Exploration of Neuroscience

Open Exploration

Open Access Review

Metastatic glioblastoma multiforme on skin and subcutaneous tissue

Maria Ciscar-Fabuel*, Alexandre De Vilalta-Bufurull, Gemma Blanch-Pujol, Marina Romero-Quintela, Gerard Plans-Ahicart, Andreu Gabarros-Canals

Department of Neurosurgery, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, 08097 Barcelona, Spain

***Correspondence:** Maria Ciscar-Fabuel, Department of Neurosurgery, Hospital Universitari de Bellvitge, L'Hospitalet de Llobregat, 08097 Barcelona, Spain. mariaciscar@bellvitgehospital.cat
Academic Editor: Katrin Sak, NGO Praeventio, Estonia
Received: August 9, 2024 **Accepted:** September 23, 2024 **Published:** October 29, 2024

Cite this article: Ciscar-Fabuel M, De Vilalta-Bufurull A, Blanch-Pujol G, Romero-Quintela M, Plans-Ahicart G, Gabarros-Canals A. Metastatic glioblastoma multiforme on skin and subcutaneous tissue. Explor Neurosci. 2024;3:539–50. https://doi.org/10.37349/en.2024.00065

Abstract

Glioblastoma multiforme (GBM) is characterized by its infiltrative growth pattern and high recurrence rate despite treatment. While local progression within the central nervous system (CNS) is the rule, manifestations outside the CNS, particularly skin and subcutaneous metastases, are very infrequent and seldom reported in the literature. The authors reviewed the current understanding of this rare condition, with the main purpose of giving visibility to its clinical presentation and prognostic implications, thus improving clinical management and encouraging research in this area. A PubMed, Cochrane Library, and EMBASE search from database inception through March 2024 was conducted. In this way, we compiled a total of thirty-five cases in our review. As far as we know, our work gathers the largest number of patients with this condition. Remarkably, we observed that the typical presentation of soft-tissue high-grade glioma metastases is the finding of subcutaneous erythematous nodules in patients previously operated on for a primary CNS tumor, within the craniotomy site and nearby, mostly in the first year after the initial surgery. It was also noted that there is a trend of developing a concomitant CNS recurrence and/or other metastases in different locations, either simultaneously or subsequently. From here, we propose some possible mechanisms that explain the extracranial spread of GBM. We concluded that a poor outcome is expected from the diagnosis of skin and subcutaneous metastases: the mean overall survival was 4.38 months. Yet, assessing individual characteristics is always mandatory; a palliative approach seems to be the best option for the majority of cases.

Keywords

Glioblastoma, metastasis, scalp, subcutaneous, skin

Introduction

Glioblastoma multiforme (GBM) is the most common malignant primary central nervous system (CNS) tumor in adults. The GBM incidence generally rises with age, with a median age at diagnosis of 64 years. In addition, an aggressive clinical course and a high rate of local recurrence define the disease, with a poor overall prognosis; being the survival rate at 2 years (95% CI) is 14.8% (14.3–15.2), and at 10 years (95% CI), 2.6 % (2.3–2.9) [1]. On the other hand, GBM typically spreads locally within the CNS, infiltrating nearby brain tissue, and making distant metastasis uncommon. However, sporadic cases of extracranial metastasis have been reported, including instances of dissemination to organs such as the lungs, liver, and bones [2–6]. Nevertheless, among the variety of patterns, the phenomenon of subcutaneous dissemination stands as a highly unusual form of recurrence. We conducted a review of the literature to provide context to this entity, its features, the different management strategies, and its natural history.

Literature review

Methods

A PubMed, Cochrane Library, and EMBASE search from database inception through March 2024 was conducted using combinations of the search terms "glioblastoma" AND "subcutaneous/skin/scalp" AND "metastasis" OR "dissemination" OR "progression." Full-text articles published in the English and Spanish literature were included if they reported on patients with this finding, despite the systemic disease progression or other concomitant findings. Reports of GBM metastasis without skin and/or subcutaneous tissue involvement were excluded. In this way, we reviewed twenty-eight articles (Table 1) and a total of thirty-four cases of soft-tissue high-grade glioma dissemination, increasing to thirty-five after including ours. As far as we know, our work gathers the largest number of patients with this condition. The previous broadest review was made by Lewis et al. (2017) [7] with seventeen cases.

Histopathology: some nuances

In the whole of the review, the histopathological exam showed a glial lineage and a high grade following the World Health Organization (WHO) classification of CNS tumors. We use the term glioblastoma, high-grade glioma, or high-grade glial tumor indistinctly. However, according to the 2021 version of this classification, the previously called GBM is divided into two different diagnoses based on IDH mutation status: glioblastoma, IDH-wildtype, CNS WHO grade 4; and astrocytoma, IDH-mutant, CNS WHO grade 4 [8]. Even though this feature is important to the current understanding of the disease, we couldn't specify the IDH mutational state of the cases compiled here because nearly all of the publications were made before this latter classification, and the information on IDH mutational state is not always given.

