and absence of prospective trials (Romero-Pérez et al., 2021):

- **Radiation therapy:** May be considered for patients with close or positive margins not amenable to re-excision, perineural invasion, or lymph node involvement. The tumor's high-grade nature suggests radiosensitivity, though specific data are lacking.
- **Chemotherapy:** No standard regimen exists. When employed for metastatic disease, regimens have typically been extrapolated from soft tissue sarcoma protocols (doxorubicin-based) or carcinoma protocols (platinum-based), with variable success.
- **Targeted therapy:** Identification of specific molecular alterations in individual tumors (e.g., PTCH1 mutations) may enable targeted approaches, though this remains investigational.

4.6.4 Surveillance

Given the substantial risk of recurrence and metastasis, close clinical surveillance is mandatory (Tsole et al., 2023):

- **Clinical examination:** Every 3-4 months for first 2-3 years, then every 6-12 months thereafter
- **Lymph node assessment:** Careful palpation of regional basins at each visit
- **Imaging:** Baseline imaging (CT, PET-CT) may be considered for high-risk patients, with subsequent imaging directed by symptoms or clinical findings

- **Patient education:** Patients should be counseled regarding signs of recurrence and need for prompt reporting of new symptoms

5. DISCUSSION

5.1 Diagnostic Challenges and Key Learning Points

The present case illustrates several critical aspects of cutaneous carcinosarcoma diagnosis and management that warrant emphasis.

5.1.1 Clinical Recognition

The clinical presentation of cutaneous carcinosarcoma is non-specific and often mimics more common skin malignancies. In this case, the lesion's ulcerated appearance, raised borders, and location in a sun-exposed area prompted a provisional diagnosis of squamous cell carcinoma—a reasonable clinical impression that would be correct for the vast majority of such lesions. The possibility of carcinosarcoma was not entertained preoperatively, reflecting its extreme rarity and lack of pathognomonic clinical features.

This case underscores the reality that cutaneous carcinosarcoma is almost invariably diagnosed histopathologically, often as an unexpected finding following excision of a lesion presumed to be conventional carcinoma. Clinicians should maintain a low threshold for considering atypical diagnoses when lesions exhibit concerning features including rapid growth, large size, deep fixation, or unusual appearance, but even these features are not specific to carcinosarcoma.

5.1.2 Histopathological Recognition

The histopathological diagnosis of cutaneous carcinosarcoma requires recognition of its biphasic nature and careful assessment of both components. Key diagnostic features illustrated in this case include:

- **Intimate admixture** of epithelial and mesenchymal elements rather than sharp demarcation
- **Transitional zones** where cells exhibit intermediate morphology
- **Malignant cytology** in both components (not merely reactive stromal changes)
- **Depth of invasion** often greater in sarcomatous component

The absence of these features in routine sections from common skin cancers explains why carcinosarcoma may be missed if not specifically considered. Pathologists must maintain awareness of this entity and thoroughly sample and examine lesions with unusual features or those arising in high-risk contexts.

5.1.3 Immunohistochemical Confirmation

This case powerfully demonstrates the essential role of immunohistochemistry in confirming the diagnosis and excluding mimics. Key contributions included:

- **Demonstration of dual differentiation:** Cytokeratin positivity in both components confirmed epithelial origin, while vimentin positivity confirmed mesenchymal differentiation in the sarcomatous component.
- **Exclusion of melanoma:** Negative SOX10 and Melan-A with only focal S100 effectively ruled out spindle cell melanoma.

- **Exclusion of specific sarcomas:** Negative smooth muscle markers, desmin, and CD34 excluded leiomyosarcoma, rhabdomyosarcoma, and angiosarcoma.
- **Support for basal cell origin:** p63 positivity in both components supported derivation from basal cell carcinoma.

Without comprehensive immunohistochemical evaluation, confident distinction from sarcomatoid squamous cell carcinoma, spindle cell melanoma, and other mimics would be impossible.

5.2 Implications of Sarcomatous Component Predominance

An important observation in this case is that the sarcomatous component accounted for the deepest level of invasion. This finding aligns with published observations that the mesenchymal element typically drives aggressive behavior and metastatic potential in carcinosarcomas (Kyrpychova et al., 2021; Satzger et al., 2022).

