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Adjunctive hyperbaric oxygen therapy with reconstruction of lower eyelid for basal cell carcinoma: A case series

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ABSTRACT

Introduction: Basal cell carcinoma (BCC) is among the most widespread non-melanoma skin cancers, with an incidence of around 80 % worldwide. Surgery is the main therapy of choice. High-pressure oxygen is used in hyperbaric oxygen therapy (HBO) to treat hypoxic tissue conditions. By using this technique, the tissue oxygen tensions increase. This is used to treat a wide range of diseases and disorders brought on by hypoxic states, circulation issues, inadequate tissue oxygenation due to vascular damage, tissue damage from infections or accidents, and impairment of tissue healing.

Cases presentation: This paper presents five cases of HBO used in the healing BCC surgery. All patients underwent wide and deep excisions with eight adjunctive sessions of HBO therapy.

Clinical discussion: The five cases of post-surgery wound healing improved significantly with HBO.

Conclusion: BCC is a condition that is frequently identified in the outpatient department. Prerequisites for a better prognosis include early diagnosis based on sound information and prompt, structured, and sufficient therapy. Our study reveals the benefit of HBO in increasing wound healing and preventing complications after surgery for BCC.

1. Introduction

Basal cell carcinoma (BCC) is among the most widespread types of non-melanoma skin cancer. The world incidence is around 80 % worldwide. BCC was first described in 1827 [1]. The main risk factor for BCC is sun exposure, and 90 % are found in fair-skinned people. The *PATCH* gene (tumor suppression receptor protein) mutation brought on by UV radiation and the *p53* gene mutation result in the loss of function of the related proteins and, ultimately, tumor suppression activity [1,2].

Areas exposed to UV radiation are the most common places where lesions appear, such as the back, face, and chest. BCC usually grows slowly for many years before presentation [3].

BCC's outward appearance varies according to the subtype. Typically, a skin-colored lump that bleeds, does not heal, and has developed slowly should raise suspicion. Spontaneous bleeding that results in a bloody crust can aid in distinguishing it from actinic keratoses and squamous cell carcinoma, which more frequently form a distinctive keratinized crust [4].

Hyperbaric oxygen (HBO) therapy is a treatment option of high-pressure oxygen to improve hypoxic tissue condition [5]. This

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increases the tissue oxygen tensions. It has been used to treat conditions with inadequate tissue oxygen delivery because of hypoxic conditions, recovery from circulation insufficiency, or vascular injury [6].

HBO therapy enhances oxygen delivery to hypoxic tissues because even when injured tissues have poor blood circulation, dissolved oxygen can still infiltrate through tissue fluid. Although the basic process of HBO therapy is relatively straightforward and involves increasing dissolved oxygen, an increase in tissue oxygen tension has several positive side effects, including creating a more conducive environment for wound repair and speeding healing [7]. This case series has been reported in line with the SCARE Guidelines 2020 [8].

2. Presentation of case

We provide five cases of HBO therapy on the healing of BCC surgery (Table 1). Consent to publish personal information was obtained from the patients orally and in writing. HBO was administered a day after surgery. The patients were given eight sessions of HBO, 8 days in a row, at a duration of 120–180 min per session, by inhalation of 100 % oxygen at a pressure of 2 ATA. The HBO therapy was carried out in two different facilities: Kandou General Hospital (KGH) and Siloam Hospital, Manado, Indonesia. KGH uses a monoplace chamber, whereas Siloam Hospital uses a multiplace chamber, but the pressure and duration of the procedure were the same.

2.1. Case 1

A 70-year-old woman presented with a 4 × 5-cm lesion on her left lower eyelid, immediately below the lower lash line. The lesion had been noticed approximately 5 years previously. The nodule had gradually moved from the distal side of the inner canthus to the proximal side. The clinical diagnosis was BCC, and the pathological examination confirmed this. Wide excision and reconstruction with a musculocutaneous transposition flap from the upper eyelid (Fig. 1A, B) with adjunctive HBO therapy were performed. The flap was completely salvaged with successful completion of the reconstruction. HBO resulted in flap survival, wound closure, and improved healing time (Fig. 1C).

2.2. Case 2

A 50-year-old man presented with a mole-like lump under the left eye. Initially, the lump was small and quickly grew. The patient also reported itching. The mass was 1 × 1 cm, and the edges were not flat (Fig. 2A, B). Reconstruction was performed by a specialist plastic surgeon (Fig. 2C). The wound healing was successful and complete (Fig. 2D). HBO resulted in faster wound closure and improved healing time. The clinical pictures at follow-up show no recurrence (Fig. 2E).