Differential diagnosis

The recognition of extracranial metastasis of GBM holds significant clinical implications, since it poses a diagnostic challenge due to its resemblance to dermatological conditions (Figure 1) such as angiosarcoma, melanoma, squamous cell carcinoma, or basal cell carcinoma [9, 10]. Nonetheless, the majority of soft-tissue metastases were found at the craniotomy site and/or nearby, in the form of subcutaneous erythematous nodules. In all cases, the soft-tissue lesions appeared after diagnosing and operating on a primary GBM, and an excisional biopsy, punch biopsy, or fine-needle aspiration confirmed the pathological anatomy.

Postulated mechanisms

With regard to high-grade glioma extracranial spread mechanisms, several have been postulated. One prominent theory suggests that tumor cells acquire invasive properties, allowing them to breach the blood-brain barrier and enter the bloodstream or lymphatic system, facilitating dissemination to distant organs. Tumor cells release pro-angiogenic factors, promoting the development of a dense vascular network that facilitates tumor growth and metastatic spread [1]. Moreover, interactions between GBM cells and the extracellular matrix (ECM) contribute to metastasis by promoting cell adhesion, migration, and invasion [11]. Angiogenesis seems to be relevant too. Immune evasion mechanisms also contribute to metastatic dissemination [1].

Table 1. Literature review of skin and subcutaneous metastasis in high-grade glial tumors

References	Age at diagnosis (years)	Sex	Primary location	Surgery (grade of resection)	Adjuvant treatment	Time from first surgery to scalp metastasis (months)	Relevant features of metastasis	CNS progression (local intracranial recurrence) simultaneously or deferred	Other manifestations after scalp metastasis	Management of scalp metastasis	Survival from scalp metastasis diagnosis (months)
Matsuyama et al., 1989 [2]	68	M	Right sylvian fissure and small masses in cisterns	GT	RT + CT	Unknown	Scalp nodule at the craniotomy site and/or nearby	Unknown	Autopsy revealed metastases to the liver, spleen, and spinal cord	Palliative approach	Unknown
Carvalho et al., 1991 [16]	26	F	Posterior right temporal	ST	RT + BT	Unknown	Scalp nodule at the craniotomy site and/or nearby	Yes, simultaneously	A cervical lymph node, and afterward other extracranial masses (not specified)	RT + CT + excision of the affected soft-tissue	Unknown
Wallace et al., 1996 [17]	41	M	Right frontal	GT	RT + CT	3	Scalp nodule at the craniotomy site and/or nearby	Unknown	Painful bilateral cervical adenopathies	RT + CT	5
	39	M	Right frontal-temporal	GT	RT	5	Scalp nodule at the craniotomy site and/or nearby	Yes, simultaneously local recurrence with extension through the overlying skull and along the anterior fossa into the right orbit	Neck and facial swelling with a preauricular lymphadenopaty	CNS surgery	7
Houston et al., 2000 [3]	19	M	Left parietal	ST	BT	10	Scalp and skull nodules in the suboccipital region	Yes, 4 months later	4 months later, a supraclavicular node and a mediastinum mass	RT + CT	7
	32	M	Left temporal	ST	BT + CT	5	Scalp nodule at one of the healed left frontal catheter sites	Yes, 2 months later	8 months later, lung and liver metastasis	Excision of the affected soft-tissue + CNS surgery after detecting CNS progression	8
Hata et al., 2001 [4]	Unknown	Unknown	Unknown	Unknown	RT + CT	Unknown	Scalp nodule at the craniotomy site and/or nearby	Yes, simultaneously local invasion of the primary tumor to the dura and skull	Multiple tumors in the lung, lymph nodes, and the heart, simultaneously	Unknown	Unknown

Table 1. Literature review of skin and subcutaneous metastasis in high-grade glial tumors (*continued*)