The biological basis for this phenomenon likely relates to the properties acquired through epithelial-mesenchymal transition, including:

- **Loss of cell-cell adhesion** enabling single-cell infiltration
- **Increased motility** facilitating tissue invasion
- **Production of matrix-degrading enzymes** enabling penetration of tissue barriers
- **Resistance to apoptosis** promoting survival in hostile microenvironments
- **Acquisition of stem cell-like properties** enhancing metastatic capacity

From a prognostic standpoint, the predominance of sarcomatous elements and their depth of invasion may be more important than overall tumor thickness in predicting outcomes, though this relationship requires further study in larger case series.

5.3 Relationship to Basal Cell Carcinoma

The presence of an identifiable basal cell carcinoma component in intimate association with sarcomatous elements, as observed in this case, supports the concept that cutaneous carcinosarcoma frequently arises through transformation of pre-existing basal cell carcinoma. This relationship carries several implications:

- **Pathogenetic insight:** The molecular mechanisms underlying basal cell carcinogenesis (particularly PTCH1 mutations and hedgehog pathway activation) likely represent early events, with subsequent acquisition of additional alterations driving sarcomatous transformation.
- **Diagnostic utility:** Recognition of residual basal cell carcinoma within a biphasic tumor supports the diagnosis of carcinosarcoma rather than primary sarcoma or other entities.
- **Prognostic significance:** Tumors arising from basal cell carcinoma may have different biological behavior than those arising de novo or from squamous cell carcinoma, though comparative data are limited.

The precise timing and triggers for sarcomatous transformation within basal cell carcinoma remain poorly understood. Potential contributing factors may include accumulation of

additional genetic alterations, changes in tumor microenvironment, immune selection pressures, or therapeutic interventions (though this patient had no prior treatment).

5.4 Treatment Considerations in the Elderly

This patient's age (87 years) raises important considerations regarding treatment aggressiveness and surveillance intensity. While cutaneous carcinosarcoma is an aggressive malignancy warranting comprehensive treatment, therapeutic decisions must be balanced against patient age, functional status, comorbidities, and personal preferences.

In this case, the patient's excellent functional status (ECOG 1) and lack of significant comorbidities supported a standard approach with wide local excision and close surveillance. However, for frail elderly patients or those with limited life expectancy, less aggressive approaches might be considered, particularly if the tumor is small and completely excised.

The decision to pursue sentinel lymph node biopsy in elderly patients requires particularly careful consideration, as the procedure carries its own morbidity and the benefit of identifying microscopic nodal disease must be weighed against the patient's ability to tolerate potential subsequent treatments (completion lymphadenectomy, adjuvant therapy) if metastases are identified.

5.5 Importance of Long-Term Surveillance

The substantial risk of late recurrence and metastasis in cutaneous carcinosarcoma mandates long-term clinical surveillance. While most recurrences occur within the first 2-3 years, late metastases have been reported up to 10 years following initial treatment, arguing for continued vigilance (Tsole et al., 2023).

The surveillance protocol implemented for this patient (clinical examinations every 3-4 months for 2 years, then every 6-12 months thereafter) represents a reasonable approach based on available evidence and expert opinion. Patient education regarding self-examination and prompt reporting of new symptoms is equally important, as early detection of recurrence offers the best chance for successful salvage therapy.

5.6 Gaps in Knowledge and Future Directions

Despite advances in understanding cutaneous carcinosarcoma, significant knowledge gaps remain:

- **Prospective data:** Virtually all published data derive from retrospective case series and case reports, with inherent selection and publication biases. Multi-institutional registries are needed to accumulate sufficient cases for meaningful analysis.
- **Molecular characterization:** Comprehensive genomic profiling of larger case series could identify recurrent driver alterations, therapeutic targets, and molecular predictors of outcome.
- **Optimal margins:** Evidence-based recommendations for surgical margins are lacking; current practice extrapolates from data on other high-risk skin cancers.
- **Sentinel node utility:** The role of sentinel lymph node biopsy requires evaluation in larger cohorts with standardized protocols and long-term follow-up.
- **Adjuvant therapy:** No prospective data guide selection of patients for adjuvant radiation or chemotherapy.

- **Targeted therapy:** Identification of actionable mutations could enable personalized approaches for advanced disease.

