Craniectomy With Soft Tissue Reconstruction for Locally Advanced Non-Melanoma Skin Cancer Ofor Scalp With Calvarial Invasion: the Nottingham

experience

Zhen Yu Wong^{1,2*}, Neil Wickham^{1*}, Shenbana Bagirathan¹, Alex Leggate², Stuart J Smith², Jonathan Pollock^{1#}

¹Department of Plastic Surgery, Nottingham City Hospital, Nottingham, England, United Kingdom ² Department of Neurosurgery, Queens Medical Centre, Nottingham, England, United Kingdom

1

*These authors have contributed equally to this work and share first authorship. #These authors have contributed equally to this work and share last authorship

Corresponding Author:

Jonathan Pollock BM, BS, BMedSci (Hons), FRCS (Plast) Department of Plastic Surgery, Nottingham City Hospital, Nottingham, England, United Kingdom Email: Jonathan.Pollock@nuh.nhs.uk

Number of tables: 2 Number of figures: 0

ABSTRACT

Introduction: Locally advanced non-melanoma skin cancer (NMSC) involving the periosteum or calvarium remain clinically challenging for patients unfit for immunotherapy due to medical comorbidities and/or frailty. This case series aims to explore outcomes for patients that underwent craniectomy and soft tissue reconstruction.

Method: Patients underwent craniectomy and soft tissue reconstruction for invasive NMSC with calvarium or periosteal invasion from 2016 to 2022 were included. Data including demographics, operative details, and clinical outcomes were sourced from Nottingham University Hospitals digital health record and the histopathology electronic database.

Result: 8 patients (Age: 78.4, 3F 5M) with significant comorbidities and varying degrees of periosteal or bone invasion fulfilled the inclusion criteria. These included four squamous cell carcinoma, two basal cell carcinoma and two pleomorphic dermal <u>sarcomasarcomas</u>. Five patients had a history of prior incomplete deep margin excision. The median soft tissue defect, tumour and bone defect size was 51.83cm², 34.63cm² and 42.25cm² respectively. Intraoperative complications included one dural tear. Four patients underwent local flap reconstruction and with split thickness skin grafting, four patients underwent free flap reconstruction. Adjuvant radiotherapy was administered to three. Complications comprised partial graft loss in two and complete graft loss in one. There was partial flap loss in one case. One patient required subsequent parotidectomy due to regional progression before achieving disease control. All patients achieved lasting locoregional disease control (average follow up 29.7 months).

Conclusion: Craniectomy with soft tissue reconstruction is a safe and effective treatment option in advanced NMSC of the scalp in patients unsuitable for immunotherapy due to frailty or medical comorbidity.

(245 words)

Keywords: free flap reconstruction of the calvarium, microsurgical reconstruction, Nonmelanoma skin cancers of the scalp

INTRODUCTION

Non-melanoma skin cancer (NMSC) has become a significant global health concern, with its prevalence reaching epidemic proportions,¹ Among the various types of NMSC, basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are the most common. The burden of NMSC continues to rise or remain at high levels, presenting a pressing challenge for healthcare providers worldwide. Up to eighty percent of cutaneous malignancies occur in the head and neck region,² secondary to the lifetime accumulation of ultraviolet radiation damage³, necessitating a meticulous and considerate approach to management.

Immunotherapy and radiotherapy have emerged as the mainstay treatment options for managing locally advanced NMSC, ⁴ However, NMSC involving the periosteum or calvarium, poses significant clinical challenges for patients who are unfit for contemporary management options due to underlying medical comorbidities and/or frailty as universally accepted treatment protocols have not yet been established. Furthermore, there is a scarcity of literature, limited epidemiological data, and poor awareness among surgeons regarding this specific subset of locally advanced non-melanoma skin cancer. The aggressive approach of resection of cranial bone and soft tissue reconstruction has gained increasing popularity in the management of locally advanced non-melanoma skin cancer (NMSC) affecting the scalp, primarily driven by its therapeutic benefits, ^{5,6}

In light of these challenges, our report aims to present our recent experience in effectively treating patients with locally advanced and recalcitrant scalp cancers through a combination of extirpation and reconstruction, without immediate cranioplasty. This case series explores the outcomes of craniectomy with flap reconstruction as an alternative approach for patients who are not suitable candidates for conventional management options.

