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Clinical and dermoscopic evaluation of the efficacy of 1064 nm Q-switched Nd: YAG laser treatment of Nevus of Ota

Ota Nevus'un 1064 nm Q düğmeli Nd: YAG lazer tedavisinin etkinliğinin klinik ve dermoskopik değerlendirmesi

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Abstract

Background and Design: Nevus of Ota is a hamartoma that present since birth or within the first year of life. Most patients suffer from depression, and laser has become the first-line treatment for this difficult-to-treat condition. There are hardly any studies regarding dermoscopic changes of the Nevus of Ota treated with Nd: YAG laser from Eastern India. This study aimed to evaluate the effectiveness, safety and side effects of 1064 nm Q-button Nd:YAG laser treatment together with dermoscopic changes in patients with Nevus of Ota.
Materials and Methods: This was a prospective observational descriptive study conducted for a period of one year in a tertiary care hospital. We included clinically diagnosed Nevus of Ota patients aged over 18 years. Exclusion criteria were acute infection or chronic diseases, pregnancy or lactation, and history of any treatment with laser or chemo-peeling. Thirty-two cases were included in the study. Photographs and dermoscopic examinations were done at every session for an average of six sessions at an interval of four to six weeks. The response to treatment was graded based on the physician's global assessment scale, and appropriate statistical tests were done using SPSS 18.
Results: Very good results with >75% improvement were seen in 12.5% of patients, and a good response i.e., 50-74% was seen in 59.37% of patients. An average response (25-49%) was seen in 18.75% of patients, while a poor response with <25% improvement was found in 9.37% of patients. After completion of laser sessions, dermoscopy was done again to compare changes, but there were no significant changes except a slight lightening of the brown-grey patchy distribution and fewer brown-grey dots. There were no changes in terminal hair, serpentine vessels, and scaling.
Conclusion: Most patients noted satisfying improvement after an average of six sessions of Nd: YAG laser therapy. Studies with a greater number of sessions can be conducted, and they may yield more improvement.
Keywords: Nevus of Ota, Nd: YAG laser, dermoscopy

Öz

Amaç: Ota Nevusu, doğumdan itibaren veya yaşamın ilk yılında mevcut olan bir hamartomdur. Hastaların çoğu depresyondan muzdariptir ve lazer artık bu tedavisi zor durum için birinci basamak tedavi haline gelmiştir. Doğu Hindistan'dan Nd: YAG lazer ile tedavi edilen Ota Nevus'un dermoskopik değişiklikleri ile ilgili neredeyse hiç çalışma yoktur. Bu çalışmada, Ota Nevus'lu olgularda 1064 nm Q düğmeli Nd: YAG lazer tedavisinin etkinlik, güvenlik ve yan etkilerinin, dermoskopik değişikliklerle birlikte değerlendirilmesi amaçlanmıştır.
Gereç ve Yöntem: Bu, üçüncü basamak bir hastanede bir yıl boyunca yürütülen prospektif, gözlemsel tanımlayıcı bir çalışmadır. Çalışmaya klinik olarak 18 yaş üstü Ota Nevus hastalarını dahil ettik. Hariç tutma kriterleri, akut enfeksiyon veya kronik hastalıklar, gebelik veya emzirme ve geçmişte lazer veya kimyasal soyma ile herhangi bir tedavi öyküsü idi. Çalışmaya 32 olgu dahil edildi. Dört ila 6 hafta arayla ortalama altı seansta her seansta fotoğraf ve dermoskopik inceleme yapıldı. Tedavi yanıtı hekimin genel değerlendirme ölçeğine göre derecelendirildi ve SPSS18 kullanılarak uygun istatistiksel testler yapıldı.
Bulgular: %12,5 hastada >%75 iyileşme ile çok iyi yanıt ve %59,37 hastada iyi yanıt (%50-74) görüldü. %18,75 hastada ortalama yanıt (%25-49) görülürken, %9,37 hastada <%25 iyileşme ile kötü yanıt bulundu. Lazer seanslarının tamamlanmasından sonra, değişiklikleri karşılaştırmak

