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Cryocarboxy Surgery: A New Addition to the Armamentarium for the Treatment of Congenital Melanocytic Nevi of the Face

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ABSTRACT

Background: *Congenital melanocytic nevi (CMN) of the face cause substantial psychological and cosmetic problems in affected patients. The treatment of giant congenital nevi has been a longstanding challenge, but currently, various treatment options, such as cryotherapy, chemical peeling, electrical cautery, laser therapy, and surgery, have been tried for the treatment of CMN. In this article, we present our experience and the outcomes of the use of controlled CO2 gas as a cryogen in the treatment of CMN.*

Methods: *This study included 28 patients with varying sizes of CMN seen from January 2014 to December 2017. Cryocarboxy surgery was performed in all cases. Results: The average evaluation score of our patients was excellent in 22 (78.6%) cases, good in 4 (14.3%) cases, satisfactory in two (7.1%) cases, and we had no poor results.*

Conclusions: *Cryocarboxy surgery is a good addition to the armamentarium for the treatment of CMN. CO2 is a cheap, non-explosive, and readily available gas.*

Level of Evidence: *Level IV, Therapeutic study.*

Keywords: Congenital melanocytic nevus; Giant nevus; Cryosurgery; Cryocarboxy; Hyperpigmentation

INTRODUCTION

The problems that congenital melanocytic nevi (CMN) cause to a patient exceed the cosmetic appearance and malignant transformations. CMN has direct and indirect effects on symptoms of depression and social anxiety in patients due to their loss of confidence and self-esteem [1]. Cryocarboxy surgery is the use of carbon dioxide gas as a cryogenic agent in the treatment of CMN.

The first reported medical application of controlled freezing for the destruction of tissues was described by Arnott (1883), an English physician who used a technique that reduced tissue temperature to approximately -20°C. Between 1819 and 1879, he published extensively on the use of cold therapy in medical treatment [2]. Solid carbon dioxide was used by Arnott (1851) as an effective method of cold therapy [2]. Pusey (1865) used solid carbon dioxide in the form of carbon dioxide snow to treat patients [3]. Campbell of Columbia University (USA) was the first to use liquefied gas in medicine. In 1899, he reported the successful use of liquefied air for the treatment of some dermatologic lesions, such as lupus erythaematosus, chancroid, nevi, warts, carbuncles, and epitheliomas [4]. However, because of its high combustibility, liquid oxygen has been forbidden for use as a cryogenic agent [5].

Because liquid nitrogen has a boiling temperature of -196°C, it has been used as a cryogenic agent. In 1950, Arlington started using liquid nitrogen in the USA by applying it with a saturated cotton swab. By 1969, Setrag and his clinical work had become one ofthe important references in the field of cold therapy. The term *"cryosurgery"* was also coined by him [6].

The work of physician Cooper and engineer Arnold is considered to be the cornerstone in the development of the modern era of cryosurgery. They invented a cryosurgical probe on which later types of probes were modelled [7].

Facial CMN is a pigmented lesion composed of nevus cells present at birth or immediately after birth. It is found in approximately 1% of neonates [8]. CMNs are classified according to their diameter. Lesions less than 1.5 cm in diameter are considered small-sized. Lesions from 1.5 to 20 cm are considered medium-sized. Lesions from 20 cm and more are considered giant melanocytic nevi [9].

Various treatment options have been used in dealing with CMN. These include chemical peeling, cryotherapy, electrical cautery, and laser. However, the results are not satisfactory [9].

CMV has potential to undergo malignant transformation, so surgery is still the preferred method of treatment of giant congenital nevi [10]. Some authors used Dermabrasion as a method of treatment [11]; however, the results are not satisfactory, and it is not currently recommended as an effective line of treatment [12]. Laser therapy may lighten the lesion, but the results are nevertheless not adequate [13,14].

In this study, we evaluated the effect of using controlled CO_2 gas as a cryogen in the treatment of CMN of the face.

MATERIAL AND METHODS

This study included 28 patients with varying sizes of CMN in the period from January 2014 to December 2017. The skin photo-type of the patients was III , IV and V, according to Fitzpatrick classification. The exclusion criteria included patients with cold urticaria, cryoglobulinemia, and cryofibrinogenemia. Eight of the patients included in this study underwent treatment with different types of lasers (Nd Yag laser, Alexandrite laser, and Q switched Ruby laser) at other centres with unsatisfactory results.

In this study, we used a machine called Cryo-S mini, SN-0776 BL. The working medium of the machine is N_2O and CO_2, and the working pressure of the machine varies between 3.5 and 5 MPa.