References	Age at diagnosis (years)	Sex	Primary location	Surgery (grade of resection)	Adjuvant treatment	Time from first surgery to scalp metastasis (months)	Relevant features of metastasis	CNS progression (local intracranial recurrence) simultaneously or deferred	Other manifestations after scalp metastasis	Management of scalp metastasis	Survival from scalp metastasis diagnosis (months)
Figueroa et al., 2002 [18]	34	M	Left temporal	P	RT	8	Subcutaneous nodule 3.5 cm anterior to the frontal scalp line and 2 cm posterior	Yes, simultaneously	No	Excision of the affected soft-tissue	5
Santos et al., 2003 [19]	42	M	Left fronto-parietal	GT	RT + CT; after, two CNS recurrences required two different surgeries and cycles of RT + CT	36	Scalp nodule at the craniotomy site and/or nearby	No	No	Excision of the affected soft-tissue	Unknown
Allan, 2004 [20]	60	M	Frontal-temporal (side not specified)	P	RT	12	Scalp nodule at the craniotomy site and/or nearby	Yes, simultaneously	No	Palliative approach	2
Moon et al., 2004 [21]	35	F	Left temporo-occipital	ST	RT; after, three CNS recurrences required three different surgeries	48	Scalp nodule at the craniotomy site and/or nearby	Yes, simultaneously. Extense leptomeningeal spread to the left temporo-occipital region	Multiple lymph adenopathies in the deep cervical region without continuity with the scalp mass, simultaneously	CT	5
Bouillot-Eimer et al., 2005 [22]	60	F	Left parietal	B	RT + CT	11	Scalp nodule at the craniotomy site and/or nearby	Yes, simultaneously. Intracraneal tumor seeding along the stereotactic biopsy trajectory	No	Excision of the affected soft-tissue	1
Jain et al., 2005 [11]	49	M	Right temporo-parietal	P	RT	10	Scalp nodule at the craniotomy site and/or nearby	Yes, simultaneously	No	Excision of the affected soft-tissue	2
Schultz et al., 2005 [10]	74	F	Left temporal	P	Unknown	12	Scalp nodule at the craniotomy site and/or nearby	Yes, simultaneously	No	Excision of the affected soft-tissue	1

Table 1. Literature review of skin and subcutaneous metastasis in high-grade glial tumors (*continued*)

References	Age at diagnosis (years)	Sex	Primary location	Surgery (grade of resection)	Adjuvant treatment	Time from first surgery to scalp metastasis (months)	Relevant features of metastasis	CNS progression (local intracranial recurrence) simultaneously or deferred	Other manifestations after scalp metastasis	Management of scalp metastasis	Survival from scalp metastasis diagnosis (months)
Saad et al., 2007 [5]	13	M	Left frontal	ST	RT + CT + antiangiogenic therapy	7	Scalp nodule at the craniotomy site and/or nearby	Yes, simultaneously intracranial and leptomeningeal spread	Multiple liver and lung metastatic nodules, simultaneously	Palliative approach	3
Mentrikoski et al., 2008 [23]	58	F	Left frontal	GT	RT + CT; after two CNS recurrences required two different surgeries and antiangiogenic therapy + RT	16	Scalp nodule at the craniotomy site and/or nearby	No	No	Unknown	Unknown
	47	M	Not specified	GT	CT	2	Scalp nodule at the craniotomy site and/or nearby	No	No	Unknown	Unknown
Senetta et al., 2009 [12]	48	F	Right fronto-parietal	GT	RT + CT	14	Scalp nodule at the craniotomy site and/or nearby	Yes, 4 months later	No	Excision of the affected soft-tissue + RT + CT	12
	53	F	Left frontal	P	RT + CT	9	Scalp nodule at the craniotomy site and/or nearby	Yes, 4 months later	3 months later, new scalp satellite lesions	RT	16
Miliaras et al., 2009 [24]	63	M	Left fronto-parietal	GT	Unknown	7	Scapular subcutaneous mass	Yes, 1 month later	No	Unknown	3
Jusué Torres et al., 2011 [25]	63	F	Right frontal	GT	RT + CT	6	Scalp nodule at the craniotomy site and/or nearby	Yes, simultaneously	No	Excision of the affected soft-tissue + CNS surgery + carmustine implants + CT + antiangiogenic therapy	Unknown
Guo et al., 2012 [26]	19	F	Pons of brain stem	Unknown	RT + CT	8	Scalp nodule at the craniotomy site and/or nearby	Yes, simultaneously	No	Excision of the affected soft-tissue + CT + RT	Unknown

Table 1. Literature review of skin and subcutaneous metastasis in high-grade glial tumors (*continued*)

