Bilateral Nevus of Ota Treated with Combination of CO_2 Fractional Laser and 1064 nm Nd:YAG Laser

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ABSTRACT
Background: Ota's nevus (nevus fuscocaeruleus ophthalmomaxillaris) was first described by Ota in 1939. It is characterized by blue–black or gray–brown dermal melanocytic pigmentation and typically occurs in areas innervated by the first and second branches of the trigeminal nerve. Mucosal pigmentation may occur involving conjunctiva, sclera, and tympanic membrane (oculodermal melanocytosis), or other sites. **Purpose:** Describe the clinical manifestation and therapy of bilateral nevus of Ota. **Case**: A 20-year-old female patient, complaint about dark patches in both of her cheek and forehead since birth. Histopathology has not been done because patient refused to do the biopsy. Diagnosis of bilateral nevus of Ota is made based on anamnesis and clinical manifestations. **Discussion:** Pasien has undergo Nd:YAG laser session for Ota's nevus and the result was not satisfactory. Now patient was given combination laser of CO_2 fractional laser and 1064 nm Nd:YAG laser for 4 sessions with 3 months interval. After four laser sessions, there has been an improvement in the lesions as the lesions is getting lighter. The purpose of CO_2 fractional laser is to increase light delivery into the tissue and for extruding material out of the skin. This laser combination aimed to increase the ability to remove pigment as an alternative method without inducing a systemic allergic reaction. **Conclusion:** Nevus of Ota is diagnosed based on clinical finding. Combination therapy of CO_2 fractional laser and1064 nm Nd:YAG is the mode of choice because of excellent results.

Keywords: bilateral nevus of Ota, fractional CO_2 laser, 1064 nm Nd:YAG laser.

ABSTRAK
Latar Belakang: Nevus Ota (*nevus fuscocaeruleus ophtalmomaxillaris*) pertama kali dideskripsikan oleh Ota pada tahun 1939. Manifestasi klinis berupa pigmentasi melanositik dermal biru-kehitaman atau abu-kecoklatan dan biasanya terjadi pada area yang diinervasi oleh cabang pertama dan cabang kedua nervus trigeminus. Pigmentasi pada area mukosa dapat melibatkan konjungtiva, sklera, dan membran timpani (melanositosis okulodermal), atau tempat lainnya.**Tujuan:** Menjelaskan gambaran klinis dan penatalaksanaan nevus Ota bilateral. **Kasus**: Perempuan, berusia 20 tahun, mengeluh bercak gelap pada area dahi dan pipi sejak lahir. Pemeriksaan histopatologi belum dilakukan karena pasien menolak untuk dilakukan biopsi. Penegakan diagnosis dari nevus Ota bilateral berdasarkan anamnesis dan manifestasi klinis. **Diskusi:** Pasien sudah pernah menjalani terapi laser Nd:YAG untuk nevus Ota dan tidak memberikan hasil yang memuaskan. Sekarang pasien sudah menjalani terapi kombinasi antara laser fraksional CO_2 dan laser Nd:YAG 1064 nm sebanyak 4 sesi. Terapi laser fraksional CO_2 bertujuan untuk meningkatkan penetrasi sinar ke dalam jaringan dan mengeluarkan material tertentu keluar dari kulit, sedangkan tujuan kombinasi terapi laser fraksional CO_2 dan Nd:Yag 1064 nm adalah untuk meningkatkan kemampuan menghilangkan pigmen sebagai metode alternatif tanpa memicu reaksi alergi sistemik. **Simpulan:** Diagnosis nevus Ota ditegakkan berdasarkan pemeriksaan klinis. Terapi kombinasi antara laser fraksional CO_2 dan laser Nd:YAG menjadi pilihan karena memberikan hasil yang baik.

Kata kunci : bilateral nevus Ota, laser fraksional CO_2, laser Nd:YAG 1064 nm.