Formatted: Check spelling and grammar

METHODS

Patient Selection

Patients underwent craniectomy and soft tissue reconstruction for invasive cutaneous malignancies with calvarium or periosteal invasion from 2016 to 2022 were included in the analysis. In Figure 1, an illustrative representation of anatomy is presented.

Classification of Comorbidities and Outcomes

Data including demographics, operative details, and clinical outcomes were sourced from Nottingham University Hospitals digital health record and the histopathology electronic database. Scalp defect and reconstruction characteristics were collected through review of medical records. Postoperative outcomes, survival, and complications were collected prospectively through communication between neurosurgeons, plastic surgeons, and clinic nurses. Partial flap loss was defined as flap necrosis that resulted in subtotal loss of flap, while complete flap loss was defined as requiring total flap debridement.

Surgical Technique

The procedures carried out within our study cohort were tailored to each patient's specific requirements, depending on the extent of resection necessary to achieve clear margins on pathology assessment. Preoperative radiological evaluations provided valuable insights, particularly in identifying cases with periosteal invasion. Surgical resection was planned in advance with all patients having either histologically confirmed deep margin involvement from previous excision or clear radiological evidence of at least periosteal involvement. Under general anaesthesia the soft tissue tumour field was widely excised. A variable sized full thickness calvarial bone excision was then performed to expose the underlying dura. Both tissue samples were sent for <u>permenantpermanent</u> section histologically assessment. Soft tissue <u>reonstructionreconstruction</u> was then undertaken using either local or free flap coverage depending on the defect size. By tailoring our surgical approach based on individual patient characteristics and employing radiological assessments with preoperative planning, we aimed to achieve complete resection with clear margins, ensuring optimal oncological outcomes for our patients.

RESULTS

Patient Characteristics

We included 8 patients (3 Female, 5 Males) with significant comorbidities and varying degrees of periosteal or bone invasion that fulfilled the inclusion criteria (Table 1). The cohort consisted of five patients with a documented history of significant cardiovascular diseases, two of whom were undergoing immunosuppressive treatment, while one patient had a concurrent diagnosis of leukaemia. The mean patient age was 78.35 (range 71-89). The median follow up was 26.5 months (interquartile range 16.5- 46.75).

TumorTumour and Resulting Defect Characteristics

These included four squamous cell carcinoma, two basal cell carcinoma and two pleomorphic dermal sarcomasarcomas. Five patients had a history of prior incomplete deep margin excision. Most cases in the study cohort were identified as primary tumorstumours, with the exception of one patient presenting with recurrent metastatic pleomorphic dermal sarcoma. The depth of invasion was on the outer table of the skull in one patient, full thickness through cranium in four patients and periosteum invasion in two patients while it remained unknown in one patient. One of the patients who had full thickness invasion through cranium also has dural involvement. None of the patients had any neoadjuvant chemotherapy or radiotherapy. Clear peripheral and deep margins were achieved for all patients. The median soft tissue defect, tumour and bone defect size was 51.83cm² (interquartile range 19.75–80.75), 30.25cm² (interquartile range 6.5–49) and 42.25cm² (interquartile range 9.7–82.03) respectively.

Reconstruction Characteristics

Cranioplasty was not performed in any of the patients. Four patients underwent local flap reconstruction and with split thickness skin grafting, four patients underwent free flap reconstruction. Adjuvant radiotherapy was administered to three with one developed osteoradionecrosis and had further craniectomy and free latissimus dorsi flap reconstruction.

Complications and Outcomes

Intraoperative complications included one primary dural tear which was repaired intraoperatively. Complications comprised partial graft loss in two, complete graft loss in one and partial flap loss in one. Graft loss was treated with regrafting in all cases and a small scalp rotation used in the case with partial flap loss. One patient required subsequent parotidectomy due to regional disease progression before achieving disease control. All patients achieved lasting locoregional disease control.

