

Super giant basal cell carcinoma: a comprehensive systematic review

Ajaipal S. Kang, MD^{a,*}, Genelia Kang^b, Harjaap S. Kathuria, BS^c

Abstract

Super giant basal cell carcinoma (SGBCC), defined as greater than 20 cm in diameter, is a rare oncological entity, with scarce literature. The authors conducted a review to characterize SGBCC, specifically with regards to age, sex predilection, risk factors, geographical location, body site, metastasis, and treatment. A systematic literature search was conducted from 1972 to 2023. All abstracts, studies, and citations were reviewed. The initial result showed 47 281 articles and were filtered down for human, skin, English language, and SGBCC. The authors identified 20 case reports for our analysis. The sample size was too small to conduct extensive statistical analysis. Majority of the cases were reported in North America and Europe. Males outnumbered almost females 2:1. The mean age was 61 years. The lesion was located on trunk in 16 out of 20 cases. In 13 out of 20 years, the lesion had been present for more than 10 years and 7 out of 20 cases reported metastasis. Several reports documented low socioeconomic status and poor mental health. Regarding treatment, 11 patients underwent surgery, radiation was utilized in 6 patients and immunotherapy (Vismodegib) in 4 patients. Although basal cell carcinoma (BCC) is known to have a favorable prognosis, SGBCC is highly aggressive with ability to metastasize. Our review reveals SGBCC is commonly diagnosed in males in their sixth decade, present for more than 10 years duration, risk factors include low socioeconomic status and poor mental health, commonly found on the trunk with a predilection for metastasis. The authors believe self-neglect is the likely etiology of the large size. Treatment options may be multimodal with a combination of surgery, radiation therapy or immunotherapy (Vismodegib).

Keywords: basal cell cancer, cutaneous malignancy, giant basal cell cancer, skin cancer, super giant basal cell cancer

Introduction

Basal cell cancer (BCC) is the most common skin malignancy in Caucasians and is usually seen on sun damaged skin^[1] with 3.6 million cases reported annually in the United States^[2]. It is typically slow growing and locally invasive. However, if BCCs are neglected, they may continue to invade deeper, destroy vital tissues, and very rarely may metastasize^[1]. Giant Basal Cell Cancer, defined as having a diameter of 5 cm, only comprises 0.5–2% of all BCCs^[2–4]. The literature links GBCC with male sex, alcohol use, poor socioeconomic status, and delay in access to medical attention^[5–7]. On the other hand, Super Giant Basal Cell Cancer (SGBCC), described with a diameter of larger than 20 cm, is known to be an aggressive oncological entity, yet is extraordinarily rare^[8,9]. Our goal was to conduct a comprehensive

^aDepartment of Surgery, UPMC Hamot, ^bNorthwest Pennsylvania Collegiate Academy and ^cLake Erie College of Osteopathic Medicine, Erie, Pennsylvania, USA

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*Corresponding author. Address: Department of Surgery, UPMC Hamot, 201 State Street, Erie, PA 16507, USA. Tel.: +814 746 6705; fax: 814 877 5205. E-mail: drjaykang@gmail.com (A.S. Kang).

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HIGHLIGHTS

- Super giant basal cell carcinoma (SGBCC) is defined as greater than 20 cm in diameter.
- A systematic literature search conducted from 1972 to 2023 identified 16 case reports only.
- Unlike basal cell carcinoma, SGBCC is highly aggressive with ability to metastasize.
- The risk factors include low socioeconomic status and poor mental health.
- Optimal treatment may be a combination of surgery, radiation therapy, and immunotherapy (Vismodegib).

review of existing literature and help characterize SGBCC, specifically with regards to age, sex predilection, risk factors, geographical location, body site, metastasis, and treatment.

Material and methods

A systematic literature search with PubMed, Google Scholar, Medline Ultimate, and Cumulative Index to Nursing and Allied Health Literature databases on 17 September 2023, was conducted using the search terms, 'basal cell cancer', 'basal cell carcinoma', 'giant basal cell cancer', and 'super-giant basal cell cancer', and 'super-giant basal cell cancer management' by the reviewers independently. The date range of publication was limited from 1972 to 2023. All abstracts, studies, and citations were reviewed. The articles involving noncutaneous melanoma, videos only, and conference abstracts were excluded. Articles in which SGBCC was not the focus, were also excluded. The reviewers discussed and reached a consensus in any disagreement about the inclusion of an article.

The final analysis included peer-reviewed English language articles involving human subjects with lesions greater than 20 cm in diameter (Fig. 1). We evaluated the literature for patient geographical location, age, sex, lesion location and duration, metastasis, other risk factors, and treatment modality of SGBCC. We summarized the results to meet our objectives. We analyzed the data in accordance with the best practice as described by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement^[10]. Twenty case reports were identified for our analysis. This work has been reported in line with AMSTAR (Assessing the methodological quality of systematic reviews).

