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CLINICOPATHOLOGICAL ANALYSIS OF GIANT BASAL CELL CARCINOMA (GBCC) CASES TREATED AT OUR INSTITUTION OVER LAST DECADE

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ABSTRACT

Background

Giant basal cell carcinoma (GBCC) is a rare and aggressive malignant neoplasm. Due to its uncommon nature and the recognized high risk of recurrence, standardized treatment guidelines are lacking.

Aims and Objectives

This study presents a clinicopathological analysis of 12 cases of giant basal cell carcinoma (GBCC) treated at our institution VIMSAR BURLA.

Methods

This clinicopathological observational study included 12 patients diagnosed with GBCC who presented to the outpatient department of General Surgery at VIMSAR Burla, Sambalpur, between November 2014 and October 2024. A clinical database was constructed to investigate the tumor's behaviour, identify prognostic factors, and evaluate optimal treatment approaches.

Results

GBCC predominantly affects elderly male patients, with the highest incidence observed in the seventh decade. The tumor typically arises from a long-standing dermal lesion, with a mean disease duration of 14.2 years. The most frequent location is the back, followed by the face and upper extremities. The nodular subtype is the most common histological variant. The average tumor size at presentation was 14.5 cm at its largest diameter. The presence of metastasis at diagnosis is a significant indicator of poor prognosis. Despite optimal therapy, 33.33% of patients experienced local recurrence or metastasis. The overall reported cure rate was 61.8%, based on a mean follow-up of 2 years. Wide local excision, with or without postoperative radio or chemotherapy, was determined to be the most effective treatment approach.

Conclusion

The optimal management of GBCC involves wide local excision to achieve histologically clear margins, often followed by adjuvant therapy. In cases of lymphatic spread, regional

lymphadenectomy is necessary. Given the elevated risk of loco regional recurrence, close and long-term follow-up is also crucial.

Keywords: Giant Basal Cell Carcinoma (GBCC), Wide Local Excision, Reconstruction.

INTRODUCTION

Basal cell carcinoma (BCC), formerly called basal cell epithelioma, is the most prevalent cancer in humans. It typically develops on sun-exposed skin, with rare occurrences on mucous membranes or the palms and soles. BCC is generally a slow-growing tumor and metastasis is uncommon. Despite its low fatality rate, BCC can cause significant local tissue damage and disfigurement if left untreated or managed poorly. Basal cell carcinoma (BCC) is the most common skin malignancy of Caucasian populations and is only rarely seen in pigmented races. It generally grows slowly and behaves in a relatively benign, less aggressive fashion. The development of BCC is a consequence of interactions between environmental factors, individual patient characteristics, and genetic predispositions. Specifically, the abnormal activation of the Hedgehog signalling pathway is a key hallmark of BCC and can interact with other cancer-related pathways such as EGFR, TGF-β, PI3K, NF-κB, and atypical protein kinase C (aPKC).[1,2] The development of basal cell carcinoma (BCC) is influenced by a variety of risk factors, which can be broadly categorized as modifiable and non-modifiable. **Modifiable risk factors** primarily involve exposure to ultraviolet (UV) radiation. This includes behaviours that increase UV exposure, such as experiencing multiple sunburns at a young age and prolonged occupational sun exposure. These factors are considered the most significant contributors to BCC development. **Non-modifiable risk factors** include inherent characteristics and conditions. An older population, due to cumulative sun exposure over their lifetime, is at higher risk. Additionally, a positive family history of BCC and certain genetic factors play a role. These include mutations in the PTCH1 and PTCH2 tumor suppressor genes, which can be inherited in an autosomal dominant pattern or arise spontaneously, commonly associated with basal cell nevus syndrome (also known as nevoid BCC syndrome or Gorlin-Goltz syndrome). Further genetic syndromes like xeroderma pigmentosum and Bazex-Dupré-Christol syndrome are also linked to an increased risk. Specifically, in the Caucasian population, certain non-modifiable factors are particularly relevant to BCC development. These include having fair skin (Fitzpatrick skin types I and II), light eye colour, blonde or red hair, freckles, using photosensitizing medications like tetracyclines, hydrochlorothiazide, and statins, and exposure to carcinogenic substances such as arsenic.[3]