References	Age at diagnosis (years)	Sex	Primary location	Surgery (grade of resection)	Adjuvant treatment	Time from first surgery to scalp metastasis (months)	Relevant features of metastasis	CNS progression (local intracranial recurrence) simultaneously or deferred	Other manifestations after scalp metastasis	Management of scalp metastasis	Survival from scalp metastasis diagnosis (months)
Amitendu et al., 2012 [27]	27	M	Right temporal	GT	After PXA diagnosis, an RT regimen was carried out	48	Scalp nodule at the craniotomy site and/or nearby	Yes, 3 months later. After excision, the histology showed anaplastic oligodendroglioma (WHO III).	6 months later, lumbosacral spinal metastasis	Excision of the affected soft-tissue + surgery of lumbosacral spinal metastasis	Unknown
Ginat et al., 2013 [28]	62	M	Left frontal extending to ependimal surface	ST	RT + CT	10	Scalp nodule at the craniotomy site and/or nearby	Yes, afterwards (unespecified)	No	Excision of the affected soft-tissue + CT + RT	3.5
Bathla et al., 2015 [14]	51	M	Left parafalcine with	GT	RT + CT	1.5	Scalp nodule at the craniotomy site and/or nearby	Unknown	No	Palliative approach	2
Anghileri et al., 2015 [6]	30	M	Left central sulcus	Unknown	RT + CT; two CNS recurrences required two different surgeries afterward	80	Frontal subcutaneous lump	No	2 months later, cervical lymph nodes and multiple lung metastasis	Excision of the affected soft-tissue	2
	43	M	Left anterior frontal	GT	RT + CT; two CNS recurrences required two different surgeries	20	Frontal subcutaneous lump	Yes, simultaneously	No	Excision of the affected soft-tissue	1
Forsyth et al., 2015 [29]	59	F	Left fronto-temporal	Unknown	RT + CT	6	Frontal subcutaneous lump	Yes, simultaneously	No	CNS surgery	Unknown
Lewis et al., 2017 [7]	47	F	Left medial cerebellar hemisphere extending to the vermis	GT	RT + CT	5	Scalp nodule at the craniotomy site and/or nearby	Yes, simultaneously ecurrence at leptomeninges, fourth ventricle, and drop metastases in the cervical vertebrae	No	RT + CT + Excision of the affected soft-tissue	Unknown

Table 1. Literature review of skin and subcutaneous metastasis in high-grade glial tumors (*continued*)

References	Age at diagnosis (years)	Sex	Primary location	Surgery (grade of resection)	Adjuvant treatment	Time from first surgery to scalp metastasis (months)	Relevant features of metastasis	CNS progression (local intracranial recurrence) simultaneously or deferred	Other manifestations after scalp metastasis	Management of scalp metastasis	Survival from scalp metastasis diagnosis (months)
Pérez-Bovet and Rimbau-Muñoz, 2018 [30]	63	F	Right fronto-parietal	ST	RT + CT	10	Scalp nodule at the craniotomy site and/or nearby and palpable nodules in the masticator muscles of the right infratemporal fossa	Yes, 4 months later	No	Excision of the affected soft-tissue + CNS surgery + CT	1.5
Magdaleno-Tapial et al., 2019 [13]	75	F	Right parietal	GT	Clinical trial with nivolumab/placebo	7	Scalp nodule at the craniotomy site and/or nearby	No	No	Palliative approach	Unknown
Moratinos-Ferrero et al., 2019 [31]	51	M	Right temporo-parietal	GT	Unknown	8	Scalp nodule at the craniotomy site and/or nearby	Yes, simultaneously	No	Unknown	Unknown
	53	M	Left temporo-parietal	GT	Unknown	18	Scalp nodule at the craniotomy site and/or nearby	Yes, simultaneously	No	Unknown	Unknown
Nakib et al., 2021 [32]	53	M	Posterior limb og the right internal capsule and right thalamus	ST	RT + CT + antiangiogenic therapy	11	Anterior-auricular side of his face is near-distant from the surgery scar	Yes, simultaneously	No	Palliative approach	4
Ciscar-Fabuel et al., 2024 [9]	48	M	Left parietal multifocal	GT	RT+CT	6	Scalp nodule at the craniotomy site and/or nearby	Yes, 1 month later	No	Excision of the affected soft-tissue	1

M: male; F: female; GT: gross total resection; RT: radiotherapy; CT: chemotherapy; ST: subtotal resection; BT: brachytherapy; CNS: central nervous system; P: partial resection; B: biopsy; PXA: pleomorphic xanthoastrocytoma; WHO: World Health Organization