Results

In terms of geographic location, nine patients were reported in North America, seven patients in Europe, and four patients in Asia (Tables 1, 2). There were 7 females and 13 males. The age range was 43–73 years with a mean age of 61 years. Most of the

lesions were located on trunk (n=16), followed by head (n=3)and extremity (n=1). The duration of the lesion ranged from 1 to 30 years, with less than 10 years in 5 patients and greater than 10 years in 13 patients. Metastasis was identified in 7 patients and 11 patients did not have any metastasis. Several reports documented mental health concerns and poor socioeconomic status as risk factors. Regarding treatment, four patients did not undergo any treatment, 11 patients underwent surgery, 6 patients were treated with radiation, 4 patients were treated with immunotherapy (Vismodegib), and 1 patient underwent chemotherapy.

Discussion

Although BCC is the most common skin cancer in the world, we only found 20 reported cases of SGBCC. In contrast to BCC's known slow progression, SGBCC is a rare, highly malignant variant that may infiltrate the deeper dermis and extradermal tissues and may metastasize^[19]. Undoubtedly, this rare entity behaves very differently than BCC and needs further characterization.



Figure 1. Systematic review of super giant basal cell cancer in literature.

Table 1				
Super giant	basal	cell	carcir	ioma.

Authors/Year/Location	Sex age (years)	Region	Time	Size (cm)	Treatment	Mets
Curry et al. 1977, Rochester, MN ^[11]	F 43	Trunk	20	28×26	Radiotherapy and chemotherapy	Yes
Lichtenstein et al. 1980, Rochester, NY ^[12]	M 64	Trunk	10	30×24	Radiation therapy	Yes
Beck et al. 1983, Hong Kong ^[13]	F 59	Trunk	> 13	40×30	None	Yes
Yamamoto et al. 1996, Japan ^[14]	M 61	Trunk	30	39×26	Surgery and radiation	Yes
Kikuchi et al. 2002, Japan ^[15]	M 63	Trunk	8	40×20	Surgery	No
Piteiro et al. 2003, Spain ^[16]	M 47	Trunk	7	28×25	Surgery	No
Northington et al. Birmingham, AL 2004 ^[1]	M 64	Trunk	20	20×30	None, death	No
Arnaiz et al. 2007, Spain ^[17]	F 73	Extremity	2	26×17	Surgery	No
Fresini et al. 2007, Italy ^[18]	M 72	Trunk	7	30×20	Radiotherapy	No
De Bree et al. 2010, Greece ^[4]	M 52	Trunk	NR	30×20	Surgery	No
Pierer et al. 2014, Italy ^[19]	F 67	Trunk	1	25×13	Surgery	NA
Desmond et al. 2015, Salem OR ^[2]	M 70	Trunk	35	20×25	No treatment, Died	Yes
Andersen, et al. 2015 Denmark ^[20]	F 73	Head	15	25×20	Vismodegib, Radiation	NR
Laageide, et al. 2020 Iowa City, IA ^[21]	F 56	Trunk	10	20×11	Surgery, Radiation, Vismodegib	No
Holzbauer, et al. 2020 Austria ^[22]	M 60	Trunk	10	20×15	Surgery	No
Hudson et al. 2020, Ontario, Canada ^[23]	M 53	Trunk	10-12	25	Vismodegib	No
Yoham, et al. 2021, Miami FL ^[8]	M 52	Head	11	21×16	None/refused/homeless	Yes
Kolitz, et al. 2021 Dallas, TX ^[24]	M 60	Trunk	NR	20×18	Surgery	No
Ahmed et al. 2022, Waterbury, CT ^[9]	F 60	Trunk	10	36.5×18	Surgery, vismodegib. then cemiplimab	Yes
Okano <i>et al</i> . 2023, Japan ^[25]	M 71	Head	10	NR	Surgery	No

Mets, Metastasis; NR, not reported.

Definition

The American Joint Committee on Cancer classification defines BCCs as T1, if they are 2 cm or less in greatest diameter, T2, if

Table 2 Compilation of results of super giant basal cell carcinomas in the literature.

Location	
North America	9
Europe	7
Asia	4
Sex	
Males	13
Females	7
Age	
Mean (years)	61
Range (years)	43–73
Body site	
Trunk	16
Head	3
Extremity	1
Duration	
> 10 years	13
< 10 years	5
NR	2
Metastasis	
No	11
Yes	7
NR	2
Treatment	
Surgery	11
Radiation	6
Vismodegib	4
Multimodal	5
None	4
Chemotherapy	1

NR, not reported.

they are more than 2 cm but not more than 5 cm in greatest diameter, and T3 or giant BCCs, if they are 5 cm or more in greatest diameter^[1]. SGBCC described with diameter of larger than 20 cm, are known to be an aggressive yet extraordinarily rare oncological entity^[8,9].