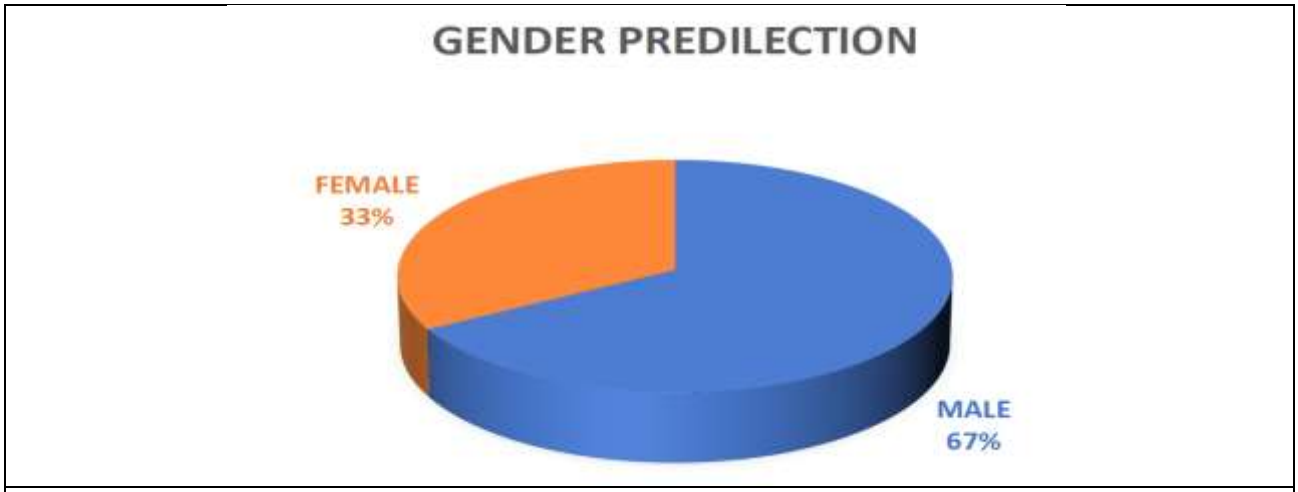
Giant BCC (GBCC) is, on the contrary, a rare skin malignancy characterized by an aggressive biological behaviour, deep tissue invasion with infiltration of the dermis and involvement of extra dermal structures such as bone, muscle and cartilage, as well as by metastasis and frequently carries a poor prognosis. According to the American Joint Committee on Cancer,[4] GBCC is defined as a tumor with a diameter larger than 5 cm. Only 1% of all BCCs achieve this size.[5] Since its first description by Eckoff[6] in 1951, data originating from large clinical series are rare due to the rarity of GBCC.

MATERIAL & METHODS

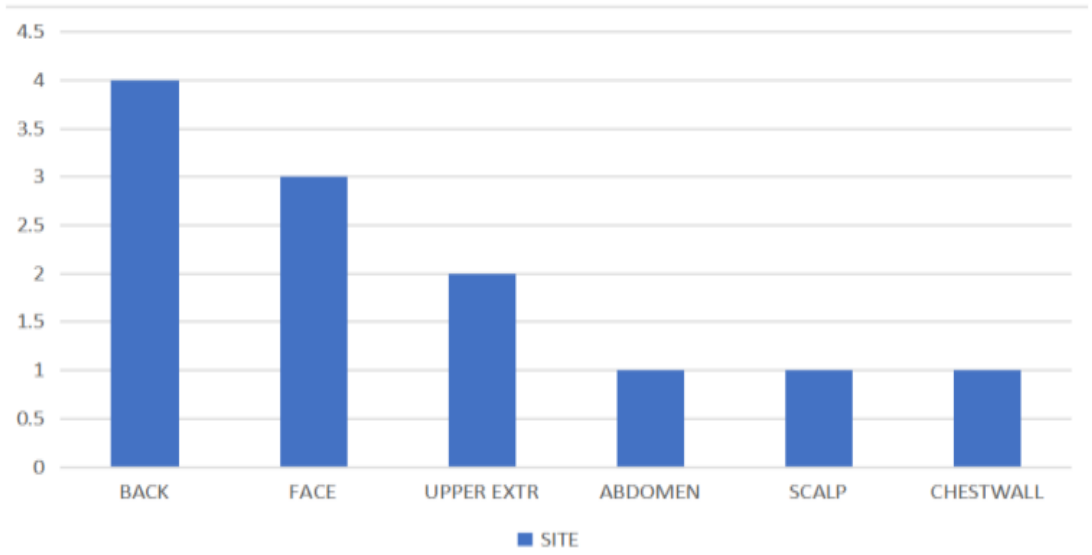
This clinicopathological observational study included 12 patients diagnosed with GBCC who presented to the outpatient department of General Surgery at VIMSAR Burla, Sambalpur, between November 2014 and October 2024. A clinical database was constructed to investigate the tumor's behaviour, identify prognostic factors, and evaluate optimal treatment approaches. The collected data included patient demographics (age, sex), tumor characteristics (location, size, histological subtype, stage), lesion history (duration, treatment history), primary management, and patient outcomes. Potential prognostic factors were assessed for their influence on outcome, and statistical significance was evaluated using a chi-squared ($\chi 2$) test and regression analysis.

