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Original Article

Sublimation of Benign Conjunctival Nevi Using Plasma-Assisted Noninvasive Surgery: A Clinical Case Series

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Abstract

Background: Conjunctival nevi (CN) are common benign ocular tumors. Given their low risk of malignancy, surgical removal of nevi is primarily requested by patients. Herein, we introduce Atmospheric Low-temperature Plasma (ALTP) as a novel noninvasive method for the removal of CN.

Methods: A clinical case series was conducted from 2020 to 2021 at the Vision Health Ophthalmic Center in Tehran, Iran. CN in one of the eyes of seven patients was treated. In all patients, the benignity of CN was confirmed by ocular oncologists. The white handpiece of the Plexr device, which generates plasma with the lowest output, was used to apply plasma spots on the nevi. In addition, the Ocular Surface Disease Index (OSDI) questionnaire was completed by all patients before and six months after the treatment.

Results: In all patients, the nevi outside the limbus area completely disappeared. The mean size of pre- and post-operative nevi was 3.89×11.7 and 0.54×1.69 mm, respectively. Results of the OSDI questionnaire showed significantly lower scores after the surgery in all patients.

Conclusion: The ALTP method is a simple, cost-effective, and office-based surgery to remove CN safely and effectively.

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Keywords ● Conjunctiva ● Nevus ● Plasma ● Sublimation ● Plasma-assisted noninvasive surgery

What's Known

- The results of animal studies showed that plasma-assisted noninvasive surgery (PANIS) is a safe method to treat various ocular disorders.
- The effectiveness of the method was shown in the treatment of conjunctival cysts, conjunctivochalasis, pinguecula, and dry eye with temporary punctal occlusion.

What's New

- The PANIS method is a simple, cost-effective, and office-based surgery to remove conjunctival nevi.
- The method removes or significantly reduces nevi without any risk of recurrence, side effects, or complications.

Introduction

Conjunctival lesions account for only 2.5% of all ocular lesions, of which more than 50% are classified as melanocytic.[1, 2] These lesions are categorized into two groups, namely nevi and other benign disorders (e.g., ephelis and lentigo), of which nevi are the most common.[3] Conjunctival nevi (CN) can be congenital with initial clinical presentations at birth, during the first six months of life, or develop in early adulthood. However, it can also occur in other age groups including older adults.[4] Hormonal changes during puberty are thought to increase cell proliferation and cause CN.[1] Demographic data indicate that CN is more common in Caucasians, and its incidence has no sex predilection. Generally, the color of nevi is brown but is unpigmented in approximately 5% of the cases. Interestingly, the color and size of benign nevi remain unchanged over time.[5]

CN are discrete, variably pigmented, slightly elevated, and

sessile lesions and may contain cysts without feeder vessels. The bulbar conjunctiva is the most common location of the lesion, however, although rare, it can be seen in the fornix and cornea. In about 90% of patients, CN is mainly located in the nasal and temporal quadrants.[6] Most conjunctival nevi are benign ocular tumors, and the risk of transformation into melanoma is less than 1%. However, despite such a low risk, regular checkups by an ophthalmologist are strongly recommended.[7-9] In general, surgery is not suggested when the clinical diagnosis of melanoma is not confirmed. However, some patients may opt for surgery because of fear of melanoma, lesion-induced ocular surface irritation, or cosmetic reasons.[6]

Given that a surgical approach is invasive and may involve complications and hospitalization, researchers investigated alternatives with lower risks and even noninvasive methods. In the late 90s, plasma (one of the four states of matter) technology was introduced as a minimally invasive treatment approach, particularly for wound healing and cancer treatment.[10] Advances in plasma therapy resulted in the development of various plasma-generating devices, such as handheld microsurgical instruments. Plasma is generated by ionizing the air between the instrument tip and the target tissue. The energy released during plasma generation sublimates the superficial tissue layer without affecting deeper layers or surrounding areas. Previous studies confirmed the safety of the Atmospheric Low-temperature Plasma (ALTP) method in rabbit eyes.[11, 12] Furthermore, the effectiveness and safety of Plasma-assisted Noninvasive Surgery (PANIS) for the treatment of ocular surface disorders were reported, e.g., in the cases of the conjunctival cyst,[13] conjunctivochalasis,[14] pingueculas,[15] and dry eye treatment with temporary punctal occlusion.[16] In line with these studies, herein, we introduce a novel noninvasive and safe plasma-based method for the removal of CN.