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için tekrar dermoskopi yapıldı, ancak kahverengi gri yamalı dağılımın hafifçe açılması ve daha az kahverengi gri nokta dışında önemli bir değişiklik olmadı. Terminal kıllarda, serpantin damarlarda ve pullanmada herhangi bir değişiklik saptanmadı.
Sonuç: Çoğu hasta, ortalama altı seanslık Nd: YAG lazer tedavisinden sonra tatmin edici bir iyileşme kaydetti. Daha fazla lazer seansları uygulayarak yapılacak çalışmalarla daha fazla iyileşme sağlanabileceği kanaatindeyiz.
Anahtar Kelimeler: Nevus of Ota, Nd: YAG lazer, dermoskopi

Introduction

Nevus of Ota (oculodermal melanocytosis) is a dermal melanocytic hamartoma that presents at birth or 1st year of life. A second peak occurs during puberty[1]. It presents as extensive bluish, patchy, dermal melanocytosis that affects the sclera and skin adjacent to the eye, distributed along the first and second branches of the trigeminal nerve. It usually presents in Asians with an incidence between 0.014% and 0.034%. It is more common in darkly pigmented individuals with skin types 3 and 4, and females are more commonly affected, with a male-to-female ratio of 1:4. GNAQ mutations have been reported in 6% of cases[1]. It is rarely associated with Nevus of Ito, Mongolian spots, Klippel Trenaunay, and Sturge Weber syndromes[1].

Tanino has classified Nevus of Ota according to its severity and distribution into 4 types.

Type 1:

A. Mild orbital type: Distribution over the upper and lower eyelids, periocular, and temple regions.

B. Mild zygomatic type: Pigmentation in the infrapalpebral fold, nasolabial fold and the zygomatic region.

C. Mild forehead type: Involvement of the forehead alone.

D. Involvement of ala nasi alone.

Type 2: Distribution over the upper and lower eyelids, periocular, zygomatic, cheek, and temple regions.

Type 3: Involves the scalp, forehead, eyebrow, and nose.

Type 4: Bilateral type[2].

Before the introduction of the laser, it was very difficult to treat Nevus of Ota. Treatment modalities included depigmenting creams, cryotherapy, dermabrasion, surgical excision, and cosmetic camouflage. Surgical treatment had the risk of hyperpigmentation and scarring[2]. Q-switched laser, where Q means Quality and Switching is a means of shuttering the laser output so that it is delivered in extremely short pulses of high-intensity radiation[3]. Q-switched Nd: YAG laser (1064 nm) emits light that can penetrate 2-3 mm deep into dermis targeting melanocytes and has thus, proven suitable for removal of deeper dermal pigment[4]. Q-switched Nd: YAG 1064 nm is best suited for the Indian skin type as this wavelength has a deeper penetration in the dermis and minimizes the risk of epidermal injury. A larger spot size causes deeper penetration and minimizes splatter and change in texture[5].

As Nevus of Ota commonly occurs on the face and affects young people, it causes severe distress and depression. The advent of Q-switched Nd: YAG (1064 nm) has brought a huge change in the treatment protocol. There are hardly any studies to see dermoscopic changes following the treatment of Nevus of Ota with Nd: YAG laser from Eastern India, hence such a study was conducted.

This study aimed to determine the efficacy, safety, and side effects of 1064 nm Q-switched Nd: YAG laser treatment in Nevus of Ota patients. We also wanted to compare dermoscopic findings in Nevus of Ota patients before and after treatment.

Materials and Methods

This was an institution-based prospective non-randomized controlled study conducted for a period of 12 months in a tertiary care hospital. A total of 32 patients were taken as samples who were clinically diagnosed as Nevus of Ota. Patients over 18 years of age who were willing to treat the disease with laser were included. Patients with any active or chronic infection, pregnant or lactating mothers, or any history of laser treatment or chemo-peeling were excluded from the study. The NRS Medical College and Hospital Institutional Ethical Committee clearance was obtained before the study (approval number: 454, date: 06.02.2019). Informed consent was obtained.