RESULTS

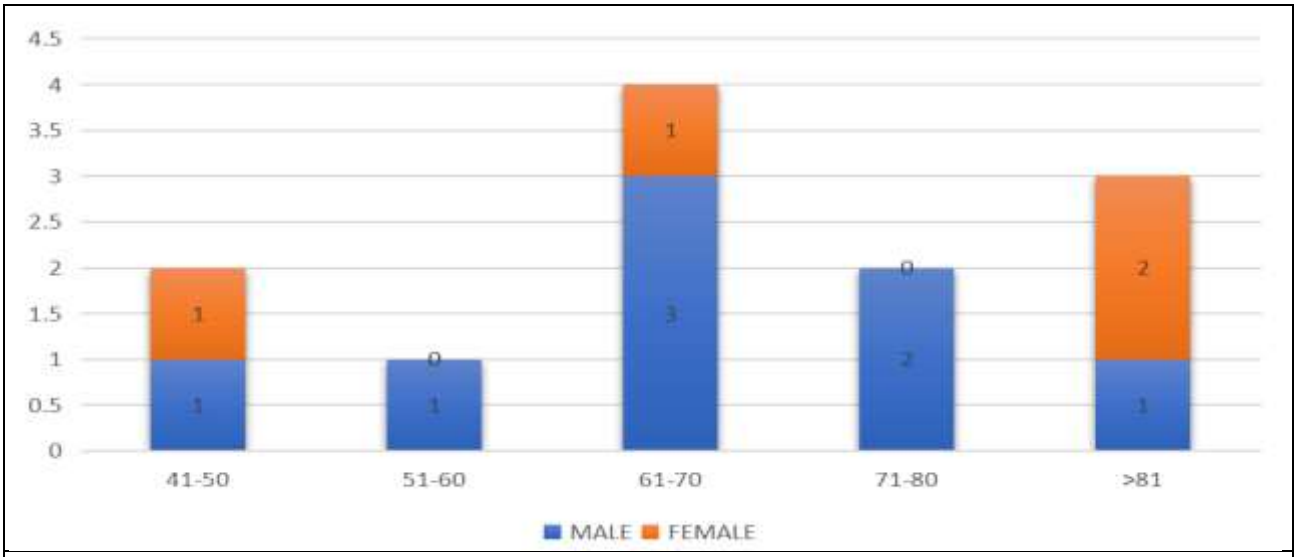
This study analysed 12 GBCC patients treated at VIMSAR BURLA over the past decade (since 2014). There were eight male patients with a mean age of 66.7 years (range 47-82 years) and four female patients with a mean age of 68.6 years (range 43-84 years). The male-to-female ratio was 2:1, indicating a sex predilection. The peak incidence occurred during the seventh decade of life for both sexes. All but one patient were of Caucasian ethnicity. Previous burns were reported in one case (8.3%), and prior X-ray exposure in three (25%). Four patients (33.33%) had a recurrence following previous BCC treatment. Alcohol abuse was documented in four patients (33.33%), and hypoalbuminemia and iron deficiency anaemia were present in 25% and 33.3% of patients, respectively. The primary anatomical sites for GBCCs were the back (33.33%, 4 patients), face (25%, 3 patients), and upper extremities (16.6%, 2 patients). The remaining cases were found on the abdominal wall, scalp and anterior chest wall (8.3% each, 1 patient per location). The average maximum tumor diameter was 14.5 cm (range: 5-40 cm), while the average duration of tumor presence was 14.2 years. Histological subtyping was performed for ten patients; nodular subtype was seen in 4 patients (40%), infiltrating lesions in 3 cases (30%), superficial tumors in one case (10%), and metatypical and morpheaform subtypes in 2 cases (20%). At presentation, eleven patients had localized disease (91.7%) while one patient (8.3%) presented with regional lymphadenopathy. All patients were node-negative except the patient with local lymphadenopathy. Wide local excision with reconstruction using grafting or flaps was the primary curative approach for 7 out of 12 patients. Local excision with adjuvant treatment was performed in four patients, whereas one patient received palliative treatment with radiotherapy or chemotherapy alone. The Mann-Whitney test identified no significant difference in follow-up time between patients with good and poor outcomes, with an average follow-up time of approximately 2 years (range: 0.75-72 months). Univariate analysis of factors such as sex, age, anatomic location, disease duration, lesion size, and histological subtype revealed no statistically significant correlation with overall prognosis. However, the presence of metastasis was identified as a significant negative prognostic factor ($\chi 2$ test, $p=0.041$). Regression analysis further indicated that the presence of metastasis tripled the risk of a poor outcome (OR=3.612). Treatment modality was also statistically significant. Patients who received surgical excision with reconstructive techniques, with or without adjuvant treatment, demonstrated a significantly better prognosis compared to patients who were managed palliatively with radiotherapy or chemotherapy alone. This association was statistically significant using the $\chi 2$ test ($p=0.004$).