We used CO_2 as the working medium and not N_2O, as it is banned from use in Egypt by law. Prior to commencing treatment, the diagnosis was confirmed by histological biopsy, as the cases were referred to us from different centres after histological diagnosis as CMN.

Local anaesthetic cream was applied to the affected area 15 minutes before the procedure. The affected area to be treated was then disinfected with chlorhexidine 10% lotion, and K-Y Jelly was applied to increase the thermo-conduction of the skin. Afterwards, a metal probe with circulating carbon dioxide was applied over the lesion for 30 seconds and then withdrawn. A thaw period of approximately 30 seconds was allowed thereafter before a second freeze-thaw cycle was initiated on the same affected area. All patients were subjected to 2 freeze-thaw cycles. All patients were also instructed to apply fusidic acid cream as a local antibiotic with a daily dressing to guard against secondary infections until complete healing occurred. The average number of treatment sessions for our patients was 6 sessions (maximum of 9 and a minimum of 3). The period allowed between treatment sessions ranged from 2 to 4 weeks, according to the healing capacity of each patient. The sessions were stopped once the complete disappearance of the hyper pigmented colour of the nevi occurred.

Patients were then scheduled for follow-up every fortnight for the first two months and then monthly thereafter. At each visit, the patient was evaluated to assess the improvement in colour, texture, and size of the hyper pigmented area. Each of the three parameters was given a score on a 4-point scale: excellent, good, satisfactory, or poor. The score was evaluated by three independent plastic surgeons in the Department of Plastic Surgery at Tanta University (the evaluations are not shared in this study) and by patients' opinions in the case of adults or those of his/her parents/legal guardians in the case of minors. Then, the average score of the three parameters was calculated. The final score was recorded 6 months after the last treatment session. The average follow-up period in our study was one and half years, with the longest period being three years and the shortest period being one year.

RESULTS

The results are tabulated in Table 1.

Age	8 m-10 y	17 patients
	11-20 y	5 patients
	Older than 20 y	6 patients
Sex	Male	18 patients
	female	10 patients
Areas involved	Forehead	4 patients
	Cheek	11 patients
	Nose	4 patients
	eyelid	2 patients
	combined	7 patients
Size	≤ 2 m	6 patients
	2-20 cm	20 patients
	≥ 20 cm	2 patients
Number of sessions	03-May	10 patients
	06-Aug	17 patients
	more	1 patient
Previous treatments	No treatment	20 patients
	Laser treatment	8 patients
Aesthetic outcome	Excellent	22 patients
	Good	4 patients
	satisfactory	2 patients

Table 1: Patient age, sex, area affected, number of sessions, previous treatments, lesion size, and aesthetic outcome.

The average age of our patients was 12.5 years (the youngest was 8 months, and the eldest was 45 years old). Eighteen patients were females, and 10 were males. The size of the lesion was ≤ 2 cm in 6 cases, 2-20 in 20 cases and ≥ 20 cm in 2 cases.

After freezing, the tissue responded predictably within minutes. It initially responded with oedema and sometimes bullae and ulceration in the first few days. This usually lasted for 5 days. The wound began to dry within 5 to 10 days after freezing, and an eschar developed. The eschar was then allowed to dry and fall off spontaneously. In all cases, wounds were usually healed within two weeks. After complete healing, the affected area was fully covered with hypo pigmented skin in the part of the lesion, and the remaining areas showed a decrease in the degree of hyperpigmentation. The other remaining hyper pigmented areas mandated repeating of the sessions after observing that the effect of the previous session was resolved. Sessions were terminated following the complete elimination of the hyper pigmented colour of the lesion.

The average evaluation score of the size, texture, and colour of the hyperpigmented nevi in our patients was excellent in 22 (78.6%) cases, good in 4 (14.3%) cases, satisfactory in 2 (7.1%) cases, and we had no poor results.

Skin hypopigmentation at the lesion sites after completion of the sessions occurred in all patients (100%). Twenty-two patients regained normal skin colour within 3-6 months, 4 patients regained normal skin colour after one year, and 2 patients remained with partial hypopigmentation after 2.5 years. In our study, during the follow-up period, 4 patients showed regimentation of the treated parts of the lesions three months after stopping the treatment sessions. This mandated reinitiation of the treatment sessions until the black to brown colour of the affected area completely disappeared (Figures 1-4).