Table 1
Characteristics of patients and treatment outcomes.

No.	HBO sessions	Onset of HBO therapy after the surgery	Type of flap	Healing time of the wound	Follow-up time and recurrence of BCC
1.	8 times	1 day	Transposition flap	3 weeks	3 months, no recurrence
2.	8 times	1 day	Transposition flap	3 weeks	1 year, no recurrence
3.	8 times	1 day	Transposition flap	3 weeks	6 months, no recurrence
4.	8 times	1 day	Transposition flap	2 weeks	1 year, no recurrence
5.	8 times	1 day	Transposition flap	3 weeks	1 year, no recurrence

2.3. Case 3

A 53-year-old woman presented with a 1.5 × 1-cm lesion on her right lower eyelid, below the lower lash line. She had first noticed the lesion approximately 3 years previously. The nodule had gradually moved from the distal side of the inner canthus to the proximal side (Fig. 3A). The clinical diagnosis was BCC, and the pathological examination confirmed this. A transposition flap was used to repair the anterior lamellar defect of the lower eyelid, and adjunctive HBO was performed. The flap was completely salvaged with successful completion of the reconstruction (Fig. 3B). HBO resulted in flap survival, wound closure, and improved healing time (Fig. 3C).

2.4. Case 4

A 49-year-old woman presented with a 1 × 1 cm lesion on her left lower eyelid, below the lower lash line. She had first noticed the lesion approximately 2 years previously. The nodule had gradually moved from the distal side of the inner canthus to the proximal side. The clinical diagnosis was BCC, and the pathological examination confirmed this. A transposition flap was used to repair the anterior lamellar defect of the lower eyelid with adjunctive HBO. The flap was completely salvaged with successful completion of the reconstruction. HBO therapy resulted in flap survival, wound closure, and improved healing time.

2.5. Case 5

A 84-year-old woman presented with a 1.5 × 0.5-cm lesion on her left lower eyelid, immediately below the lower lash line. She had first noticed the lesion approximately 4 years previously. The nodule had gradually grown toward the lacrimal tarsus in one direction. The clinical diagnosis was BCC, and the pathological examination confirmed this. A transposition flap was used to repair the anterior lamellar defect of the lower eyelid with adjunctive HBO therapy. The flap was completely salvaged with successful completion of the reconstruction. HBO resulted in flap survival, wound closure, and improved healing time.

3. Discussion

BCC is a reasonably common cancer, frequently identified in outpatient departments. Early diagnosis based on good knowledge and prompt, structured, and adequate therapy are prerequisites for a better prognosis. Surgical treatment has the highest success compared to other methods. Following surgical removal of BCCs with primary tumors up to 1.5 cm in diameter, the results of a 5-year follow-up suggest that recurrences occur in 12 % of instances. In comparison, they occur 23 % of the time in primary carcinomas larger than 3 cm in diameter [9].

In other procedures, such as Mohs surgery, the intraoperative examination of the wound edges for the presence of tumor cells is part of the microscope-controlled surgery—electric cauterization or cryotherapy can only be done in relatively small tumors. The relapse rate of the other methods besides surgery is up to 50 %. Only superficial BCCs are acceptable for laser therapy. More than 80 % of BCC patients treated by CO_2 laser saw complete clearance after just one session [9].

The fundamental goals of reconstructive alternatives should be primary wound healing, safeguarding crucial structures, contour restoration, and maximizing functional and aesthetic benefits. The paramedian forehead flap has become the preferred technique for reconstructing nasal BCC. However, it does not apply to the severe midface and nasal abnormalities in giant nasal BCC, leaving only other local flaps, regional flaps, and microsurgical free flaps as alternatives [10]. In these case series, we use references based on the study of Cordoro et al. [11], where the wound healing phase in patients with BCC until the re-epithelialization process reaches 3 weeks. The removal of stitches in the eyelid area is from the 5th day after the operation. It depends on the patient's condition and risk factors.

Fig. 1. (A) The patient during surgery and (B) after the surgery. The picture shows significant improvement of the postoperative lesion and (C) complete healing after 3 months of follow-up.