At the first visit, detailed history, clinical examination, photographs, and dermoscopy were done and recorded in a predesigned proforma. "Progressive" was defined as an increase in the size of the lesion, darkening of the color, and involvement of new areas/mucosa during the last 1 year and vice versa for "non-progressive." Before the first session, patients were advised to use sunscreen at least 15 days prior and to continue it throughout the laser sessions. Hydroquinone or azelaic acid cream was given to patients having tanning. Topical anesthesia with a eutectic mixture of lignocaine and prilocaine was used almost 1.5 hours before occlusion. Both the patient and attending doctors wore proper protective measures for the eyes. The area within the orbital area was not treated as it was covered by an eye shield. For all patients, the laser was started with 7 J/cm2 (Harmony XL, Alma Laser, Israel), which was further increased to 9 J/cm2 gradually with each sitting with a spot size of 5 mm under topical anesthesia. The entire lesion was covered with a single pass. An interval of one month on average was kept for each patient. Any immediate side effects were noted. Objective clinical assessments were done by two dermatologists who evaluated the photographs and dermoscopy taken at the first and last visit, and the results were classified as excellent/very good (>75% improvement), good (74%-50 improvement), fair/average (49-25% improvement), poor (<25% improvement).

Statistical analysis

Data was analyzed with an appropriate statistical method using SPSS18.

Results

During the study period from March 2019 to February 2020, 32 clinically confirmed patients of Nevus of Ota were enlisted. The prevalence of Nevus of Ota was 0.015% among all the patients attending dermatology outpatient department during the study period.

In the study, female preponderance was found with 30 females (93.75%). The Female to male ratio was 15:1. Tanino type 2 was the most common presentation, both in men (100%) and women (73.3%). The second most common type was Tanino type 1 (16.6%), followed by type 4 (6.66%) and type 3 (3.33%).

The age of onset of Nevus of Ota ranged from birth to 26 years, with a mean age of onset being 1.812±1.029 years. The median age of onset was one year [95% confidence interval: 1.44 to 2.18]. Maximum patients i.e., 56.25% were in the age group of less than one year.

A progressive nature was found in 17 patients. When the age of onset was above one year, the progressive and non-progressive natures were equally distributed. Eye involvement was higher in patients with an onset of less than one year.

Type 2 was the most common Tanino finding in all age groups with 58.3% in less than one year, followed by 25% in 11-20 years, 12.5% in 2-10 years, and 4.1% in >20 years age group (p=0.021).

A family history of Nevus of Ota was not found in any of the patients. No history was found for any developmental delay, history of seizures, or problems with vision. Few patients had used a triple regimen (containing hydroquinone, retinoid, and steroid) for Nevus of Ota earlier without any response.

In the study, we found mostly Fitzpatrick skin types 4 and 5. The maximum number of patients had skin type 4 i.e., 23 (71.87%), while 9 (28.12%) had skin type 5.

The most common type of presentation was Tanino type 2 (75%); type 4 (i.e., bilateral type) was found in only 6.25% of cases, while the lowest presentation was type 3 (3.125%). The most common color of Nevus of Ota was slate gray color (91%) followed by deep brown (6%) and the rest light brown.

Eye involvement was seen in 18 patients (56.25%). Two (6.25%) patients had another nevus. One of them had Becker's nevus, while the other one had a port wine stain.

Dermoscopy findings

Out of 32 patients, all had a brown-gray structureless area with a patchy distribution (100%) (Figure 1).

Scattered brown-gray dots were seen in 28 patients and terminal hair was found in seven patients.

Perifollicular hypopigmentation was found in nine patients, serpentine vessels were seen in seven patients, and mild scaling was found in five patients (Image 1).

After completion of laser sessions, dermoscopy was done again, but there was no significant change except a slight lightening of the brown-grey patchy distribution and fewer brown-grey dots. There were no changes in terminal hair, serpentine vessels, and scaling (Image 2).