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INTRODUCTION

Ota's nevus (nevus fuscocaeruleus ophthalmomaxillaris) was first described by Ota in 1939.[1,2] It is characterized by blue–black or gray–brown dermal melanocytic pigmentation and typically occurs in areas innervated by the first and second branches of the trigeminal nerve.[1] Mucosal pigmentation may occur involving conjunctiva, sclera, and tympanic membrane (oculodermal melanocytosis), or other sites.[1]

Nevus of Ota were subclassified as mild (type 1), moderate (type 2), intensive (type 3), and bilateral (type 4).[1] Bilateral cases should be differentiated from

Hori nevus, which is acquired, does not manifest mucosal involvement and less pigmented.[1]

Nevus of Ota is the commonest in Asian patients and affects between 0.014% to 0.034% of the Asian population.[2] The age of onset is bimodal, with larger peak at birth or soon after and a smaller peak at adolescence.[2] Nearly all lesions appear by 30 years of age.[2] The condition is more common in females, with a male:female ratio of 1:4.8.[2]

Cosmetic and psychological disturbances common concerns to affected individuals who may delay treatment because of doubt about final satisfactory fading.[2] Treatment options were limited prior to the advent of lasers.[2] Q-switched Nd:YAG lasers have been used successfully to treat nevus of Ota lesions.[2]

We report a case of bilateral nevus of Ota in a 20-year-old female patient, dark patches in both of her cheek and forehead since birth, who got clinical improvement by combination of CO_2 fractional laser and Nd:YAG laser. This report discusses about the clinical presentation, diagnosis, and treatment.

CASE REPORT

A 20-years-old female, came to Dermatology and Venerology Outpatient Clinic of Dr. Soetomo General Hospital Surabaya on June 12th 2014 with main complaint dark patches in both of her cheek and forehead since birth. The dark patches was getting wider along with patient's growth. She never complained about itchy, numbness or pain sensation on her cheek. She had no complained about visual disturbances or dizzy.

There were no history of food and drug allergy in the patient and her family, history of atopi in the patient and her family, and none of the family member has the same complaint. She had history of applying topical medication (multiple cream from beauty clinic) and already had Nd:YAG laser treatment before in private beauty clinic for 4 sessions but the complaint still persist.

General physical examination was compos mentis, look well with no sign of anemic, icterus, cyanotic or respiratory distress. The blood pressure was 110/70, pulse rate was 96 times per minute, respiratory rate 20 times per minute and body temperature was 36,3 °C. No abnormalities found on thorax and abdominal examination. No swelling on his extremity.

The dermatological examination on forehead, temporal, and cheek region revealed there were hyperpigmented macule, sharply marginated, bluish in color, vary in size and from okuli dextra region there was an episcleral pigmentation.

Figure 1. Hyperpigmented macule, sharply marginated, bluish in color, vary in size in cheek region and episcleral pigmentation in okuli dextra.

Figure 2. Hyperpigmented macule, sharply marginated, bluish in color, vary in size in forehead and temporal region.

Laboratory result revealed the complete blood count all within normal limit. The histology examination has not been done yet because patient still refuse to do the biopsy. Patient has been consulted to ophtalmologist and the result is all within normal limit. The patient's visus is normal (6/6) and the pigmentation limited in the right sclera region. The tonometry and funduscopy examination also revealed normal result and no sign of glaukoma in this patient.

The diagnosis of this patient is Nevus of Ota. The differential diagnosis of nevus of Ota include phakomatosis pigmentovascularis, acquired bilateral nevus of Ota-like macules (ABNOM), nevus of Ito