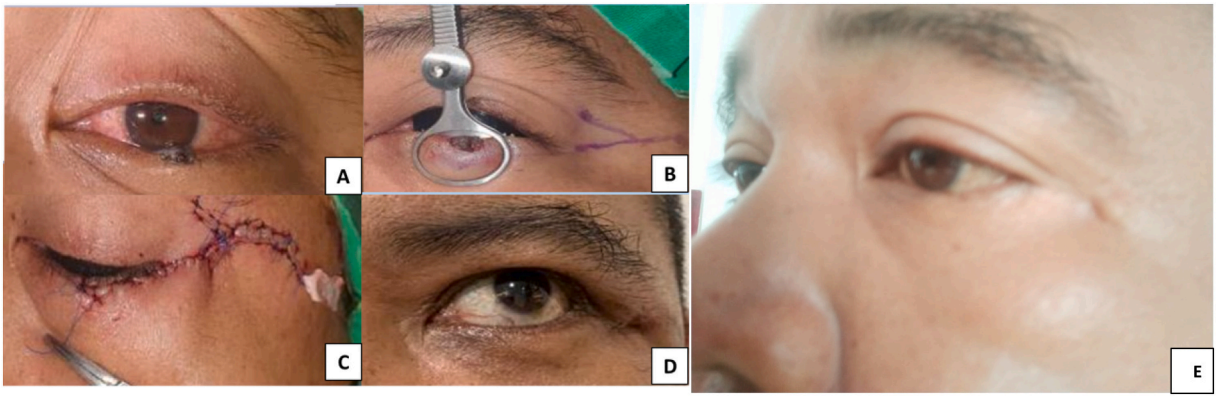

Fig. 2. (A) In the periorbital region, an irregular-shaped, soft mass, 1 × 1 cm in size. (B) Excision design with ink and chalazion forceps used for fixation. (C) The mass was removed. (D) 2 weeks after reconstruction. (E) A year after reconstruction.

A reverse reconstruction ladder has been recommended, where significant or composite defects are treated using the microsurgical free flap as the first option. The free flap gives the newly created tissues a strong blood supply, enough volume to regain function and form, and radiation resistance. However, it requires more time and thorough training during surgery due to the poor skin color match, donor site

Fig. 3. (A) In the periorbital region, an irregular-shaped, soft mass, 1.5 × 1 cm in size. Excision design with ink. (B) The mass was removed. (C) Completed healing after 6 months follow-up.

morbidity, and large tissue bulk. The regional flap has the same problems as the free flap but requires less time during surgery and uses simpler tools and techniques [10].

To reconstruct lower eyelid deformities, two techniques exist. The first involves direct closure with either a semicircular Tenzel flap or lateral cantholysis for tiny defects up to 30 %. The second method is for moderate-sized defects up to 50 % of the length of the eyelid, divided into the posterior and anterior lamella. Hughes's (modified) tarsoconjunctival flap is a part of the posterior lamella. Full-thickness skin grafts, Tripier flap unipedicles, and cheek skin advancement are examples of anterior lamella [12].

HBO acts through both direct and indirect effects. Both hyperoxia and increased pressure are primary impacts. Antimicrobial effects, a reduction in ischemia-reperfusion injury, and wound healing are secondary consequences of regulated oxidative stress. Wound healing is the result of both systemic and local effects.

Systemic effects lead to better progenitor stem cell homing to the site of injury and mobilization and release from bone marrow. A pronounced oxygen gradient, the recruitment of macrophages, and the release of numerous growth factors are some of the local effects. Neovasculogenesis and collagen production are the outcomes of both systemic and local effects, and both of these promote wound healing. The same mechanisms that produce HBO's positive effects can also lead to certain patients experiencing its known adverse effects [13].