Improvement of patients after laser treatment

The rate of improvement of the lesion of Nevus of Ota was decided based on photographs taken before the start of treatment and after the end of treatment. Most of the patients had significant improvement. Very good results with >75% improvement (Image 3, 4) were seen in 12.5% of patients, and good response i.e., 50-74% was seen in 59.37% of patients. Average response (25-49%) was seen in 18.75% of patients, while a poor response with <25% improvement was found in 9.37% of patients only (Image 5, 6).

Very good response (75%) was seen in patients with an age of onset between 1-10 years. Whereas good response with 50-74% improvement was seen in patients with an age of onset less than one year (68.4%). Poor response <25% improvement was seen in the onset less than one-year group (66.6%) (p=0.018) (Table 1).

The mean number of sessions done was 6.5±1.319. In patients with six or less than six sessions, a very good response was not found in any patient. Good response was seen in 35.7% of patients. In patients with >6 sessions, a very good response was seen in 21.05% and a poor response in 5.26% (p=0.0013) (Figure 2). Twenty-one patients (65.6%) had more than 50 percent improvement with a total cumulative dose of more than 50 J/cm^2 (Table 2).

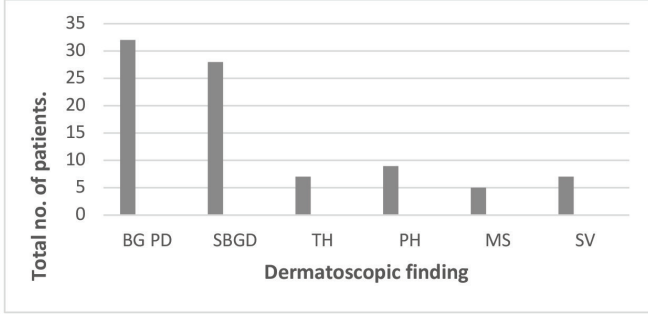

Figure 1. Dermoscopy findings

BG PD: Brown and gray structureless areas with patchy distribution, SBGD: Scattered brown-gray dots, TH: Terminal hair, PH: Perifollicular hypopigmentation, MS: Mild scaling, SV: Serpentine vessels

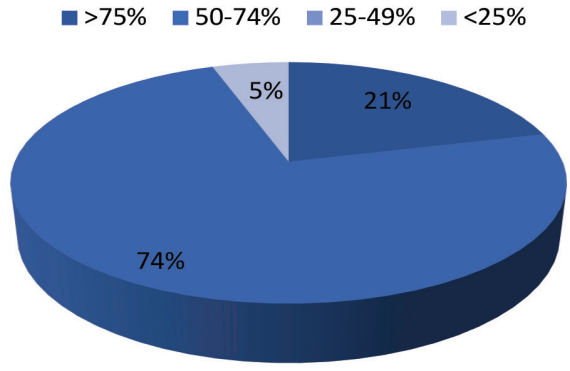

Figure 2. Improvement in patients with >6 sessions of laser

Table 1. Age of onset and response to laser treatment (p=0.018)

Age of onset	>75% improvement	50-74% improvement	25-49% improvement	<25% improvement
<1 year	0	13 (40.6%)	3 (9.3%)	2 (6.25%)
1-10 years	3 (9.3%)	0	1 (3.1%)	0
11-20 years	1 (3.1%)	5 (15.6%)	1 (3.1%)	1 (3.1%)
>20 years	0	1 (3.1%)	1 (3.1%)	0
(n=32)	4 (12.5%)	19 (59.4%)	6 (18.8%)	3 (9.4%)

In skin type 4, a very good response was seen in 17.3 % of patients, while in skin type 5, there were none. In type 4, 60.86% of patients had 50-74% improvement. In skin type 5, 55.55% of patients had a good response while 44.44% had an average response (p=0.045).

In type 1 Tanino presentation most of the patients (80%) had a good response to treatment.