DISCUSSION

This case series presents a group of high-risk patients who underwent surgical treatment for locally advanced non-melanoma skin cancer (NMSC) affecting the scalp. The collaboration between neurosurgeons and plastic surgeons was crucial in managing the extensive extirpative and reconstructive challenges posed by these patients, considering the size and depth of the tumorstumours. The resulting full-thickness defects exposed the intracranial contents, making it impractical to use interim dressings until the final pathology report was available due to the high risk of complications such as intracranial infection, cerebrospinal fluid (CSF) leak, or haemorrhage from the sagittal sinus. The treatment goals in these cases encompass three main objectives. Firstly, the aim is to eliminate the tumortumour and compromised tissues completely. Secondly, immediate and stable tissue coverage is provided to address the full-thickness defects. Lastly, the ultimate objective is to enable patients to resume their normal daily activities. Achieving these goals required a multidisciplinary approach, which proved successful in accomplishing complete surgical excision and immediate single-stage soft tissue reconstruction.

Plastic and reconstructive techniques play a crucial role in managing extensive bone and soft tissue defects of the skull, particularly after oncological resections, to achieve optimal oncological and aesthetic outcomes.⁷ To facilitate the early and comprehensive reconstruction of both soft tissue and bone, it is advisable to plan these procedures in an interdisciplinary board involving specialists from neurosurgery and plastic and reconstructive surgery. In cases involving large resections, plastic surgery involvement from the initial stages becomes imperative. Currently, there is a scarcity of studies that have reported outcomes of single-stage microvascular scalp and calvarial reconstructions. The variability in surgical outcomes among individuals is primarily influenced by the depth and degree of invasion of the defect, as well as the presence of comorbidities. Our study's results are comparable to findings from other similar studies which are summarized in Table 2.⁸⁻¹⁴ Generally, a low incidence of locoregional recurrence and a relatively longer disease-free survival are considered satisfactory outcomes, particularly considering the high-risk nature of this patient population. Despite the need for a clear algorithm to guide decision-making in this regard, one of the main obstacles is the relatively small size of the population available for study. Further research and a larger patient cohort are

Formatted: Check spelling and grammar

Formatted: Check spelling and grammar

necessary to address this limitation and propose a comprehensive algorithm for managing these cases effectively.

Furthermore, a significant portion of the challenges encountered in these cases are related to complications associated with soft tissue reconstruction. This highlights the importance of optimizing and carefully selecting the appropriate flap reconstruction techniques for individual patients. While no clear guideline exists for these specific patients, the decision is typically left to the judgment of the operating surgeon. In addition, the use of adjuvant or neoadjuvant radio-chemotherapy has been shown to improve disease outcomes15, but it can compromise the quality of flap reconstruction. In our approach, we have chosen to avoid immediate cranioplasty. This decision is based on the high rate of complications historically associated with cranioplasty in similar clinical scenarios involving radiation and infection or contamination,¹⁶ A retrospective review conducted by Afifi et al. demonstrated an unacceptably high major complication rate of 38% in 13 patients who underwent simultaneous methylmethacrylatemethyl methacrylate-based cranioplasty and microvascular soft-tissue reconstruction,¹⁷ Although the absence of immediate calvarial reconstruction may result in abnormal cranial contour and the lack of solid protection for the intracranial contents¹⁸, we have found that these limitations are acceptable within this specific patient population, primarily due to their advanced age and associated lifestyle. Unlike individuals in their younger years who may experience scalp and cranial defects from traumatic events, all of our patients were in their seventh through ninth decades of life..life. This older group of patients, who were dealing with persistent cancers, prioritized curative resection and the ability to resume their baseline activities. Delaying cranial reconstruction was deemed the safest approach to achieve these goals. Consequently, our patients are required to follow standard precautions for individuals without solid protection of their intracranial contents.