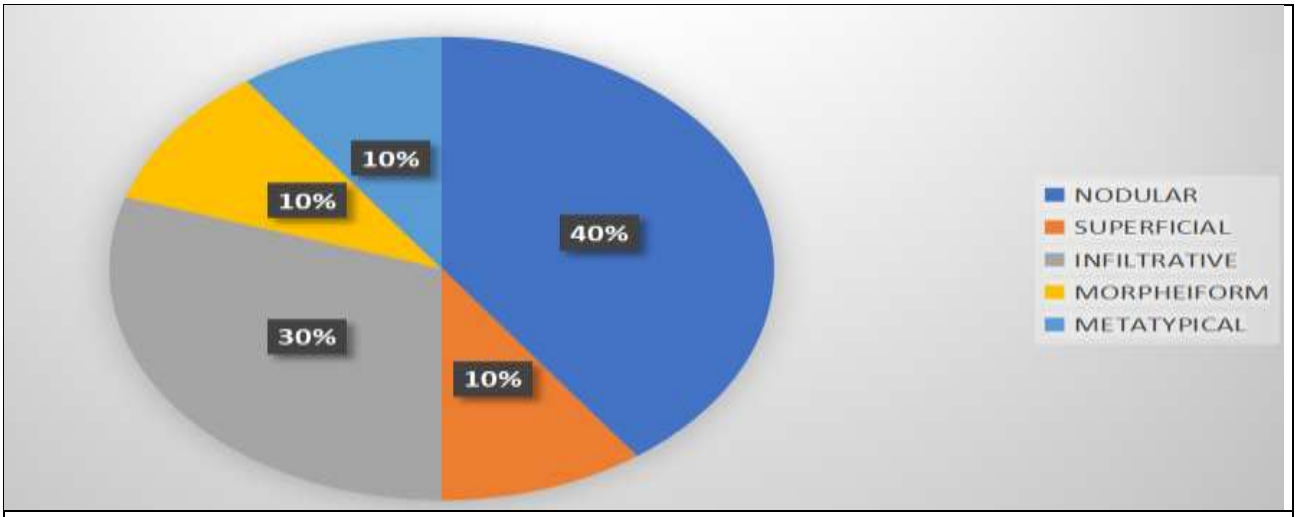
Graph 1: Distribution



Graph 2: Distribution according to anatomical site



Graph 3: Age Incidence



Graph 4: Histological Subtypes

DISCUSSION

Giant basal cell carcinomas (GBCCs) are rare oncological entities, with limited documentation in medical literature, primarily consisting of isolated case reports. Studies, including one by Betti et al.[5] suggest an incidence of approximately 0.5%-1% of all basal cell carcinomas (BCCs). While a tumor diameter exceeding 5 cm is generally considered a GBCC, classified as T3 according to the TNM system,[7] some researchers define giant tumors as those measuring 10 cm or more.[8] BCCs are believed to originate from pluripotent epithelial cells within the epidermis and hair follicles. While BCCs typically exhibit a slow growth rate, averaging around 1 mm in diameter per year according to Ono et al.[9] prolonged presence can lead to significant size and aggressive behavior. The primary etiology for BCC is ultraviolet radiation exposure. Additionally, they can occur in association with specific conditions such as basal cell nevus syndromes, xeroderma pigmentosum, albinism, and nevus sebaceous. Other associations include trauma (chronic leg ulcers, vaccination scars), immunosuppression, and exposure to arsenic, X-rays, and coal-tar derivatives.[10] The underlying causes of GBCCs are less defined. Sahl et al.[8] suggest neglect as the primary factor, resulting in continuous tumor growth spanning 10 to 20 years. GBCCs are more frequently seen in individuals with poor socioeconomic conditions or physical/psychiatric conditions impacting their judgment or access to medical care. Randle et al.[7] highlight that although neglect contributes to large tumor size, inadequate treatment of smaller lesions, which leads to recurrence, is critical in the development of such large tumors. This study reinforces the role of prolonged neglect in large tumors, with inadequate initial treatment being a less common factor. Chronic alcoholism, which can impair host immune response, was observed in a minority of patients in this study. The presented data showed that the mean patient age was around 67, with a clear male predominance – consistent with other studies. While BCCs are most prevalent in the head and neck (approximately 80%) due to sun exposure, GBCCs demonstrate a different anatomical distribution, occurring more frequently on the trunk, particularly the back, where they may remain unnoticed for extended periods.[10] This observed distribution is also consistent with previous literature.[8,11] GBCCs on the face or neck are less likely due to prompt medical attention. GBCCs on the anterior chest wall are unusual, and there have been reports of cases that were inoperable.[12] The size of these tumors is usually correlated with duration of existence, rather than rapid growth, though they can exhibit highly aggressive development in younger patients.[13] The mean lesion diameter in the reviewed cases was 14.77 cm.

