

Original Article

Q-switched ruby laser therapy for acquired bilateral naevus of Ota-like macules in Chinese

Q 開關紅寶石激光在華人後天對稱性太田痣樣斑的治療研究

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Objectives: To evaluate the efficacy and safety of Q-switched ruby laser (QSRL) for Chinese patients with acquired bilateral naevus of Ota-like macules (ABNOM). **Methods:** Thirty Chinese female patients were enrolled. QSRL therapy was performed at intervals of three to six months, with the following parameters: spot size, 6 mm; pulse duration, 20 ns; fluence, 2.5-3.5 J/cm². **Results:** Twenty-six patients achieved good to excellent clearance after one to seven (mean 3.2) treatments. Repeated treatments led to enhanced efficacy. Nine developed transient post-laser hyperpigmentation while two developed persistent hypopigmentation. **Conclusions:** QSRL provides a safe, effective and economical treatment modality for ABNOM in Chinese.

目的：評價 Q 開關紅寶石激光對華人後天對稱性太田痣樣斑的治療成效和安全性。方法：有三十個中國女性患者參加。以以下參數，每隔三至六個月內進行 Q 開關紅寶石激光治療：光點大小 6 毫米；脈衝持續時間，20 納秒；流量 2.5-3.5 焦耳 / 平方厘米。結果：經過一至七次（平均 3.2）治療後，二十六例患者獲得好至極好的療效。多次治療可提高療效。九例患者出現短暫色素沈著，兩例出現持久性色素減退。結論：Q 開關紅寶石激光是治療後天對稱性太田痣樣斑的一種安全、有效及經濟的方案。

Keywords: Acquired bilateral naevus of Ota-like macules, efficacy, safety, Q-switched ruby laser

關鍵詞：後天對稱性太田痣樣斑、療效、安全性、Q 開關紅寶石激光

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Introduction

Acquired bilateral naevus of Ota-like macules (ABNOM), or Hori's macule, is a circumscribed dermal melanocytosis first described in 1984.¹ Clinically characterised by small, bilateral, brown or grey patches over the face, ABNOM is not uncommon among Asian populations including Chinese.²⁻⁵ ABNOM derived its name from naevus of Ota due to similar histological patterns: scattered bipolar melanocytes within the upper and middle dermis.¹ However, ABNOM assumes distinctive features in comparison to naevus of

Ota, e.g. bilateral lesions universally involving malar area, occurrence during adolescence or adulthood and a lack of ocular or mucosal involvement. It is increasingly recognised as a cosmetic problem because of its prevalence and long lasting nature. Naevus of Ota has been successfully managed with Q-switched (QS) laser systems, which specifically target the melanosomes as the chromophore on the basis of selective photothermolysis.⁶ Likewise, QS lasers have also gained popularity for ABNOM treatment. QS ruby laser (QSRL), QS alexandrite laser (QSAL) and QS Nd:YAG laser (QSNYL) have all been introduced with varying degrees of success.⁷⁻¹⁴

QSRL emits radiation at a wavelength of 694 nm. It is highly absorbed by melanosomes in pigment-laden cells and has proved effective and safe for multiple skin pigmentary disorders in various populations.⁶ QSRL was reported to be highly effective for Thai patients with ABNOM.⁷ However, limited data are available on its use in Chinese populations. In the present study, we retrospectively evaluated the efficacy and safety profile of QSRL in treating Chinese patients diagnosed with ABNOM.

Material and methods

Study population

Thirty Chinese female patients with ABNOM were enrolled and characterised as Fitzpatrick skin phototype III or IV (Table 1). None of them reported any previous treatments for their lesions. Patients who had medical conditions e.g. active infections, photosensitivity, pregnancy, lactation or malignancy, which rendered them unfit for the study, were excluded. Informed consent was all obtained. The age of the patients at their first visits ranged from 20 to 49 years (mean age 29.5 years). The colour of the lesions was categorised into three types: blue (3/30, 10%), brown (13/30, 43.3%) and slate-grey (14/30, 46.7%). In terms of lesion distribution, all patients had mottled or confluent

grey, brown to bluish macules on both malar regions. In addition, lesions were observed on the temple (36.7%, 11/30), forehead (13.3%, 4/30), upper eyelids (6.7%, 2/30), root of nose (16.7%, 5/30) and alae nasi (20%, 6/30).

Treatment protocol

The patients were treated with the SINON ruby laser system (Wavelight, Erlangen, Germany) with the following parameters: spot size, 6 mm; pulse duration, 20 ns and fluence, 2.5-3.5 J/cm². The therapeutic endpoint was determined as immediate whitening following laser radiation. The treatment interval was set at three to six months. The mean number of treatment sessions was 3.2 (range one to seven). After each session, the patients were instructed to apply fusidic acid cream (Fucidin®; LEO Pharma, Ballerup, Denmark) as well as a broad-spectrum sunscreen. Bleaching agents, mainly 3% hydroquinone cream, were also used when laser-induced hyperpigmentation occurred.