HBO may be an effective adjuvant in the treatment of surgical injuries, and its early administration may improve results. HBO provides additional aid when wounds do not respond to conventional medical care for healing. The importance of this method in accelerating neovascularization and epithelialization during wound healing has been demonstrated in animal models. According to reports, host factors such as tissue inhibitor of metalloproteinase-1 (TIMP-1), matrix metallopeptidase 9 (MMP-9), and tumor necrosis factor are upregulated as a result of these occurrences in accelerating wound healing. Normobaric oxygen therapy and HBO therapy were evaluated in a rabbit model of irradiated tissue, revealing again that O_2 is necessary at higher pressures to cause an angiogenic effect. More in vivo studies have suggested that the pressure created by HBO influences the rate at which stem cells proliferate in small intestinal crypts and increases angiogenesis in the chorioallantoic membrane of *Gallus gallus* embryos. In a clinical trial, HBO was administered to patients with chronic non-healing wounds (wounds that had not healed in more than 20 months) for a standard 20 sessions (five treatments per week). As a result, vascular endothelial growth factor (VEGF) and interleukin-6 (IL-6) levels were elevated, but endothelin-1 levels decreased. This is due to the stimulation of vascular tone, angiogenesis, and host wound resolution factors. Nitric oxide is upregulated by HBO, which increases the efficiency of vasculogenesis and contributes to a reduction in the size of lesions [5].

Absolute contraindications to HBO include a blood gas analysis–measured PaO_2/FiO_2 ratio of 200, non-drained pneumothorax, claustrophobia, psychiatric problems, and seizures. Limited risks associated with HBO can make receiving effective treatment more difficult. Two classifications exist in HBO side effects: pressure-related

complications and oxygen-related issues.

Barotrauma is the first category. This can happen in any sealed, air-filled cavity. Around 2 % of patients who are awake experience middle ear barotrauma, whereas unconscious patients can avoid it by using trans-tympanic breathing tubes. Rarely, during decompression, individuals with an airway blockage may experience pulmonary barotrauma (pneumomediastinum, subcutaneous emphysema, intrapulmonary hemorrhage, tension pneumothorax [PTX], and simple PTX). The second category is further divided into three different complications: ophthalmologic, neurologic, and pulmonary. Myopia alteration is the most frequent ocular side effect of HBO therapy. The incidence of oxygen seizures is around 0.01 % of treatments, without any indication of long-term sequelae. Pulmonary oxygen toxicity (interstitial edema, alveolar edema, intra-alveolar hemorrhage) is not a realistic issue because it requires sustained hyperbaric dosage exposure [13–15].

Follow-up evaluation of the patients was carried out 6 months to 1 year after the procedure. The clinical pictures (Figs. 2 and 3) of the patients at follow-up show no recurrence. This is also supported by a review article by Feldmeier et al. [16], where HBO therapy was reported to reduce the incidence of recurrence in cancer patients. According to the literature, cancer growth is not accelerated by intermittent HBO in either primary or metastatic cancer. Similarly, no concrete evidence suggests that HBO causes or fosters the development of cancer de novo. Between 1966 and 2001, many experimental animal investigations have been undertaken expressly to examine the effect of HBO on malignant tumor growth and metastasis. They have been unable to show that HBO has an effect that promotes tumor growth. Marx [16,17] observed 405 individuals who had delayed radiation injury and found that those who received HBO had a lower risk of recurrence. The review article by Feldmeier et al. does not provide strong evidence to support the hypothesis that considerable immune suppression, free radical–induced damage, or mutations resulting in carcinogenesis may increase malignant development in hyperbaric patients [16].

A limitation of our study is that since the rates of epithelization in the HBO therapy and control groups were not contrasted, no conclusive correlation could be drawn. Future studies should investigate HBO uses further for treating surgical wounds.

4. Conclusion

BCC is a condition frequently identified in the outpatient department. Prerequisites for a better prognosis include early diagnosis based on sound information and prompt, structured, and sufficient therapy. We presented five cases of post-surgery wound healing in BCC that improved significantly with HBO. Our study reveals the benefit of HBO in increasing wound healing and preventing post-surgery BCC complications.

Ethical approval

Ethical Approval was waived by the authors institution.

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CRediT authorship contribution statement

Mendy Hatibie Oley and Maximillian Christian Oley: Conceptualization, Methodology, Software. Mendy Hatibie Oley, Maximillian Christian Oley, Deborah Florencia Gunawan, and Andi A. Rangan: Data curation, Writing-Original draft preparation. Muhammad Faruk: Visualization, Investigation. Mendy Hatibie Oley and Maximillian Christian Oley: Supervision. Muhammad Faruk and Angelica Maurene Joicetine Wagiu: Software, Validation. Muhammad Faruk and Angelica Maurene Joicetine Wagiu: Writing-Reviewing and Editing. All authors read and approved the final manuscript.

Guarantor

Mendy Hatibie Oley and Maximillian Christian Oley

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Patient consent

Written informed consent was obtained from the patient for publication of this case series and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Declaration of competing interest

N/A

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