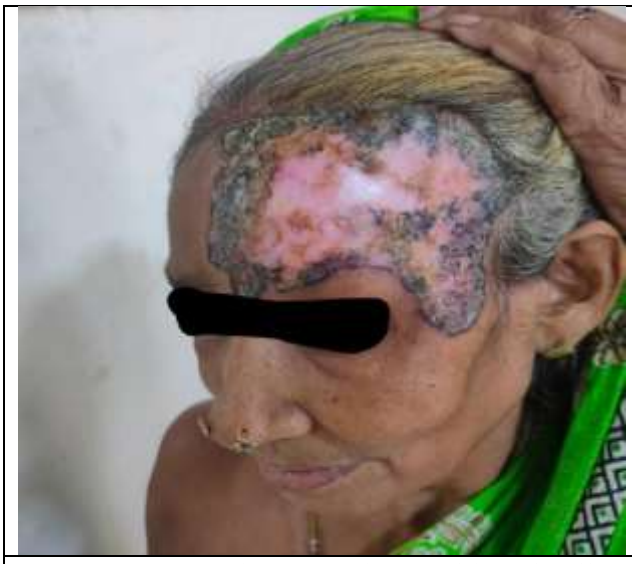


Figure 1 & 2 – advanced basal cell carcinoma (BCC) on the scalp & forehead

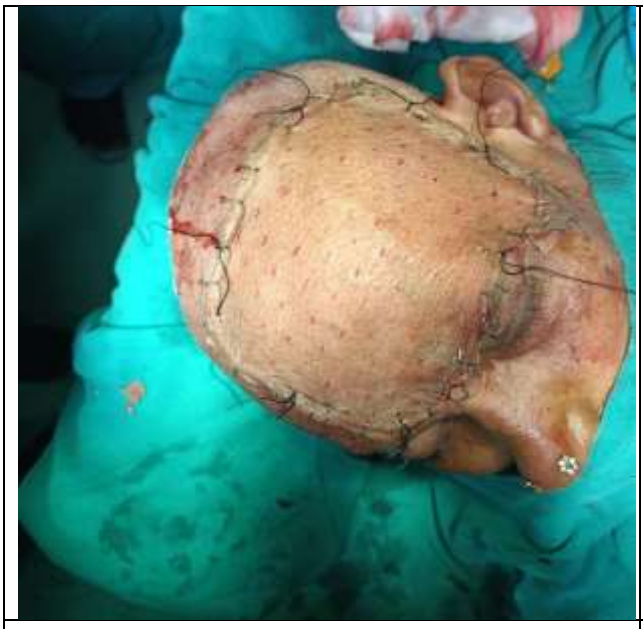


Figure 3 - Immediate post op picture after SSG

Figure 4- follow up picture after 6wks

Iron deficiency anemia and hypoproteinaemia are commonly observed in patients with giant basal cell carcinomas (GBCCs), likely resulting from intermittent tumor bleeding and serum loss.[14] Histologically, up of different subtypes of basal cell carcinoma (BCC) have been identified.[15] The histological subtype is considered a contributing factor in GBCC development, with certain subtypes demonstrating a more aggressive clinical course. GBCCs can be broadly classified as either non-aggressive (nodular and superficial subtypes) or aggressive (morpheaform, micronodular, and metatypical subtypes).[7,16] Randle et al.[7] reported that approximately 72% of GBCCs were micronodular or infiltrative. The World Health Organization (WHO) classification,[16] currently the most widely accepted due to its simplicity and reproducibility, distinguishes between nodular, superficial, and infiltrative types, as well as micronodular, fibroepithelial, metatypical, and keratotic types.

While metastasis is rare in typical BCCs (0.1% incidence), it is even less frequently reported in GBCCs[17]. BCCs primarily metastasize to lymph nodes but can also spread through the bloodstream to organs and bones,[18] potentially causing myelophthisic anemia.[19] and secondary amyloidosis in the kidney, spleen, and intestines.[20] In our study, 8.3% of patients presented with metastases. GBCCs show a greater tendency to metastasize, particularly when they reach a size of 10 cm or larger.[7] Lo et al[21] found that large lesions and deep invasion accounted for 75% of metastatic BCCs. Snow et al.[22] reported a 45% incidence of metastasis or fatal outcomes in tumors exceeding 10 cm, with an average duration of 22 years for these larger BCCs. It is currently believed that the histological subtype does not correlate with metastasis occurrence.[18] The average survival time following metastatic spread of GBCC is only 8 to 10 months.

Treatment for GBCCs, similar to other BCCs, involves wide surgical excision with clear margins. However, detailed information on resection margins is limited in GBCC records. For small primary lesions (<1 cm), a 2-4 mm clinical margin is usually adequate, while larger lesions, which are more likely to involve subclinical extension, require 3-5 mm clinical margins. Treatment of GBCC often necessitates reconstructive procedures, such as split-thickness skin grafts or free flaps, to cover the defect. Histological margin control is crucial in minimizing recurrence risk, and Moh's micrographic surgery is reported to achieve a 99% cure rate.[23] Breuninger et al.[24] demonstrated that the risk of tumor residue increases with tumor size, with a 68% risk for GBCCs larger than 5 cm, compared to 14% and 4% for BCCs smaller than 2 cm and 1 cm, respectively.[7] In some instances, GBCCs affecting the extremities may necessitate amputation.[11] Additionally, regional lymphadenopathy