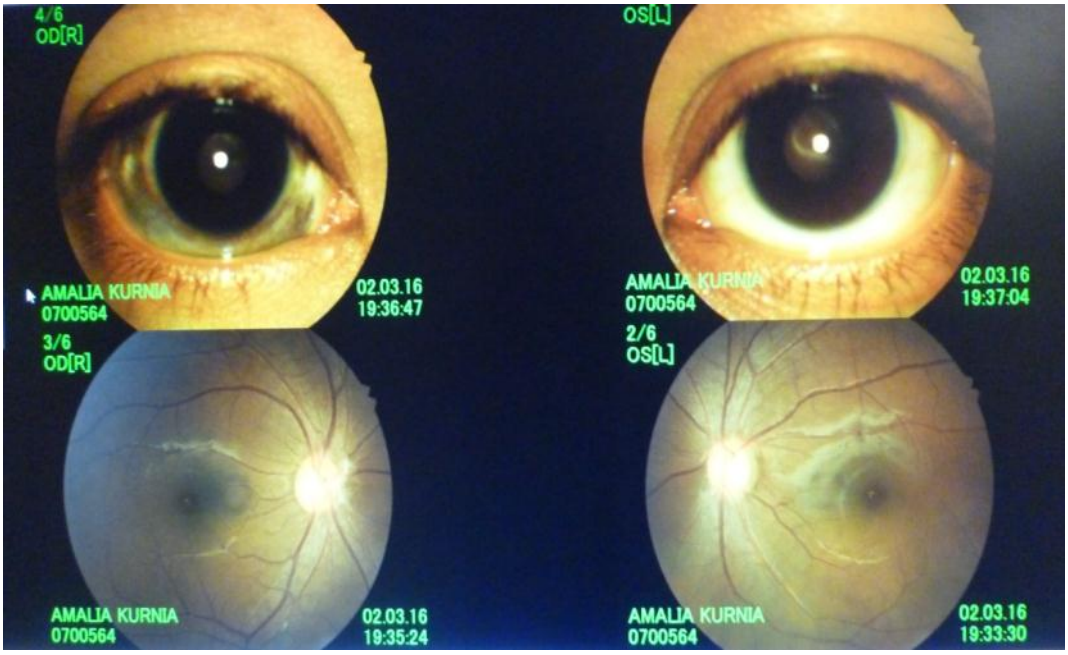

Figure 3. Result of eye examination. The pigmentation limited in the right sclera and the funduscopy showed no abnormalities.

The patient was treated with CO_2 fractional laser and Nd:YAG laser 1064 nm for 4 sessions and the lesion became lighter. The progression and improvement of the patient can be seen in the figures and table below:

Figure 4. 1st Laser session: 1 day after laser

Figure 5. 2nd Laser session: before laser

Figure 6. 3rd Laser session: 3 days after laser

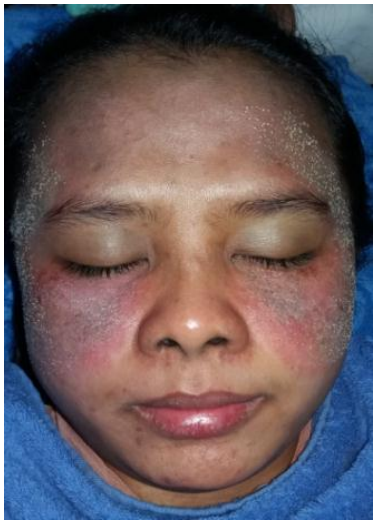

Figure 7. 4th Laser Session: 10 minutes after laser

Table 1. Course of the disease

	April 15th 2015	May 20th 2015	August 19th 2015	Dec 04th 2015	March 04th 2016
Subjective:					
Dark patches	+++	+++	++	++	+
Objective:					
Forehead, temporal, cheek region:					
Hyperpigmented macule	+++	+++	++	++	+
Okuli Dextra:					
Episcleral pigmentation	+	+	+	+	+
Assessment:	Bilateral Ota's Nevus	Bilateral Ota's Nevus	Bilateral Ota's Nevus	Bilateral Ota's Nevus	Bilateral Ota's Nevus
Planning diagnostic	Complete Blood Count Consult to Ophtalmologist				
Planning therapy					
Priming (Hidroquinon 4%, sunblock SPF 30 lotion, tretinoin 0.05%)	+				
CO_2 Fractional Laser	-	+	+	+	+
Nd-Yag Laser 1064 nm	-	+	+	+	+

Notes :
+++ : thick pigmentation
++ : pigmentated area decrease by 10%

DISCUSSION

Nevus of Ota or nevus fuscocaeruleus ophthalmomaxillaris was first described by the Japanese dermatologist Ota in 1939 as a dermal melanocytic hamartoma that presents as bluish hyperpigmentation along the ophthalmic, maxillary and mandibular branches of the trigeminal nerve.[1,3] It is most frequently seen in the Asian population, has a female predominance, and is usually congenital, although appearance in early childhood or at puberty has been described.[1,4]