Evaluation of response and safety profile

The response to QSRL treatment was clinically assessed by two separate, blinded dermatologists using digital photographs taken before and after each treatment session. A quartile grading system based on the percentage of pigment clearance was used for the evaluation: grade 1, 0-25% clearance-poor response; grade 2, 26-50% clearance-moderate response; grade 3, 51-75% clearance-good response; grade 4, 75-100% clearance-excellent response. Correlation between the number of sessions, colour of lesions and the therapeutic outcomes were also analysed. Side effects, e.g. hyperpigmentation, hypopigmentation and scarring, were also recorded at each follow-up visit.

Table 1. The collected data of the patients enrolled in the study

Patient	Skin type	Age	Colour of lesions	Number of treatment	Therapeutic response grade	Adverse effects
T2472	III	38	Brown	3	4	N
T2476	III	23	Brown	1	3	N
T2510	III	35	Brown	3	4	N
T2525	III	22	Slate-grey	2	2	N
T2527	III	24	Slate-grey	5	4	N
T2540	III	30	Brown	6	4	N
T2546	III	22	Brown	3	4	N
T2561	III	30	Brown	3	4	N
T2595	III	21	Brown	4	4	PLH
T2628	III	20	Slate-grey	5	4	PLH
T2687	III	26	Slate-grey	3	4	N
T2716	III	22	Slate-grey	2	4	PLH
T2737	III	23	Brown	3	4	PLH
T2746	IV	35	Blue	2	2	N
T2825	III	26	Slate-grey	5	4	PLH
T2838	III	41	Brown	1	4	PLH
T2877	III	26	Slate-grey	7	4	PLH
T2879	III	32	Slate-grey	2	4	N
T2890	IV	40	Brown	5	4	PLHo
T2912	III	49	Blue	5	4	PLHo
T2913	III	24	Slate-grey	3	4	N
T3000	III	25	Slate-grey	3	4	N
T3010	III	27	Brown	5	4	N
T3016	IV	28	Slate-grey	3	4	N
T3041	III	35	Brown	1	2	PLH
T3214	III	26	Slate-grey	1	4	N
T3247	IV	41	Brown	4	3	N
T3316	III	27	Slate-grey	2	3	N
T3453	III	39	Blue	2	1	PLH
T3732	III	36	Slate-grey	1	3	N

N: none; PLH: post-laser hyperpigmentation; PLHo: post-laser hypopigmentation

Statistical analysis

Spearman's rank correlation coefficient test was performed to determine the significance of effect on therapeutic outcome of the number of treatment sessions and the colour of lesions. Chi-square test for trend was also used to detect the association between the colour of lesions and post-laser complications. Statistical analysis was conducted using IBM SPSS version 16.0 (IBM Corporation, Somers, NY, US). The level of significance was defined as $p < 0.01$.

Results

Data of the study are summarised in Table 1. Of all 30 treated patients, 86.7% of the patients showed good to excellent responses (50% ~ 100% clearance) after one to seven (mean 3.2) treatment sessions. Twenty-two (73.3%) showed excellent responses with more than 75% clearance, 12

(40%) of whom achieved complete clearance without recurrence upon follow-up (up to 6 years) (Figure 1). Four patients (13.3%) showed good, three (10%) moderate and only one (3.3%) poor response to the QSRL treatment. A significant correlation was found between the number of treatment sessions and therapeutic outcomes ($r = 0.531$, $p = 0.003$). Repeated treatments led to enhanced lesion clearance. The average number of sessions for excellent responses was four, compared with two and 1.7 for good and moderate results, respectively. After two treatments, 19 out of 25 (76%) patients demonstrated good or excellent responses; 18 out of 19 (94.7%) patients who were treated for three times achieved the same results (Table 2). Complete clearance was observed after a mean number of 4.4 sessions. On the other hand, therapeutic outcomes were not statistically correlated with the colour of lesions before the first treatment started ($p = 0.217$). Good or excellent responses were observed in 92.7% (13/

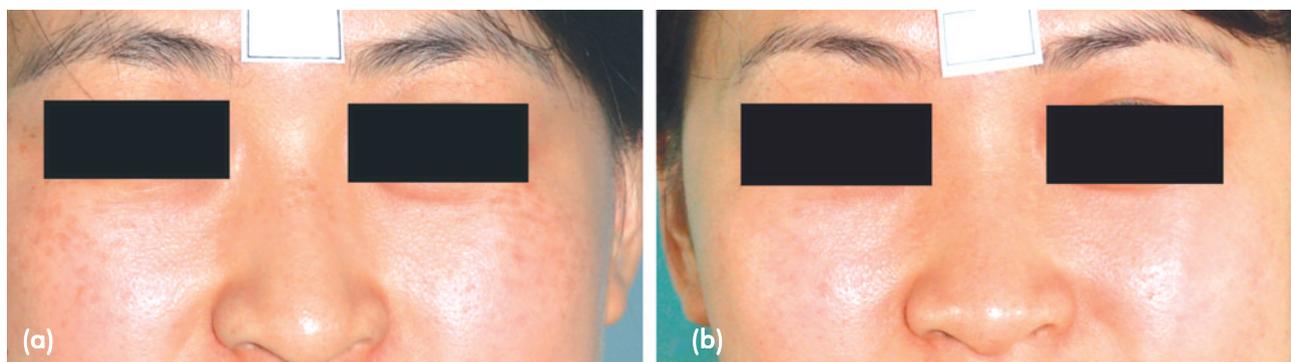


Figure 1. (a) A baseline view of 21-year-old female patient with ABNOM; (b) Almost complete clearance was achieved after three treatment sessions.