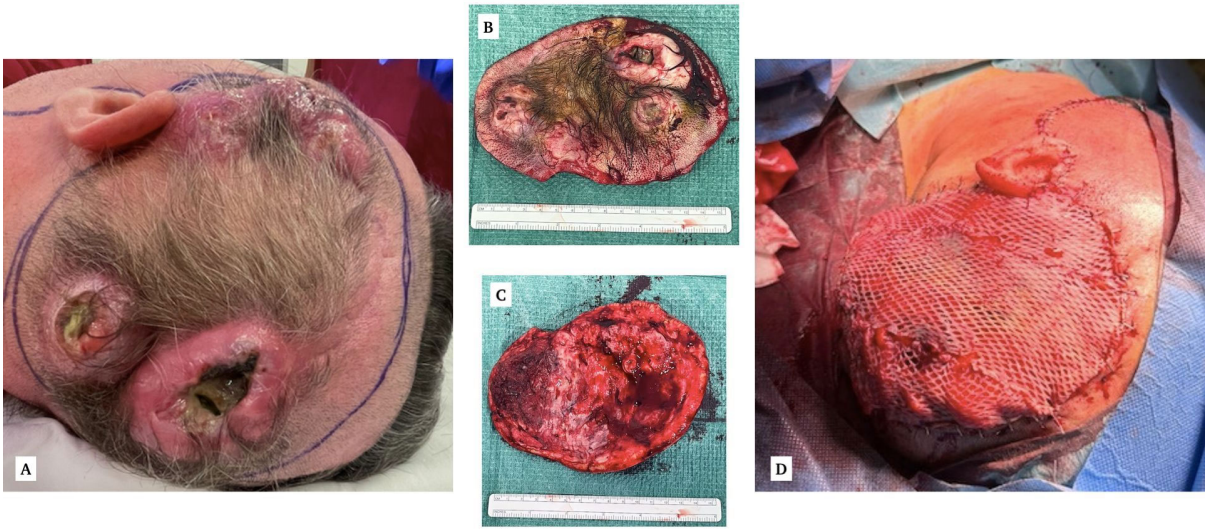

Figure 1. The case treated in our center. A: Macroscopic appearance of the scalp nodules, two of which have visible necrosis and suppuration. **B**: Surgical piece, external. **C**: Surgical piece, internal. **D**: Final result after covering the defect with a thoracodorsal artery perforator (TDAP) flap and split-thickness skin grafts. Reprinted from Ciscar-Fabuel et al. [9].

And when we focus on skin and subcutaneous GBM spread, tumor cells may undergo epithelial-mesenchymal transition (EMT), a process associated with increased migratory and invasive capabilities, furthering metastasis. Senetta et al. [12] described two cases of GBM skin metastases in the absence of intracranial progression, associated with a shift toward a mesenchymal immunophenotype (reduction of GFAP and EGFR staining paralleled by increased vimentin and YKL-40 expression), suggesting the selection of a therapy-resistant subpopulation of neoplastic cells in the metastatic sites, induced either by treatment [radiotherapy (RT)-induced morphological changes] or determined by the tumor environment.

Population distribution and predictable evolution of the disease

Also, among the thirty-five cases, the mean age was 47.21 years, the youngest being 13 years [5] and the oldest 75 [13]. About sex distribution, there were 21 males and 13 females (1 of the cases was not defined). The average time from the first surgery to skin and/or subcutaneous metastasis was 14.36 months. The standard deviation is 16.49 months, suggesting a wide range of values. The minimum time to metastasis recorded was 1.5 months [14], and the maximum was 80 months [6]. A larger number of patients experienced metastasis earlier (within the first few months from primary tumor diagnosis): the median time from the first surgery to skin and/or subcutaneous metastasis was 9.5 months, with 25% of the cases having metastasis by 6 months and 75% by 12.5 months. Comparatively, CNS recurrences of GBM are seen mostly between 6 and 9 months [15]. We couldn't find a statistically significant correlation among the grade of resection [gross total (GT), subtotal (ST), partial (P), biopsy (B)] and time to metastasis. On the other hand, 55.8% of patients (19 out of 34) had CNS progression by the time metastasis was found. In addition, another 9 patients had a CNS progression afterward. This means that 82.35% of patients (28 out of 34) had CNS progression at the same time or after diagnosing the skin and/or subcutaneous dissemination. Conspicuously, 26.47% of them had metastasis in different locations (9 out of 34), such as lymph nodes, lungs, liver, or spleen, simultaneously or afterward [2–6]. Though not in all cases was an extension study conducted; in the majority, just a head computerized tomography scan was performed.

Management and prognosis

Finally, regarding the management, some authors, including us, advocated for surgery to achieve the highest cytoreduction and to avoid local, and/or systemic complications; nonetheless, it must be taken into account that other complications from surgery can occur (local pain, bleeding, infection, or ulceration are some examples). Other authors combined RT and chemotherapy (CT) schemes, while others directly chose a palliative approach. In any case, this doesn't seem to have a significant impact on overall survival. We observed a mean survival time from scalp metastasis of 4.38 months, with a standard deviation of 3.89. The

shortest survival time from metastasis recorded was 1 month our case [9] the longest was 16 months [10]. The median survival time from metastasis was 3 months, and most patients passed away within 5 months or less from scalp metastatic disease (Figure 2). Meanwhile, the median overall survival after high-grade glioma CNS recurrence ranges from 3 to 9 months [15].