Figure 1: (a) Right lateral view of a 25-year-old male with cmn occupying most of the left cheek (approximately28 cm in diameter) (b) right lateral view of the same patient after two years follow up (c) right olique view of the same patient (d) right oblique view after two years of follow up showing excellent results.

Figure 2: (a) 8-year-old boy with cmn at the right ala of the nose, approximately 2 cm in diameter (b) before the third cryocarboxy session showing hypopigmentation but still some areas of hyperpigmentation (c) one-year follow-up after the last session (total 6 sessions) showing excellent results.

Figure 3: (a) Right lateral view of a child aged 8 months with cmn occupying the glabellar region, the upper right-hand side of the nose, the medial side of the lower eyelid and part of the cheek (approximately 10 cm in diameter) (b) 1-year follow:up after the last session (total of 5 sessions), showing excellent results (c) frontal view of the same patient, pre-cryocarboxy surgery (d) frontal view of the same patient one year after the last session, showing excellent results.

Figure 4: (a) lateral view of a 12-year-old female with cmn occupying the right ala of the nose and extending to the dorsum of the nose (approximately 8 cm in diameter) (b) lateral view of the same patient after one and a half years of follow:up after the last session (total 6 sessions), showing excellent results (c) frontal view of the same patient, pre-cryocarboxy surgery (d) frontal view of the same patient after one and a half years of follow-up after the last session, showing excellent.

No complications were observed in our cases during the follow: up period, including infection, bleeding, hypertrophy, atrophic scarring or deformity.

DISCUSSION

CMN usually present with an increased number of nevus cells. This may affect the epidermis, the dermis, or both. Hair follicles, sebaceous glands, sweat glands, nervous tissue, and blood vessels may be involved. In some cases, the nevus cells may be found in the subcutaneous tissue [15]. In CMN, the lesions may appear brown in some cases; in other cases, they may appear black. The more superficial the lesion, the more visible it is, and the lighter it is in colour. It may be modular or flat. The size of the lesion usually increases as the age of the patient increases, and the lesion may also change in character and colour [16].

The treatment options for CMN should take into account the fact that these types of lesions, especially those exceeding 20 cm in diameter, have the potential for malignant changes and present cosmetic problems for patients [17,18]. Therefore, the treatment should try to remove nevus cells and produce good cosmetic results. Trials to remove CMN have been performed in the neonatal period in some cases. Dermabrasion [19] and curettage [20] have been performed at this early age to remove as much as possible of the concentration of nevus cells. This technique helps reduce the number of nevus cells but fails to remove them completely.

CO_2 laser or Erbium-YAG laser therapy has been used to remove the nevi of the CMN from the epidermis to the upper dermis. However, it has been found that the laser effect may extend to affect the deep dermis, or even deeper, leaving a hypertrophic or a depressed scar

[21,22]. The recovery time after the application of laser therapy may be very long in some cases, and in other cases, the nevus cells may exist in the deep dermis, making them difficult to remove effectively [23].

Different types of Q-switched lasers are used in the treatment of CMN. The Q-switched Nd-YAG laser, the Q-switched ruby laser, and the Q-switched alexandrite laser, which all have pigmentation as their main target, have been used to remove CMN. However, recurrence is very common 24.

The long-pulsed Nd-YAG laser has been used for the treatment of CMN. Alshami (2013) reported the occurrence of atrophic and hypertrophic scars in 9.4% and 6.0% of the cases, respectively, as well as recurrence in 25 patients out of the 352 patients included in his study [25].

Expanded skin flaps or full:thickness skin grafts have been used effectively for the reconstruction of the nasal dorsum, periorbital region, and eyelid areas [26], but the cosmetic appearance was usually unsatisfactory.

Cryosurgery has been described in a plethora of studies. Some authors used liquid nitrogen as a cryogen, which can lower the temperature to -196°C [27,28]. In one study, nitrous oxide was used as a cryogen (-88°C) [29], and in another study, solid carbon dioxide was used as a cryogen [30]. In our study, carbon dioxide gas (-78°C) was used as the cryogen. We found that -78°C was sufficient to produce the desired results in the treatment of CMN.

The mean age of patients in our study was 12.5 years (8months-45years). Other studies reported the age of their patients to be 2 years [31] or 3 months [32].

The mean number of treatment sessions in our study was 6 [3,9]; the variability in the number of sessions in our patients was because the colour of the CMN differed from one patient to another, and deeper and therefore darker lesions needed more sessions than the superficial, lighter ones. Other studies reported performing an average of 5.8 sessions [30], 2.4 sessions [31] or 2.7 sessions [32].