Patients and Methods

A clinical case series was conducted from 2020 to 2021 at the Vision Health Ophthalmic Center, Tehran, Iran. Patients aged 33-64 years suffering benign CN were eligible to participate, excluding those with the possibility of nevus malignancy. Accordingly, seven patients were included in the study. The patients were informed about the plasma treatment method, and written informed consent was obtained for their participation and publication of clinical findings and images. The study was performed according to the Helsinki Declaration and approved by the Ethics Committee of Semnan University of Medical Sciences (IR.SEMUMS.REC.1398.321).

One eye was treated in each of the seven patients (five women and two men). Six patients had a lesion in the left eye and one patient in the right eye. The position of CN was in the temporal quadrant (n=6) or nasal quadrant (n=1). In all patients, the benignity of CN (e.g., presence of cystic lesions, no bleeding, lack of arteries, etc.)[17, 18] was confirmed by ocular oncologists. In addition, no change in the color, shape, and size of nevi was detected. Slit lamp examination (magnification at 10×) was performed before and six months after the plasma treatment, and the size of nevi was measured. In addition, the Ocular Surface Disease Index (OSDI) questionnaire was completed by all patients before and six months after surgery to assess their satisfaction. The questionnaire assessed ocular irritations related to dry eye symptoms and their effect on vision-related function. The OSDI score represents the severity of dry eye disease, namely normal (0-12 points), mild (13-22 points), moderate (23-32 points), and severe (33-100 points).[19, 20] The treatment was performed using a plasma generator device (Plexr PLUS, GMV Srl, Rome, Italy). The device includes three color-coded handpieces, of which the white plasma-generating handpiece with the lowest output (V_{p-p}=500 V, power=0.7 W, frequency=75 kHz) was used.

Surgical Technique

The surgical method was optimized to sublimate the target tissue. As a topical anesthetic, tetracaine 0.5% (Sina Darou, Tehran, Iran) was used for three times every five minutes. The patients were positioned behind the slit lamp, and the white handpiece was used to apply plasma spots on the nevus surface. Since the procedure sublimates the target tissue only, the process continued until the pigmented nevus disappeared (appendix 1: Supplementary video). Precautions were taken to prevent conjunctival tears and avoid the corneal limbus area, as it contains stem cells. The surgeries were performed by the first author. After surgery, all patients had to instill ciprofloxacin (0.3%) eye drops (Sina Darou, Tehran, Iran) into the treated eye every six hours and betamethasone (0.1%) eye drops (Sina Darou, Tehran, Iran) every four hours for one week. The latter was tapered off over one month.

Results

As expected, the surgery did not cause any

Table 1: The results of pre- and post-operative nevi size, OSDI questionnaire scores, and characteristics of the patients

	Sex	Eye	Position	Age (years)	Pre-operation size (mm)	Post-operation size (mm)	Pre-operation OSDI	Post-operation OSDI
1	Female	OS	Temporal	33	5.4×12.16	1.5×3.6	34	8.2
2	Female	OS	Temporal	59	3.1×19.27	0.06×2.05	27.7	0
3	Female	OS	Nasal	64	6.7×9.48	0	42.4	5
4	Female	OS	Temporal	38	1.2×12.59	0.05×0.02	32.2	11
5	Male	OS	Temporal	33	5.04×10.76	1.2×2.07	51	15.4
6	Male	OD	Nasal	45	3.04×7.4	1.01×4.1	25.8	8.7
7	Female	OS	Temporal	48	2.8×6.54	0	22	0
Mean				45.7±11.3	(3.89±1.7)× (11.17±3.9)	(0.54±0.6)× (1.69±1.6)	33.58±9.3	6.9±5.2

OS: Oculus sinister, OD: Oculus dexter, OSDI: Ocular surface disease index

significant effect on the measured vision parameters. Table 1 shows a comparison between the size of nevi before and after the surgery for each patient. Similar comparisons for the shape and color of nevi are presented in figure 1. In all patients, the nevi outside the limbus area completely disappeared. However, as mentioned earlier, plasma was not applied to the limbus area, and thus the part of the nevi extending into this area remained unchanged (patients 1 and 3). The results of pre- and post-operative OSDI questionnaire showed significantly lower scores after the surgery in all patients (table 1). In terms of postoperative patient satisfaction, all participants confirmed that they would opt for the procedure on the other eye with CN and will recommend the surgery to other patients.