Figure 8. **A.** Hyperpigmentation around the orbita. **B.** The hyperpigmentation extends into the sclera.[1]

Two peak ages of onset, in early infancy and early adolescence suggest a probable hormonal influence.[3] The prevalency of Nevus of Ota in Japan lies between 0.2% to 1%.[2] In Indians it is comparatively rare with the male to female sex ratio being 1:4.8, women being more frequently affected than men.[3] It is usually unilateral and bilateral involvement is described in less than 5% of cases.[3]

The pigmentation of Ota's nevus is composed of flat blue black or slate grey macules intermingled with small brown specks.[3] The intensity of pigmentation may be influenced by fatigue, menstruation, insomnia and weather.[3] Mucosal pigmentation may occur involving conjunctiva, sclera, and tympanic membrane (oculodermal melanocytosis), or other sites.[1] Ocular melanosis in 22-77% cases is almost always ipsilateral and deep in the conjunctiva.[1,3] Pigmentation may also affect the sclera, cornea, iris, choroid and less commonly the optic nerve, retrobulbar fat, orbit, periosteum and extraocular muscles.[3] The pigmentation of mucous membranes of the head and neck is variable; tympanic membrane being most frequently affected although nasal, buccal, pharyngeal and rarely palatine mucosa may be involved.[5] At present, it is believed that nevus of Ota is caused by heteroplasia that occurs in melanocyte migration during embryonic development.[6]

In our report, the patient is female, age 20 years old with the symptom dark patches both in her cheek, and forehead since birth. The dark patches was getting wider along with patient's growth. She never complained about itchy, numbness or pain sensation on her cheek. She had no complained about visual disturbances or dizzy. From physical examination there were hyperpigmented macule, vary in size, bluish in color, sharply marginated, and from okuli dextra region there was an episcleral pigmentation. The symptom of the patient is suitable with the symptom of bilateral nevus of Ota.

Histology in nevus of Ota typically shows darkly pigmented, spindle shaped dendritic melanocytes in the upper and mid dermis.[3] In this case, the histopathology examination has not been done yet because the patient still refuse to do the biopsy.

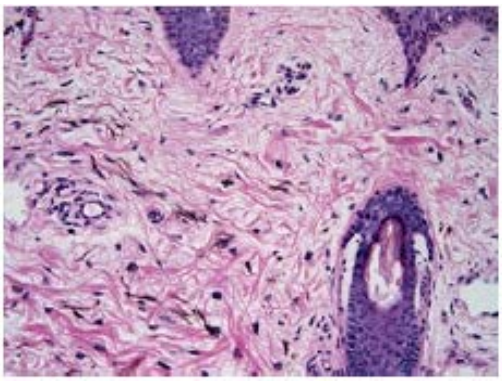

Figure 9. 10X photomicrograph showing dendritic melanocytes in the upper dermis.[3]

Nevus of Ota involves innervated areas of the first branch (V1) and second branch (V2) of the trigeminal nerve mainly affects the eye region and pars zygomatica, and the color of the skin lesion is brown or blue, the diameter of the area is 1–10 cm or larger.[6] The **i**nnervations area of trigeminal nerve branches were shown in Figure 10.[6]

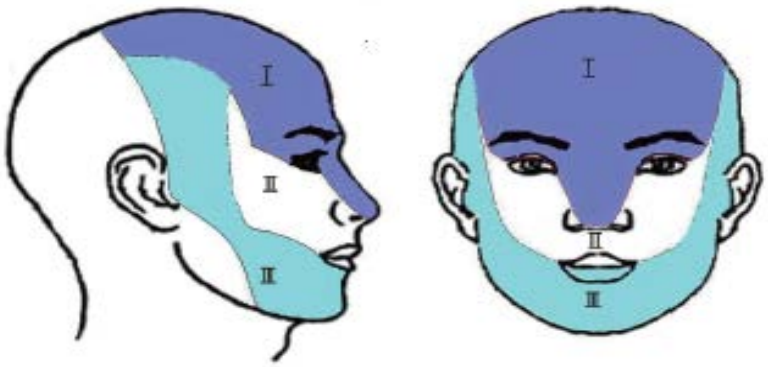

Figure 10. Innervations area of trigeminal nerve branches. I: Innervations of ophthalmic nerve; II: Innervations of maxillary nerve; III: Innervations of mandibular nerve.[6]