Limitation

There are several limitations that need to be acknowledged regarding the current body of literature discussed in the preceding paragraphs. Firstly, there is a lack of direct comparative studies that examine the outcomes of non-surgical versus surgical treatment versus conservative management approaches for the conditions under consideration. <u>Due to the rare nature of the condition, regrettably, the formation</u> of a control group for comparative analysis with alternative techniques proved unattainable. This gap

Formatted: Check spelling and grammar

Formatted: Not Highlight

hinders our ability to make definitive conclusions regarding the relative effectiveness of these different treatment modalities. Furthermore, the existing evidence base is not robust, with limited high-quality studies available to inform clinical decision-making. Several drawbacks of a retrospective case series include dependence on retrospective data, relying on medical record availability and accuracy; susceptibility to selection bias as investigators self-select cases. The scarcity of good evidence restricts the ability to establish strong recommendations or guidelines regarding optimal management strategies for patients with extensive bone and soft tissue defects of the skull. Our results may be influenced by additional confounding factors, such as demographics and disease progression, and the small sample size, necessitating careful consideration when interpreting the findings and their applicability to the general population. The variability in the nature of the diseases encountered, such as differences in tumortumour characteristics, adds complexity and makes direct comparisons challenging. This variability highlights the need for more tailored and individualized approaches to treatment, taking into account the specific characteristics of each patient's condition. To address these limitations, future research should prioritisze the prospective investigation of patient-reported outcomes, longitudinal assessment of disease-specific mortality risks, as well as the evaluation of surgical revision rates and complications while comparing different therapeutic options. However, we anticipate difficulties in recruiting a sufficient number of patients. By focusing on these aspects, a more comprehensive understanding of the optimal treatment strategies and their associated outcomes can be gained, aiding clinicians in making informed decisions and improving patient care.

Conclusion

Craniectomy with soft tissue reconstruction is a safe and effective treatment option in advanced cutaneous malignancy of the scalp in patients unsuitable for immunotherapy due to frailty or medical co-morbidity. Further studies are necessary to optimise the approach through multidisciplinary collaborations.

DECLARATIONS

Funding

No funding was required for this study.

Conflicts of Interests

All authors have no conflicts of interests.

Ethical Statement

The study was conducted in accordance with the Declaration of Helsinki. The study was exempted from IRB review.

Acknowledgements

All authors have made substantial contributions to all of the following: (1) the conception and design of the study, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, (3) final approval of the version to be submitted. No writing assistance was obtained in the preparation of the manuscript. The manuscript, including related data, figures and tables has not been previously published and that the manuscript is not under consideration elsewhere.

Authors' Contributions

All authors approve the final version of the manuscript, including the authorship list and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Conceptualisation and Design: NW, AL, SJS, JP Acquisition of Data: ZYW, NW, SB Analysis and Interpretation of Data: ZYW, NW, SB, AL, SJS, JP Writing – original draft: ZYW, NW, JP Writing – review & editing: SB, AL, SJS, JP