often warrants radical lymph node dissection. Destructive methods such as electrodessication and curettage are more effective for smaller tumors. Radiotherapy and topical chemotherapy are typically reserved for elderly patients or those who are not suitable surgical candidates.[25,26] The presence of metastasis at presentation is a significant adverse prognostic factor. In the studies by Beck et al.[20] and Schwartz et al.[19] treatment was ineffective in achieving disease control in metastatic cases, leading to rapid death. These findings emphasize the importance of early detection and prompt surgical intervention.

Treatment strategy is a key prognostic factor; complete surgical excision, with or without adjuvant therapy, is associated with lower recurrence rates and improved survival. Clear microscopic margins are essential for long-term survival in GBCCs. Chemotherapy or radiotherapy alone appears insufficient for local control. While a few studies Rossi et al.[25] and Copcu et al.[27] reported efficacy with chemoradiotherapy, these studies lacked longer-term follow-up data. Due to a lack of adequate long-term follow-up data, particularly for elderly patients, it is challenging to draw firm conclusions regarding overall mortality across all disease stages. In our dataset, follow-up data was available for just 8 cases, with follow-up ranging from 3 weeks to 72 months. This clinicopathological analysis revealed that 8.3% of patients died from the disease, 25% experienced tumor recurrence or distant metastasis, with patients being followed up for approximately 2 years.

CONCLUSION

This review highlights that early detection of suspicious skin lesions, coupled with aggressive surgical treatment and dedicated long-term follow-up for cancer monitoring, can improve patient outcomes. Effective treatment of GBCCs should consider the following: (i) the aggressive nature of the tumor necessitates early recognition and intervention; (ii) obtaining adequate surgical margins, ideally at least 2.5-3 cm; (iii) the importance of histological margin control in reducing recurrence risk; (iv) limited role of radiotherapy and chemotherapy to palliative care for selected patients; and (v) the need for long-term follow-up of previously treated patients due to high recurrence potential.

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