The first branch-ophthalmic nerve: the lacrimal nerve innervates the upper eyelid; the frontal nerve innervates the skin of forehead and calvaria; the nasociliary nerve innervates the dorsum nasi. The second branch-maxillary nerve: the infraorbital nerve innervates the skin of the lower eyelid, the alae of the nose, the upper lip; and the zygomaticus nerve innvervates the skin of zygomatic region and the temporal region. The third branch-mandibular nerve: the buccal nerve innvervates the skin of the cheek; the auriculo-temporal nerve innervates the skin of the temporal region and scalp; the mental nerve innervates skin of the mentum and lower lip.[6]

Tanino classified nevus of Ota into 4 types according to the skin lesion involvement area[6]. It was described in the table 2 below.

Table 2. Tanino's Classification

Type	Affected areas
I (Mild)	
Ia	Eye region type, the pigmentation macules involved skin of the upper and lower eyelid, orbit, and part of the temporal region
Ib	Zygomatic region type, the pigmentation macules involved the skin of the lower eyelid and zygomatic region
Ic	Forehead type
Id	Nostril type
II (Moderate)	The pigmentation macules involved skin of the upper and lower eyelid, orbit, zygomatic region, cheek, temporal region, nasion, and alae of nose
III (Severe)	The pigmentation macules involved the scalp, forehead, upper and lower eyelid, orbit, zygomatic region, cheek, temporal region, nasion, alae of nose, and posterior and superior area of auricle
IV (Bilateral)	Bilateral type

There is new classification of nevus of Ota according to the innervation area of the trigeminal nerve branches as below, named PUMCH classification (table 3 and Figure 9).[6]

There is a comparison of the PUMCH classification with Tanino's classification as followed in table 4.[6]

Table 3. Peking Union Medical College Hospital (PUMCH) Classification

Type		Affected areas
I		Pigmentation macules involving one branch of the trigeminal nerve
	Ia	Pigmentation macules involving innervation area of first branch (ophthalmic nerve) of trigeminal nerve
	Ia1	Pigmentation macules involving forehead, i.e. innervation area of frontal nerve
	Ia2	Pigmentation patch involving forehead and eyelid, i.e. innervation area of frontal nerve and lacrimal nerve
	Ib	P igmentation macules involving innervation area of second branch (maxillary nerve, V2) of trigeminal nerve
	Ib1	Pigmentation macules involving lower eyelid and inferior area of lower eyelid, i.e. innervation area of infraorbital nerve
	Ib2	Pigmentation macules involving lower eyelid, zygomatic region, temporal region, i.e. innervation area of infraorbital and zygomatic nerves
	Ib3	Pigmentation macules involving skin of alae of nose, i.e. innervation area of infraorbital nerve
	Ic	Pigmentation macules involving innervation area of third branch (mandibular nerve, V3) of trigeminal nerve
II		Pigmentation macules involving two branches of the trigeminal nerve
	IIa	Pigmentation macules involving the first and second branches (ophthalmic and maxillary nerves; V1 + V2) of the trigeminal nerve
	IIa1	Pigmentation macules involve orbit, i.e. innervation area of lacrimal and infraorbital nerves
	IIa2	Pigmentation macules involving orbit, zygomatic region, temporal region, i.e. innervation area of infraorbital and zygomatic nerves
	IIa3	Pigmentation macules involving forehead, orbit, zygomatic region, and temporal region, i.e. innervation area of lacrimal, infraorbital and zygomatic nerves
	IIb	Pigmentation macules involving skin of the zygomatic region, temporal region, cheek, anterior auricle, i.e. innervation area (maxillary nerve and mandibular nerve; V2 + V3) of the second and third branch of trigeminal nerve
III		Pigmentation macules involving the first, second and third branches (ophthalmic, maxillary, and mandibular nerves; V1 + V2 + V3) of the trigeminal nerve
	IIIa	Pigmentation macules involving skin of orbit, zygomatic region, temporal region, cheek, anterior auricle, i.e. innervation area of the first, second and third branches (ophthalmic, maxillary, and mandibular nerves; V1 + V2 + V3) of the trigeminal nerve
	IIIb	Pigmentation macules involving skin of forehead, orbit, zygomatic region, temporal region, cheek, anterior auricle i.e. innervation area of the first, second and third branch (ophthalmic, maxillary, and mandibular nerves; V1 + V2 + V3) of the trigeminal nerve
IV		Bilateral pigmentation maculeses respectively involve innervation areas of one or more branches of the trigeminal nerve
	IVa	Pigmentation macules are symmetrical
	IVb	Pigmentation macules are asymmetrical
V		Nevus of Ota combined complications