The histological biopsy of CMN in this study showed that in ten cases, the lesions were superficial, and the melanocytes were confined to the superficial dermis. In this type of lesion, 3-5 sessions were sufficient to remove the CMN. Among the remaining 18 cases, 15 had lesions in the lower half of the reticular dermis, and the remaining three had lesions extending to the subcutaneous tissue. This type of deep lesion required more sessions (6-9 sessions) to eliminate the CMN. The same results were reported by Barnhill and Fleischli [33]. They reported that histologically, most CMNs involved the lower half of the reticular dermis (89%), and 11% infiltrated the subcutaneous tissue. The same observations were reported by Kono et al [34]. They found that the response to treatment of CMN to the combined normal-mode ruby laser (NMRL) and Q-switched ruby laser (QSRL) was correlated with the histologic depth of the nevo-melanocytic nests. The response was more significant in the superficial intradermal type than in the deeper lesions.

In our study, we used two thaw cycles at the same site. Using the two thaw cycles helped us to shorten the time of skin exposure during the sessions so that it would be superficial, and at the same time, we were certain that the superficial layers were affected. We found that this is better than one thaw cycle with a prolonged exposure time. This is because the longer time of cryo exposure may cause deeper layers to be affected, and this may result in such post:cryo exposure complications as hypertrophic scars. Most authors reporting the use of cryosurgery used 2 freeze-thaw cycles [28-30], while others used only one freeze-thaw cycle [32-35].

The average follow-up period in our study was one and half years (one to three years). The variability in the follow-up period of our patients was because the earlier the cases presented in our study, the longer the follow-up time has been. Other studies have reported different follow-up periods varying from 8 months [19] or 9 months [20] to 11 months [35]. The longer follow up period in our study gave us the chance to observe that there has been no recurrence in 24 cases. The remaining 4 cases that showed recurrence 3 months after the cessation of sessions showed no recurrence during the follow-up period, after performing

additional sessions until the hyperpigmentation completely disappeared.

Regarding the effect of using cryosurgery for the treatment of CMN during the follow: up period, our study showed complete disappearance of lesions in all patients, even in those that showed reappearance of the hyperpigmentation after the cessation of treatment sessions. In another work [27], partial improvement of the lesion in 71% of cases was reported, in addition to complete disappearance in the remaining cases. Another study [27] reported complete disappearance in 67% of cases, while the improvement was partial in the remaining cases.

The use of cryosurgery for the treatment of CMN has many advantages, including short recovery time, the absence of surgical scars, less pain due to the anaesthetic effect of freezing on nerve endings, and the avoidance of collagen destruction [27].

One of the unavoidable complications of cryosurgery is hypopigmentation, but studies and clinical experience have shown that repigmentation often occurs over the course of several months. The source of repigmentation is the undamaged melanocytes within hair follicles or the migration of melanocytes from the edge of the healthy skin that surround the lesion [27].

In the present study, post:cryosurgery hypopigmentation occurred in all cases (28 cases, 100%). However, in 22 cases (81.25%), hypopigmentation improved spontaneously within 6 months. Another four cases regained normal pigmentation after one year, and two cases regained most of the pigmentation after two and a half years. Those two cases were on the eyelids, and we think the explanation is that the eyelid has a very thin skin, which needed less exposure time during cryo sessions. Similar results were reported [30], who reported that in 20 cases of cutaneous haemangiomas treated with liquid nitrogen cryotherapy, repigmentation occurred in all cases within 4 months.

Using liquid nitrogen with a temperature of -196°C, Kagami et al. found it to cause selective necrosis of the vascular component and to preserve the surrounding and underlying tissue, which helped with the healing of the skin and repigmentation [30]. In our study, we did not use liquid nitrogen because we do not have the appropriate machine. Instead, we used the Cryoflex machine with CO_2 as the cryogenic agent with a temperature of approximately -78°C, which we found to be excellent, providing the opportunity for rapid re- epithelialization and the initiation of repigmentation from the surrounding skin and remaining adnexa.

CONCLUSION

In this article, we endeavoured to introduce a new line of treatment for giant CMN. We hope that the method of treatment presented in this study can solve the problem of CMN regardless of patient age and gender. In this study, we introduced a new technique that is inexpensive, non-explosive, and easily applicable. We hope that this technique will help surgeons avoid surgery, which can cause many complications.

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- This article was approved by Tanta University's Ethical Committee (2014/01/9).
- Written informed consent was obtained in all cases, either from patients or from their parents/legal guardians, if they were minors.

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