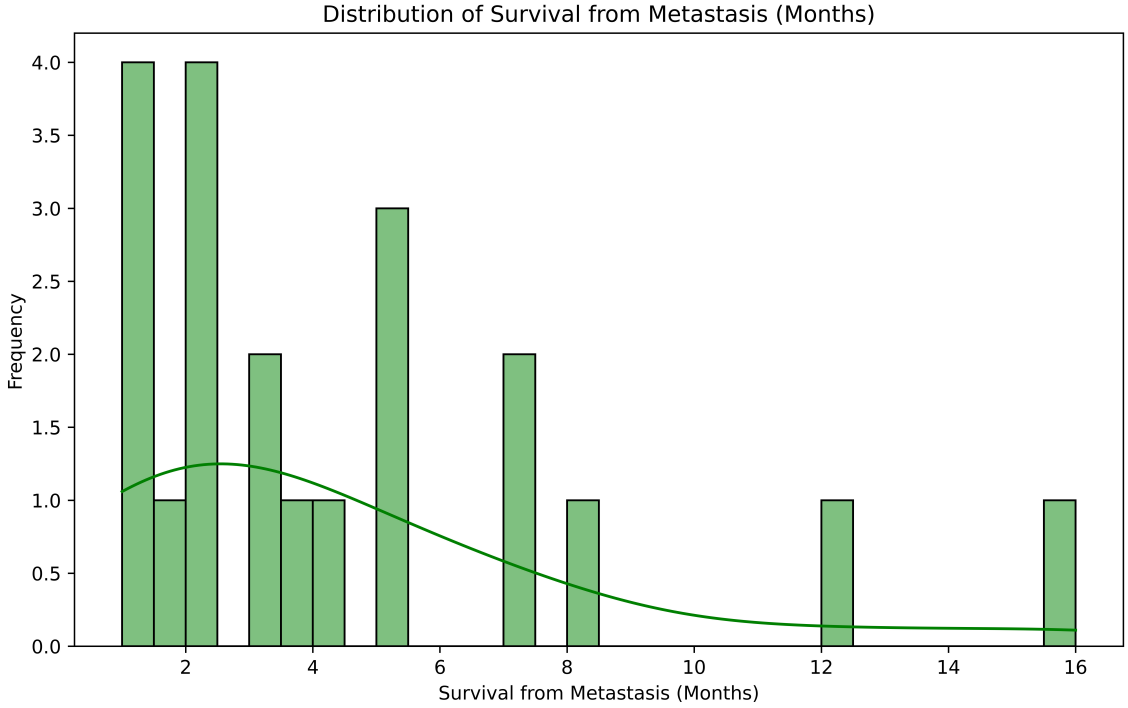

Figure 2. Survival from scalp metastasis (months). This histogram with a kernel density estimate illustrates the spread and central tendency of the survival times from metastasis. In quartiles: 25% of patients had a survival time of 2 months or less, 50% had a survival time of 3 months, and 75% of 5 months

Conclusions

This review highlights a rare form of progression of the more frequent malignant primary CNS tumor. GBM still presents a profound oncological challenge. The majority of cases reviewed debuted with scalp erythematous nodules located within the surgical scar or close to it. In any event, if extracranial recurrence of high-grade glioma is suspected, histopathological confirmation is always necessary for a definitive diagnosis.

The median time from the first surgery to skin and/or subcutaneous metastasis was 9.5 months, with 25% of the cases having metastasis by 6 months and 75% by 12.5 months. Thus, we can affirm that most of the skin and subcutaneous metastasis of GBM occurs within the first year following primary surgery. It doesn't differ greatly from CNS recurrences of GBM that largely happen between 6 and 9 months after the first surgery [15]. We must also note that 82.35% of patients had CNS progression at the same time or after the diagnosis of skin and/or subcutaneous dissemination, and 26.47% had metastasis in different locations (lymph nodes, lungs, liver, or spleen are some examples) [2–6]. In this way, we consider it appropriate to perform a new computerized tomography brain scan and an extension study before decision-making. The extension study should include at least a blood test with hepatic and renal profiles, and a thoracoabdominal computerized tomography scan in order to rule out systemic dissemination. Besides, we perceive this condition as a poor prognostic factor since the mean survival time from the diagnosis of scalp metastasis was 4.38 months, and most of the patients, more precisely 75%, passed away before 5 months. For its part, an isolated CNS recurrence entails an overall survival that ranges from 3 to 9 months. This doesn't seem to make a difference between both forms of recurrence but emphasizes the importance of palliative care, where excisional surgery of the scalp lesions seems suitable if the metastatic form of the disease endangers the patient's quality of life, yet does not have a statistically significant impact on the prognosis as we mentioned before, and it can be with different complications such as bleeding, ulceration, or infection.

In this respect, the main limitation of our review was its retrospective and observational nature. We couldn't establish a consensus regarding management, where the only mandatory aspect seems to be the unique patient attributes (age, performance status, presence of concomitant CNS recurrence…) in the risk-benefit balance of each decision. Moreover, for the reasons given above, we couldn't compile information about immunohistochemistry, which at present seems very important to understanding the mechanisms driving glioblastoma recurrence and may be a therapeutic key in the foreseeable future. It is our hope to enhance awareness of this condition among the neurosurgical and medical community, as well as to stimulate further research and collaborative efforts to gain a better understanding of the pathophysiology, and in this way, develop tailored therapeutic approaches for improved patient outcomes.