6. CONCLUSIONS

6.1 Summary of Key Findings

This comprehensive case report and literature review describes an 87-year-old male patient with cutaneous carcinosarcoma arising from pre-existing basal cell carcinoma on the posterior scalp. Key findings include:

1. **Clinical presentation:** The lesion presented as a rapidly evolving, ulcerated scalp lesion clinically mimicking squamous cell carcinoma, highlighting the non-specific clinical features of this rare entity.
2. **Histopathological features:** The tumor demonstrated characteristic biphasic morphology with intimately admixed basal cell carcinoma and high-grade pleomorphic spindle cell sarcoma components, with the sarcomatous element accounting for deepest invasion (8.2 mm, pT3).
3. **Immunohistochemical profile:** Dual expression of epithelial markers (cytokeratins) in both components, with vimentin positivity restricted to the sarcomatous component, confirmed the biphasic nature and excluded diagnostic mimics.
4. **Treatment and outcome:** Complete surgical excision with clear margins (>6 mm) was achieved, and the patient remains under close clinical surveillance without evidence of recurrence at 6 months.

6.2 Clinical and Pathological Implications

This case reinforces several critical principles for clinicians and pathologists:

1. **Maintain diagnostic vigilance:** Cutaneous carcinosarcoma, though rare, should be considered in the differential diagnosis of atypical cutaneous malignancies, particularly those with rapid growth, large size, or unusual appearance in elderly patients.
2. **Recognize the limitations of clinical diagnosis:** Clinical appearance is non-specific and unreliable for distinguishing carcinosarcoma from more common skin cancers; histological diagnosis is essential.
3. **Appreciate the essential role of immunohistochemistry:** Comprehensive immunohistochemical evaluation is mandatory for accurate diagnosis and exclusion of mimics; a limited panel risks misclassification.
4. **Understand prognostic implications:** Diagnosis of carcinosarcoma fundamentally alters prognosis compared to conventional basal cell carcinoma, warranting more aggressive surgical approach and closer surveillance.
5. **Acknowledge the importance of complete excision:** Clear surgical margins are the most important determinant of outcome; re-excision should be pursued when margins are positive or close.

6.3 Learning Points

Based on this case and review of the literature, the following learning points are emphasized:

- **Cutaneous carcinosarcoma is rare but clinically significant** due to its aggressive biological behavior and poor prognosis compared to conventional non-melanoma skin cancers.
- **Most cases arise from pre-existing basal cell carcinoma** or squamous cell carcinoma, likely through epithelial-mesenchymal transition and divergent differentiation.
- **Immunohistochemistry is crucial for diagnosis**, demonstrating dual epithelial and mesenchymal differentiation and excluding mimics including sarcomatoid carcinoma, spindle cell melanoma, and atypical fibroxanthoma.
- **The sarcomatous component typically determines tumor depth** and drives aggressive behavior, with deeper invasion and greater metastatic potential than the associated epithelial component.
- **Complete surgical excision with clear margins** is the cornerstone of treatment, with wider margins recommended than for conventional carcinomas.
- **Close long-term surveillance is mandatory** due to significant risks of local recurrence, regional metastasis, and distant dissemination.
- **Multi-disciplinary management** involving dermatologists, surgeons, pathologists, and oncologists optimizes outcomes for patients with this rare malignancy.

6.4 Final Remarks

Cutaneous carcinosarcoma represents a fascinating and clinically important entity at the intersection of epithelial and mesenchymal neoplasia. Its rarity belies its significance as a model for understanding tumor progression, epithelial-mesenchymal transition, and the biological determinants of aggressive behavior. For the individual patient, accurate diagnosis carries profound implications for treatment and prognosis, underscoring the importance of maintaining diagnostic vigilance and employing comprehensive pathological evaluation when encountering atypical cutaneous malignancies.

This case adds to the growing literature on cutaneous carcinosarcoma, reinforcing established concepts while highlighting ongoing challenges in diagnosis and management. As molecular techniques continue to advance and our understanding of tumor biology deepens, improved characterization of these rare tumors may ultimately enable more personalized approaches to treatment and surveillance. Until such time, meticulous clinical assessment, complete surgical excision, and diligent follow-up remain the cornerstones of optimal patient care.

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