Discussion

The effectiveness of the PANIS method for the removal of CN was demonstrated. The results showed that the method eliminated or significantly reduced nevi without any risk of recurrence, side effects, or complications. Postoperative OSDI questionnaire scores were significantly reduced, indicating patients' high level of satisfaction with the outcome of the treatment.

CN are generally benign lesions with a very low risk of transformation into melanoma. In

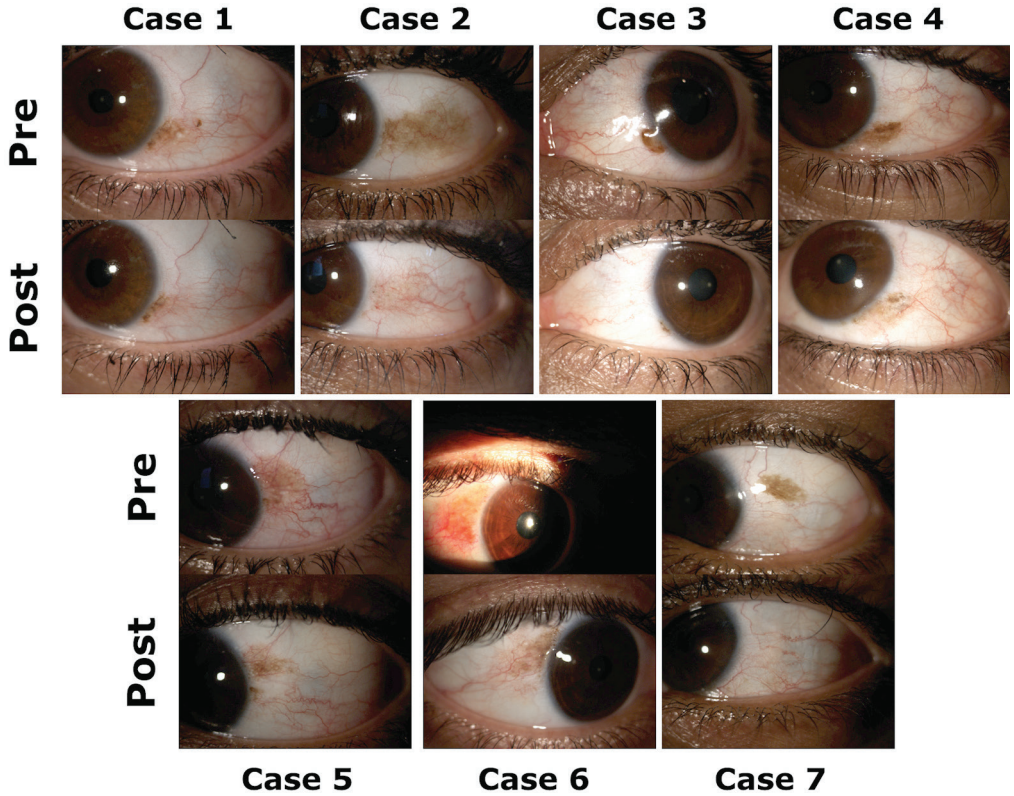

Figure 1: Significant postoperative improvement of the shape and color of conjunctival nevus was achieved in all patients. Nevi, in as far as they did not extend into the limbus area, completely disappeared in two patients (cases 3 and 7) and significantly reduced in size in other patients.

most cases, regular checkups of these lesions by an ophthalmologist can help early detection of potential eye disorders. Despite the low risk of malignancy, surgical removal of nevi is primarily requested by patients.[17, 21, 22] The main reason for such a decision varies from the fear of melanoma to lesion-induced ocular surface irritation and cosmetic reasons.[17] Demographic data indicate that about 40% of patients with CN opt for surgery to remove the lesion.[17, 21] In Saudi Arabia, for example, 38% of the patients opted for surgery for cosmetic reasons, whereas in Belgium it was only 12%. In both countries, surgery was indicated by an ophthalmologist in less than 8% of the cases.[17, 21] In our study, based on clinical evidence and expert opinion, the benignity of CN was confirmed in all the patients. Therefore, the request for surgery by our patients was either for cosmetic reasons or ocular surface irritation.