Body site

In contrast to BCCs, which are often found in the sun-exposed areas of the head and neck, SGBCC are most found on areas covered by clothing and typically expand because of ongoing neglect by the patient^[2,4,15,19,23]. Our study found that the most common location was the trunk (13), followed by head (2) and lower extremity (1).

Geographical location

In terms of geographic location, nine patients were reported in North America, seven patients in Europe, and four patients in Asia. This information is noteworthy that these diagnosis are being mostly reported from western countries with seemingly better resources and access for care of perspective patients. We are not suggesting that this entity is not found in the rest of the continents, but there have not been any reports to that account.

Risk factors

SGBCC are most often reported in those with low socioeconomic status. Additionally, physical or mental disability may impede healthcare access and the disease progresses unnoticed^[23]. Severe autism, schizophrenia, self-neglect, lack of insurance, inadequate treatment of previous tumors, chronic alcoholism, and avoidance of medical care have been reported^[1,4,8,9,20-24]. In some of these cases, patients' noncompliance has made management challenging^[20]. The aggressive histological subtype, recurrence, and radiation are additional risk factors^[14]. Our study found that the average age of presentation is in the sixth decade of life, with

an average duration of evolution is greater than 10 years and it is more prevalent in Caucasian males. In African Americans, it is virtually nonexistent^[9]. In the absence of any identifiable specific histologic factors in the reported specimens, we believe selfneglect is the likely etiology of the large size of these lesions. There is certainly an opportunity to educate the mental health patients, their families, and providers about the existence of this rare but serious entity.

Treatment

Because of the rarity of such extensive lesions, there is no consensus on treatment^[2,9]. When possible, the surgical approach is the treatment of choice^[4,19]. Whereas a 4 mm margin of excision is acceptable in excision of BCC^[26], complete excision of aggressive and large BCC requires margins of 13 mm or more^[4]. Lymphadenectomy may be considered in cases of lymphatic spread^[8]. There is a definite role for Mohs surgery for complete excision^[25]. Patients with large exophytic lesions amenable to resection did rather well in terms of mortality compared with the patients who were not surgical candidates^[9,11].

In 2012, United States Food and Drug Administration approved orally available Vismodegib, a hedgehog pathway inhibitor, for locally advanced and metastatic BCC^[2,9,19,25]. Despite the relatively low response rates of 30 and 43% for metastatic and locally advanced BCC, this is still a viable option^[2]. The most common adverse effects are muscle spasms, weight loss, and reduced appetite^[9]. This drug has also been used for tumor debulking as well as an adjunct therapy following surgical resection^[19,23]. Although surgery still plays a major role in the treatment, four recent patients were successfully treated with Vismodegib^[9]. For surveillance, some authors have advocated regular 3-monthly clinical follow-up visits, including yearly MRI examinations^[19], but patient compliance may prove to be challenging. Finally, treatment options may be multimodal with a combination of surgery, radiation therapy, or immunotherapy (Vismodegib).

Metastasis

Although only 0.03% of BCCs are found to have metastases, it has been estimated that BCCs larger than 5 and 10 cm in diameter are associated with chances of metastases or death of ~25 and 50%, respectively^[4]. Giant BCC may also lead to severe morbidity and death in the absence of metastasis, because of its complications including severe anemia and hypoproteinemia caused by continuous blood and exudate loss, serious infection, and sepsis^[13,14,16]. Thus, staging work-up with imaging should be considered as part of the work-up.

Limitations

We acknowledge numerous limitations, beginning with very sparse published data. In absence of randomized controlled trials, meta-analysis or case series, we only identified 20 case report articles. The lack of more extensive data precluded any meaningful statistical analysis. We also concede that this study suffers from potential referral, detection, or selection biases.

Future directions

We propose that actual incidence of this entity is higher than the published data. Large cohort, multicenter studies may be needed to further characterize SGBCC. We also believe there is an opportunity to educate and integrate mental health providers and social workers as part of the care team to address the social and economic conditions impacting this diagnosis^[2].

Conclusions

The extremely rare SGBCC, is understudied and poorly characterized. SGBCC is highly aggressive, usually located at sites covered by garments, linked to low socioeconomic status and poor mental health, with increased risk for metastatic disease, severe morbidity, and poor prognosis. Optimal treatment may consist of a combination of surgery, radiation therapy, and immunotherapy. It is noteworthy that patient neglect, denial, and mental health are almost always at the backdrop of this phenomenon.

Ethical approval

Given this is a systematic review of already published literature, the formal ethics approval is not required.

Consent

Respectfully this is a systematic review, hence informed consent was not required.

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Author contribution

A.S.K.: concept, data collection, data analysis, and manuscript; H.S.K., R.R., G.K., and R.R.: manuscript.

Conflicts of interest disclosures

No conflicts of interest from any author.

Research registration unique identifying number (UIN)

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Data availability statement

All data used in the study are publicly available.

Provenance and peer review

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