REFERENCES

- 1. Hu W, Fang L, Ni R, Zhang H, Pan G. Changing trends in the disease burden of non-melanoma skin cancer globally from 1990 to 2019 and its predicted level in 25 years. *BMC Cancer.* Jul 30 2022;22(1):836. doi:10.1186/s12885-022-09940-3
- Khalid A, van Essen P, Crittenden TA, Dean NR. The anatomical distribution of non-melanoma skin cancer: a retrospective cohort study of 22303 Australian cases. ANZ J Surg. Dec 2021;91(12):2750-2756. doi:10.1111/ans.17030
- 3. Leiter U, Garbe C. Epidemiology of melanoma and nonmelanoma skin cancer--the role of sunlight. *Adv Exp Med Biol.* 2008;624:89-103. doi:10.1007/978-0-387-77574-6_8
- Stratigos AJ, Garbe C, Dessinioti C, et al. European interdisciplinary guideline on invasive squamous cell carcinoma of the skin: Part 2. Treatment. *Eur J Cancer*. Mar 2020;128:83-102. doi:10.1016/j.ejca.2020.01.008
- Ziegler A, Walker R, Varvares M. Oncologic Outcomes of Invasive Squamous Cell Carcinoma of the Scalp Requiring Resection of Cranial Bone. J Neurol Surg A Cent Eur Neurosurg. Jul 2016;77(4):308-11. doi:10.1055/s-0035-1567859
- Raza SM, Ramakrishna R, Weber RS, et al. Nonmelanoma cutaneous cancers involving the skull base: outcomes of aggressive multimodal management. *J Neurosurg.* Sep 2015;123(3):781-8. doi:10.3171/2014.10.jns141037
- 7. Vogt PM, Mett TR, Broelsch GF, et al. Interdisciplinary reconstruction of oncological resections at the skull base, scalp and facial region. *Surg Oncol.* Sep 2017;26(3):318-323. doi:10.1016/j.suronc.2017.06.006
- Lipa JE, Butler CE. Enhancing the outcome of free latissimus dorsi muscle flap reconstruction of scalp defects. *Head Neck*. Jan 2004;26(1):46-53. doi:10.1002/hed.10338
- Kwon CS, Awar OA, Ripa V, Said G, Rocka S. Basal cell carcinoma of the scalp with destruction and invasion into the calvarium and dura mater: Report of 7 cases and review of literature. *J Clin Neurosci.* Jan 2018;47:190-197. doi:10.1016/j.jocn.2017.09.028
 Sleiwah A, Mughal M, Thomas N, Roblin P, Townley W, Jeannon JP. Locally Advanced Scalp
- Sleiwah A, Mughal M, Thomas N, Roblin P, Townley W, Jeannon JP. Locally Advanced Scalp Tumors: Clinical and Survival Outcomes of a Tertiary Unit. *Ann Plast Surg.* Sep 1 2021;87(3):271-277. doi:10.1097/sap.00000000002673
- 11. Soma PF, Chibbaro S, Makiese O, et al. Aggressive scalp carcinoma with intracranial extension: a multidisciplinary experience of 25 patients with long-term follow-up. *J Clin Neurosci.* Sep 2008;15(9):988-92. doi:10.1016/j.jocn.2007.09.014
- 12. Marijon P, Bertolus C, Foy JP, et al. Custom surgical management of invasive malignant tumors of the scalp. *Acta Neurochir (Wien)*. Dec 2020;162(12):2991-2999. doi:10.1007/s00701-020-04525-0
- Leach GA, Pflibsen LR, Mathew DP, Sharma AD, Reid CM, Holcombe TC. The Role of Resection of the Outer Table of the Cranium in Locally Invasive Primary Squamous Cell Carcinoma of the Scalp. J Craniofac Surg. Sep 1 2022;33(6):1860-1864. doi:10.1097/scs.00000000008696
- Cho GJ, Wang F, Garcia SM, et al. Recalcitrant Invasive Skin Cancer of the Scalp: Combined Extirpation and Microsurgical Reconstruction Without Cranioplasty. *J Craniofac Surg.* Mar 2017;28(2):325-330. doi:10.1097/scs.00000000003384
- 15. McDowell L, Yom SS. Locally advanced non-melanomatous skin cancer: Contemporary radiotherapeutic management. *Oral Oncol.* Dec 2019;99:104443. doi:10.1016/j.oraloncology.2019.104443
- Alkhaibary A, Alharbi A, Alnefaie N, Oqalaa Almubarak A, Aloraidi A, Khairy S. Cranioplasty: A Comprehensive Review of the History, Materials, Surgical Aspects, and Complications. *World Neurosurg.* Jul 2020;139:445-452. doi:10.1016/j.wneu.2020.04.211
- Afifi A, Djohan RS, Hammert W, Papay FA, Barnett AE, Zins JE. Lessons learned reconstructing complex scalp defects using free flaps and a cranioplasty in one stage. *J Craniofac Surg.* Jul 2010;21(4):1205-9. doi:10.1097/SCS.0b013e3181e17c1e
- Chao AH, Yu P, Skoracki RJ, Demonte F, Hanasono MM. Microsurgical reconstruction of composite scalp and calvarial defects in patients with cancer: a 10-year experience. *Head Neck.* Dec 2012;34(12):1759-64. doi:10.1002/hed.21999

Formatted: Check spelling and grammar

FIGURE AND TABLE LEGENDS

Figure 1: (a) Anatomical Demarcation of Calvarium, (b) Anatomical Layers of Scalp

Table 1: Current case series

Table 2: Summary of similar studies employing excision and soft tissue reconstruction for locally

advanced skin cancer with calvarium invasion