The choice of CN surgery is primarily motivated by cosmetic reasons and therefore has a direct impact on the patient's appearance and self-confidence, indicating the importance of further improvement of surgical techniques. One of the most common surgical methods is full-thickness excision of the entire lesion using a surgical microscope. This invasive method not only requires general anesthesia but also has the potential consequence of changing scleral exposure. In this method, the conjunctival lesion is removed together with a margin of healthy tissue and then sutured. Complications associated with this surgery include conjunctival edema and congestion.[23] Surgical excision and reconstruction via amniotic membrane transplantation is another invasive method used in patients with large conjunctival lesions.[24, 25] Despite the proven effectiveness of this method, the surgery entails various side effects. Argon laser photoablation for CN is an alternative treatment to invasive surgery. In this method, after topical ocular anesthesia with proparacaine, laser ablation is applied directly to the CN. In addition to its safety and effectiveness, the main advantages of this method over classical surgery are the absence of intraoperative hemorrhage, low recurrence rate, simplicity of the procedure, and good cosmetic results.[26, 27] However, some studies indicated that improper use of argon laser can cause postoperative complications such as ciliary body and choroidal detachment,[28] subretinal neovascularization,[29] and ocular inflammation.[30] Pattern scan laser (PASCAL) photocoagulation is another method to remove superficial CN.[31] It is claimed that this method does not have the disadvantages of the argon laser method. However, based on our literature survey, only one study reported its application. Hence, further studies are required.

In recent years, plasma has been introduced as a novel noninvasive method to treat various disorders. Previous studies reported the success of this method in removing benign nevi on different parts of the body and excess skin from the eyelid area.[32, 33] As mentioned earlier, PANIS is a safe and successful method to treat various eye diseases.[13-16] To the best of our knowledge, this is the first study that proposed a plasma-based technique to remove CN. The method included several advantages, such as simplicity of use, noninvasiveness, lower costs compared to other methods, and the possibility of office-based surgery. Unlike invasive surgical procedures, PANIS only required local anesthesia without the need for an incision, hemostasis, suture, and postoperative hospitalization. The results of our previously published animal studies showed that the application of plasma does not cause inflammation, necrosis, or any persistent histopathological changes in the scleral tissue. We also showed that the method only affects the superficial tissue layer without affecting the sclera and muscles.[11, 12] Moreover, the Plexr device sublimates the target tissue at temperatures slightly higher than room temperature (30-60 ˚C). Therefore, thermal injury to deeper layers and surrounding tissue did not occur.

Based on our results, ALTP applied by the white handpiece of the Plexr plasma generator successfully sublimated CN. However, plasma was not applied to the limbus area, as it contains stem cells. Therefore, the part of the nevi extending into this area remained unchanged. The result of the OSDI questionnaire showed the patients' postoperative satisfaction. This could be due to a decrease in corneal elevation resulting in a better distribution of the tear film on the ocular surface. Given the small number of patients in the present study, for more reliable data, it is suggested to perform the PANIS method with a larger number of patients and long-term follow-up assessment.

Conclusion

The PANIS method is a simple, noninvasive, and office-based surgery to remove the CN safely and effectively. Furthermore, ophthalmologists can easily acquire the required surgical skills. PANIS is an appropriate alternative to other methods for CN treatment.

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Authors' Contribution

F.N: Study design and supervision, data analysis, and performing the surgeries; K.J: Study design; NSN: Research conceptualization and data curation; Sh.E: Data gathering, data analysis; All authors actively participated in drafting, reviewing, and finalizing the manuscript. All authors have read and approved the final manuscript 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.

Conflict of Interests: None declared.

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