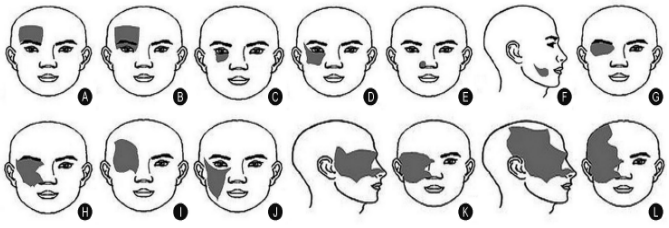

Figure 11. PUMCH classification of nevus of Ota. **A:** Type Ia1; **B:** Type Ia2; **C:** Type Ib1; **D:** Type Ib2; **E:** Type Ib3; **F:** Type Ic; **G:** Type IIa1; **H:** Type IIa2; **I:** Type IIa3; **J:** Type IIb; **K:** Type IIIa; **L:** Type IIIb.[6]

Table 4. Comparison of the PUMCH classification with Tanino's classification.[6]

PUMCH Classification	Tanino's Classification
IIa1	Ia
Ib1, Ib2	Ib
Ia1	Ic
Ib3	Id
IIIa	II
IIIb	III
Iva Ivb	IV
Ia2, Ic, IIa, IIa3, Iib	-

Based on Tanino's classification, this case include in type IV while from PUMCH classsification include in type IVA because the clinical manifestation appear symmetrically.

The development of laser and then later the theory of selective photothermolysis revolutionized the treatment of nevus of Ota. Due to the current Q-Switched laser systems such as Q-switched ruby[8], Q-switched alexandrite (QS Alex)[9] and Q-switched neodymium: yttrium-aluminum-garnet (QS Nd:YAG)[10,11] have been obtaining complete clearing of the nevus with few adverse effects. With t he introduction of Nd:YAG and Alexandrite laser technologies, Q-switched laser treatment for nevus of Ota had become the method of choice.[7] Selective photothermolysis with Q switched ruby laser is considered to be a safe and effective treatment for this pigmentation.[7]

Serafettin try to elucidate the efficacy and safety of 1064 nm Q-switched Nd:YAG laser treatment for nevus of Ota which include four cases in the study.[12] After an average of five treatment sessions, all four patients showed significant cosmetic improvement with no side effects observed.[12] This 1064 nm Q-switched Nd:YAG laser represents a safe and effective method to treat nevus of Ota.[12]

There are no specific laboratory test that have been shown to be helpful in making the diagnosis which is usually based on clinical features. The investigations are aimed at excluding other diagnostic possibilities and assessing the extent of other organ involvement such as the eyes. This patient has been consulted to an ophtalmologist and the result is all within normal limit.

The diagnosis of nevus of ota in this case was based on anamnesis and physical examination. In this patient we have already perform complete blood count. The result all within normal limit. The histopathology examination has not been done because patient refused to do the biopsy.

To diagnose nevus of Ota, there is no definitive test. The anamnesis and clinical manifestation should raise concern. There was no literature which mention that punch biopsy of the skin must be done because the diagnosis can be established from only clinical manifestations.