For type 2 Tanino presentations, 15.7% had a very good response, while 47.3% had a good response. The average response was seen in 21.05% and the rest had a poor response.

Type 3 Tanino presentation was seen only in one patient with 50-74% improvement.

Type 4 presentation was found in two patients, one of the patients had >75% improvement that had undergone eight sessions, while the other had a 25-49% response after six laser treatments (p=0.624).

Image 1. Dermoscopic image before laser showed diffuse patchy grey pigmentation (Black asterisk)

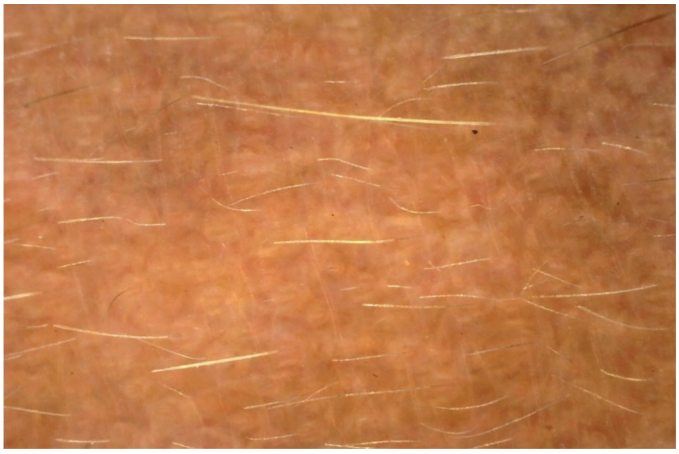

Image 2. Dermoscopic image after 6 sessions of laser treatment showed reduced patchy grey-brown pigmentation

We summarized the characteristics of patients with >75% improvement. Patients having >75% improvement had a greater number of laser sessions with skin phototype 4. Eye lesion was seen in only one patient who also had bilateral involvement of Nevus of Ota.

Complications

Immediate complications were seen in 10 out of 32 patients.

Three patients had only erythema, three had both erythema and a burning sensation while the remaining four had only a burning sensation.

A few patients complained of increased pigmentation after a few sessions of laser, though we did not observe the same upon examining the patients and comparing them with previous pictures. No other late complications such as hypopigmentation or atrophy were observed in any patient.

Discussion

The prevalence of nevus of Ota in our hospital outdoor attendees was around 0.015, which is almost the same as other studies (0.014-0.034)[1,3]. Among the 32 patients of Nevus of Ota, 30 were female and the male-to-female ratio was found to be 1:15. However, one study conducted on an Asian population showed a male to female ratio as 1:4[2]. The sex ratio difference may be due to the rarity of the disease and patients coming for their cosmetic purposes. Our study showed the mean age of onset to be 1.812 years. In our study, 56.25% of patients had their onset before one year of age, while 25% developed

Image 3. P1 before Nd: YAG laser

Table 2. Rate of improvement and total cumulative frequency used (p=0.001)

Total cumulative dose (J/cm²)	>75% improvement	50-74% improvement	25-49% improvement	<25% improvement	Total (%)
>50 J/cm²	4 (12.5%)	17 (53.1%)	0	0	21 (65.6%)
<50 J/cm²	0	2 (6.2%)	6 (18.8%)	3 (9.4%)	11 (35.4%)
	4 (12.5%)	19 (59.4%)	6 (18.8%)	3 (9.4%)	32

after 10 years of age, mainly during puberty. This is consistent with a study that showed 60% of patients developed within one year of age[6]. They mentioned two peaks of onset: one at birth and another during the second decade of life.