Abbreviations

CNS: central nervous system

CT: chemotherapy

GBM: gioblastoma multiforme

IDH: isocitrate dehydrogenase

RT: radiotherapy

WHO: World Health Organization

Declarations

Author contributions

MCF: Writing—original draft, Writing—review & editing, Formal analysis, Investigation, Methodology. ADVB: Conceptualization, Data curation, Project administration, Supervision, Validation, Writing—original draft, Writing—review & editing. GBP: Investigation, Methodology, Visualization. MRQ: Project administration, Visualization. GPA and AGC: Supervision, Validation, Visualization.

Conflicts of interest

The authors declare that there are no conflicts of interest.

Ethical approval

Not applicable.

Consent to participate

The informed consent to participate in the study was obtained from all participants.

Consent to publication

The informed consent to publication was obtained from relevant participants.

Availability of data and materials

The primary data for this review were sourced online from databases listed in the methods. Referenced articles are accessible on PubMed, EMBASE, and the Cochrane Library. Additional supporting data are available from the corresponding author upon request.

Funding

Not applicable.

References

1. Weller M, Wick W, Aldape K, Brada M, Berger M, Pfister SM, et al. Glioma. Nat Rev Dis Primers. 2015;1:15017. [DOI] [PubMed]
2. Matsuyama J, Mori T, Hori S, Nakano T, Yamada A. Gliosarcoma with multiple extracranial metastases. Case report. Neurol Med Chir (Tokyo). 1989;29:938–43. Japanese. [DOI] [PubMed]
3. Houston SC, Crocker IR, Brat DJ, Olson JJ. Extraneural metastatic glioblastoma after interstitial brachytherapy. Int J Radiat Oncol Biol Phys. 2000;48:831–6. [DOI] [PubMed]
4. Hata N, Katsuta T, Inoue T, Arikawa K, Yano T, Takeshita M, et al. Extracranial metastasis of glioblastoma to the lung and heart with a histological resemblance to small cell carcinoma of the lung: an autopsy case. No Shinkei Geka. 2001;29;433–8. Japanese. [PubMed]
5. Saad AG, Sachs J, Turner CD, Proctor M, Marcus KJ, Wang L, et al. Extracranial metastases of glioblastoma in a child: case report and review of the literature. J Pediatr Hematol Oncol. 2007;29:190–4. [DOI] [PubMed]
6. Anghileri E, Castiglione M, Nunziata R, Boffano C, Nazzi V, Acerbi F, et al. Extraneural metastases in glioblastoma patients: two cases with YKL-40-positive glioblastomas and a meta-analysis of the literature. Neurosurg Rev. 2016;39:37–46. [DOI] [PubMed]
7. Lewis GD, Rivera AL, Tremont-Lukats IW, Ballester-Fuentes LY, Zhang YJ, Teh BS. GBM skin metastasis: a case report and review of the literature. CNS Oncol. 2017;6:203–9. [DOI] [PubMed] [PMC]
8. Louis DN, Perry A, Wesseling P, Brat DJ, Cree IA, Figarella-Branger D, et al. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. Neuro Oncol. 2021;23:1231–51. [DOI] [PubMed] [PMC]
9. Ciscar-Fabuel M, De Vilalta-Bufurull A, Blanch-Pujol G, Romero-Quintela M, Plans-Ahicart G, Gabarros-Canals A. Glioblastoma multiforme recurrence on skin and subcutaneous tissue: a case report. Explor Neurosci. 2024;3:520–6. [DOI]
10. Schultz S, Pinsky GS, Wu NC, Chamberlain MC, Rodrigo AS, Martin SE. Fine needle aspiration diagnosis of extracranial glioblastoma multiforme: Case report and review of the literature. Cytojournal. 2005;2:19. [DOI] [PubMed] [PMC]
11. Jain N, Mirakhur M, Flynn P, Choudhari KA. Cutaneous metastasis from glioblastoma. Br J Neurosurg. 2005;19:65–8. [DOI] [PubMed]
12. Senetta R, Trevisan E, Rudà R, Benech F, Soffietti R, Cassoni P. Skin metastases of glioblastoma in the absence of intracranial progression are associated with a shift towards a mesenchymal immunophenotype: report of two cases. Acta Neuropathol. 2009;118:313–6. [DOI] [PubMed]
13. Magdaleno-Tapial J, Valenzuela-Oñate C, Pérez-Pastor G, Alegre de Miquel V. Skin Metastasis of Glioblastoma Multiforme: A Case Report and Literature Review. Actas Dermosifiliogr (Engl Ed). 2019;110:780–3. [DOI] [PubMed]
14. Bathla G, Gupta S, Moritani T. Primary leptomeningeal glioblastoma with systemic metastases-case report and review of literature. Clin Imaging. 2015;39:672–6. [DOI] [PubMed]
15. Nahm J, Sinha M, Schumann EH, Vu M, Hsu SH, Zhu JJ. Overall survival in patients with recurrent glioblastomas with combination chemotherapy and tumor treating fields (TTF). J Clin Oncol. 2023;41:e14057. [DOI]
16. Carvalho PA, Schwartz RB, Alexander E 3rd, Loeffler JS, Zimmerman RE, Nagel JS, et al. Extracranial Metastatic Glioblastoma: Appearance on Thallium-201-Chloride/Technetium-99m-HMPAO SPECT Images. J Nucl Med. 1991;32:322–4. [PubMed]
17. Wallace CJ, Forsyth PA, Edwards DR. Lymph node metastases from glioblastoma multiforme. AJNR Am J Neuroradiol. 1996;17:1929–31. [PubMed] [PMC]
18. Figueroa P, Lupton JR, Remington T, Olding M, Jones RV, Sekhar LN, et al. Cutaneous metastasis from an intracranial glioblastoma multiforme. J Am Acad Dermatol. 2002;46:297–300. [DOI] [PubMed]