The differential diagnosis of nevus of Ota include phakomatosis pigmentovascularis, acquired bilateral nevus of Ota-like macules (ABNOM), nevus of Ito.[1]

Phakomatosis pigmentovascularis is defined as an association of widespread vascular nevus with extensive pigmentary nevus.[13] Phacomatosis pigmentovascularis more common in women than in men. Systemic involvement is not unusual, and include ocular and neurologic disorder such as Sturge-Webber disorder, Klippel-Trenaunay syndrome, or intracranial arteriovenous malformation.[14,15]

Acquired bilateral nevus of Ota-like macules is a pigmentary disorder that was first described by Hori et al in 1984, is clinically characterized by speckled or confluent brownish-blue or slate-gray pigmentation over the face, and histologically characterized by diffuse upper dermal melanocytosis.[1,16] The sites that are involved include the malar regions, the temples, the root of the nose, the alae nasi, the eyelids, and the forehead.[1,16] One or more sites may involved. Pigmentation occurs in a symmetrical bilateral, has a late onset in adulthood, and does not involve the mucosa.[14]

Nevus of Ito is a congenital dermal melanocytosis first described by Ito in 1954 as nevus fuscocaeruleus acromiodeltoideus.[1] Nevus of Ito is the same as nevus Ota but located in different sites.[14] It can be considered as a variant of nevus of Ota but with involvement of the acromioclavicular and deltoideal region.[1] Clinical, demographical, and histological characteristics are similar to nevus of Ota and both lesions can occur simultaneously.[1]

Most patients seek treatment early in life due to the psychological trauma and cosmetic disfigurement.[2] The treatment options for nevus of Ota prior to the advent of lasers has been limited.[17] These included cryotherapy, dermabrasion, surgical

excision, and cosmetic camouflage.[17] The surgical treatment options were associated with significant scarring and permanent pigment alteration.[17] Laser therapy is the mode of choice because of excellent results in short duration but cost and availability are the limiting factors.[18] Q switched (QS) lasers have changed the management of pigmentary lesions to a great extent.[17]

Three types of Q-switched lasers have been used widely to treat nevus of Ota. These include the Q-switched 694 nm Ruby laser, Q-switched 755 nm Alexandrite laser and the Q-switched 1064 nm Nd:YAG laser. Previous studies have shown that all of them were able to provide excellent results in treating nevus of Ota. The first prospective study comparing the clinical efficacy of Q-switched Alexandrite and Q-switched 1064nm Nd:YAG laser in the treatment of nevus of Ota among Hong Kong patients was done by Chan HH et al. Their findings indicate that Q-switched 1064nm Nd:YAG laser is more effective than Q-switched alexandrite in the lightening of nevus of Ota. In darker skinned (Fiztpatrick skin type IV-VI), the Q-switched Nd:YAG laser at 1064 nm is usually the safest laser to lighten a nevus of Ota. In lighter-skinned patients, Q-switched ruby laser at 694nm and Q-switched alexandrite laser at 755nm can also be used. Currently there is no effective treatment for the scleral pigmentation of nevus of Ota. Q switched lasers QS Nd:YAG (1064 nm), Ruby (694 nm) and Alexandrite (755 nm) produce ultrashort bursts of laser light that specifically target the melanosomes in the dermal melanocytes.[17,19]

In addition to local thermal destruction and stimulation, fractionated devices may also play an important role for drug delivery into the tissue and for extruding material out of the skin, as in the studies by Haedersdal et al.[20] This has also been recently reported by Ibrahimi et al using an ablative fractionated erbium : YAG laser to treat an allergic tattoo reaction with success.[20] Conventional treatment of allergic tattoo reactions with a Q-switched laser alone could likely increase immunogenicity of the tattoo pigment post-treatment and the risk of a systemic allergic response, the ablative fractional laser has shown the ability to remove allergic tattoo pigment as an alternative method without inducing a systemic allergic reaction.[20]

Patient already had laser treatment (Nd:YAG laser) before in private beauty clinic for 4 sessions but the complaint still persist and no improvement because the defect area was large so it needed more laser session. Now patient was treated with Nd:YAG laser combined with CO_2 laser since since 10 months ago. Each laser session repeated every 3 months, using wavelengths 1064 nm. After four laser session, there has been an improvement in the lesions as the lesions is getting lighter. The prognosis of this case is good.

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