In our study, 75% of patients belonged to Tanino type 2, followed by Tanino type 1 (15.6%). In a study from Mangalore in 2008, Tanino type 2 was seen in 33.3%, while type 3 and 4 each were 20%[2]. Teekhasaenee et al.[7] reported that 27% each belonged to types 2 and 3. Thirty patients had unilateral involvement, while two patients had bilateral involvement. Bilateral involvement is rare, with only 6.25%. A large study of 240 Nevus of Ota patients from Tokyo reported that only 4% had bilateral involvement[8]. Eye involvement was seen in 18 patients (56.25%) in our study. In our study 18 (56.25%) patients had both dermal and ocular involvement, while 14 (43.75%) patients had only dermal involvement. In another study, 60% had both dermal and ocular involvement, and 40% had only dermal involvement, similar to our study[2]. We did not observe any cases of glaucoma in our study which have been reported by Khawly et al.[9] We did not find any palatal involvement in our study, while Rathi[10] have reported palatal involvement. Nevus of Ota was found along with a port-wine stain in one patient and with Becker's nevus in another. Reinke et al.[11] have reported a case of Nevus of Ota with hemangioma and Takayasu arteritis.

In a study by Ömer Faruk Elmas, the most common dermoscopic finding was a brown and gray structureless area with patchy distribution observed in all cases and brown dots in a few cases. Terminal hair and serpentine vessels were seen in a few cases[12]. In our study, all patients had a structureless brown-gray area, and most of the patients had brown dots. A few patients had terminal hair, mild scaling, perifollicular hypopigmentation, and serpentine vessels.

In our study, very good results (>75%) were seen in 12.5% of patients and a good response (50-74%) was seen in 59.37% of patients. An average response was seen in 18.75% of patients, while a poor response (<25%) was found in 9.37% of patients. A direct proportion was found between the total number of sessions and the rate of improvement. We did not find any significant relationship in response to laser therapy with respect to Fitzpatrick skin type, involvement of eyes, and bilateral distribution. One earlier study observed that 66% of patients had >60% improvement[13]. The therapeutic response was directly proportional to the number of treatment sessions. Another study done on 50 Indian patients showed that there was a total improvement in 8%, marked improvement in 22%, moderate improvement in 38%, and 32% of patients reported less than 25% improvement[3] (Table 3).

One recent case report in Asian patients suggested that two sessions of the Q-switched laser performed one year apart had an excellent result with a 95% clinical response without any side effects. Their study showed that Q-switched Nd: YAG laser is an effective treatment for Nevus of Ota, and a large number of sessions is not essential for an excellent response[14]. However, we observed that a greater number of sessions gave better results.

Image 4. P1 after 6 sessions of Nd: YAG laser

Image 5. P2 before Nd: YAG laser

Image 6. P2 after 6 sessions of Nd: YAG laser

Table 3. Comparison of different studies on the effectiveness of Nd: YAG laser

Sl no	Study on effectiveness of NdYAG laser (n)	Excellent improvement (%)	Marked improvement (%)	Moderate improvement (%)	Mild improvement (%)
1	Our study (32)	12.5	59.37	18.75	9.37
2	Kar et al.[3] (50)	8	22	38	32
3	Sharma et al.[5] (25)	60		32	8
4	Aurangabadkar[13] (50)	66		33	-

Study Limitations

Limitations of our study include a small sample size and being a single-center study. As the study period was short, follow-up could not be done for recurrence for a long duration. Our findings can be extrapolated to a larger population with a greater number of sessions to validate our findings.

Conclusion

Most of the patients had a satisfying response with an average number of six sessions of Q-switched Nd: YAG laser. There were no significant side effects except for a slight lightening of the brown-grey patchy distribution and fewer brown-grey dots in dermoscopy after laser sessions.

Ethics

Ethics Committee Approval: The NRS Medical College and Hospital Institutional Ethical Committee clearance was obtained before the study (approval number: 454, date: 06.02.2019).
Informed Consent: It was obtained.
Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.B., C.T.D., S.D., A.A., Concept: S.B., C.T.D., S.D., A.A., Design: S.B., C.T.D., S.D., A.A., Data Collection or Processing: S.B., C.T.D., S.D., A.A., Analysis or Interpretation: S.B., C.T.D., S.D., A.A., Literature Search: S.B., C.T.D., S.D., A.A., Writing: S.B., C.T.D., S.D., A.A.
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