19. Santos AV, Saraiva PF, Santiago B. Extracranial metastasis of glioblastoma multiforme. Acta Med Report. 2003;16:209–11. Portuguese. [PubMed]
20. Allan RS. Scalp metastasis from glioblastoma. J Neurol Neurosurg Psychiatry. 2004;75:559. [PubMed] [PMC]
21. Moon KS, Jung S, Lee MC, Kim IY, Kim HW, Lee JK, et al. Metastatic glioblastoma in cervical lymph node after repeated craniotomies: report of a case with diagnosis by fine needle aspiration. J Korean Med Sci. 2004;19:911–4. [DOI] [PubMed] [PMC]
22. Bouillot-Eimer S, Loiseau H, Vital A. Subcutaneous tumoral seeding from a glioblastoma following stereotactic biopsy: case report and review of the literature. Clin Neuropathol. 2005;24:247–51. [PubMed]
23. Mentrikoski M, Johnson MD, Korones DN, Scott GA. Glioblastoma multiforme in skin: a report of 2 cases and review of the literature. Am J Dermatopathol. 2008;30:381–4. [DOI] [PubMed]
24. Miliaras G, Tsitsopoulos PP, Markoula S, Kyritsis A, Polyzoidis KS, Malamou-Mitsi V. Multifocal glioblastoma with remote cutaneous metastasis: a case report and review of the literature. Cent Eur Neurosurg. 2009;70:39–42. [DOI] [PubMed]
25. Jusué Torres I, Jerez Fernández P, Ortega Zufiría J, Rodríguez Barbero JM. Skin spread from an intracranial glioblastoma: case report and review of the literature. BMJ Case Rep. 2011;2011: bcr0920114858. [DOI] [PubMed] [PMC]
26. Guo L, Qiu Y, Ge J, Zhou D. Glioblastoma multiforme with subcutaneous metastases, case report and literature review. J Korean Neurosurg Soc. 2012;52:484–7. [DOI] [PubMed] [PMC]
27. Amitendu S, Mak SK, Ling JM, Ng WH. A single institution experience of the incidence of extracranial metastasis in glioma. J Clin Neurosci. 2012;19:1511–5. [DOI] [PubMed]
28. Ginat DT, Kelly HR, Schaefer PW, Davidson CJ, Curry W. Recurrent scalp metastasis from glioblastoma following resection. Clin Neurol Neurosurg. 2013;115:461–3. [DOI] [PubMed]
29. Forsyth TM, Bi WL, Abedalthagafi M, Dunn IF, Chiocca EA. Extracranial growth of glioblastoma multiforme. J Clin Neurosci. 2015;22:1521–3. [DOI] [PubMed]
30. Pérez-Bovet J, Rimbau-Muñoz J. Glioblastoma multiforme metastases to the masticator muscles and the scalp. J Clin Neurosci. 2018;53:237–9. [DOI] [PubMed]
31. Moratinos Ferrero L, Lara Almunia M, González Jiménez V, Brell Dovall M, Ibáñez-Domínguez J. METÁSTASIS CUTÁNEAS Y GLIOBLASTOMA. REVISIÓN DE LA LITERATURA Y PRESENTACIÓN DE DOS CASOS. Neurocirugía. 2019;30:65. Spanish.
32. Nakib CE, Hajjar R, Zerdan MB, Darwish H, Zeidan Y, Alame S, et al. Glioblastoma multiforme metastasizing to the skin, a case report and literature review. Radiol Case Rep. 2021;17:171–5. [DOI] [PubMed] [PMC]