Table 2. Number of patients and therapeutic grading for each treatment session

Treatment number	Poor	Moderate	Good	Excellent	Total
4~7	0	0	0	16	16
3	0	1	3	15	19
2	1	5	8	11	25
1	7	14	7	2	30

14) of patients with slate-grey coloured lesions, 92.3% (12/13) with brown-coloured lesions and 33.3% (1/3) with blue-coloured lesions.

Out of 30 patients treated with QSRL, nine (30%) developed transient post-laser hyperpigmentation (PLH) which generally resolved in 2 to 6 months. Meanwhile, two (6.7%) patients (T2890 and T2912) experienced persistent but acceptable post-laser hypopigmentation (PLHo) after multiple sessions, which lasted for three and four years respectively (Figure 2). No significant correlation was found by Chi-square test for trend between the colour of lesions and the occurrence of pigmentary complications ($p=0.984$ and 0.108 , for PLH and PLHo respectively). Neither scarring nor permanent textural changes were observed.

Discussion

ABNOM is a common skin dyspigmentation in Chinese. A population-based study by Sun et al. indicated a prevalence of 0.8% in Taiwan, with a female: male ratio of 6:1.² One recent large-scale cross-sectional study conducted in Shanghai, China found ABNOM in 2.5% of the study population.⁵ A significant female predominance was also noted with a female: male ratio of 9:1. In the present study, consistent with the epidemiological data, all patients were female. A lack of male patients may be due to the relative

rarity of ABNOM in Chinese males and less cosmetic concern of this group.

As with naevus of Ota, QS lasers have become the primary treatment modalities for ABNOM. Although multiple laser systems have been introduced, QSRL may seem superior to others in terms of efficacy (Table 3). Kunachuk et al. first reported the use of the QSRL in 140 Thai patients with ABNOM.⁷ After an average of 2.3 treatment sessions at intervals of one to six weeks, 93.6% of the patients achieved complete clearance, 7% developed PLH and 5.7% developed PLHo. In combination with topical tretinoin and hydroquinone, Momosawa et al reported that all the 19 Japanese patients with ABNOM who were treated by QSRL showed a good to excellent (>50%) clearance after two or three treatment sessions.¹⁵ PLH occurred in 10.5% of them. With the use of QSAL, Lam et al first reported a greater than 50% clearance in 80% of 32 Hong Kong Chinese female patients with two to eleven (mean seven) treatments every two to four weeks.⁸ However, 50% of the patients developed PLHo while 12.5% PLH. A later study by Kagami et al reported a greater than 50% clearance in only 45.8% of the Japanese patients with ABNOM after one to six sessions at a three-month interval.⁹ QSNYL has also been tried with good but somewhat variable results, with mean treatment sessions required to achieve a greater than 50% clearance ranging from 2.8 to 4.6.¹⁰⁻¹⁴



Figure 2. (a) A baseline view of 49-year-old female patient with ABNOM; (b) Post-laser hypopigmentation occurred after the fourth session and persisted for four years.

The data of our study clearly demonstrated that QSRL is very effective and safe for Chinese patients with ABNOM. It took an average of two sessions to achieve a greater than 50% clearance, and 4.4 for complete clearance. More treatment sessions lead to better therapeutic outcomes, consistent with previous reports.^{9,13,14} Compared with published studies using QSRL, our study showed a similar efficacy but more treatment sessions seemed to be required for complete lesion clearance. This discrepancy may be due to varied laser instruments and treatment intervals. A short interval (2.2 weeks in average) was used by Kunachuk et al. and subsequent treatments were performed even before post-laser dyspigmentations may have

appeared.⁷ Shorter intervals may keep the epidermis hypopigmented and enhance the penetration of QS lasers into deeper dermis during the whole treatment course.¹⁶ However, they may also lead to a higher risk of hypopigmentation, a particular concern for QSRL use in darker complexions (Fitzpatrick skin type III to V).¹⁷ Consequently, a conventional three to six-month interval was adopted in our practice.

Epidermal hyperpigmentation is a distinctive feature observed in ABNOM.¹⁸ Epidermal melanin and melanocytes are competing chromophores for QS lasers when managing dermal melanocytosis, which may increase the risk of post-

Table 3. Case series of ABNOM patients treated with Q-switched lasers

No. of patients/sex	Laser	Parameters J/cm ² (Spot size, mm)	Treatment interval	Total no. of sessions (mean)	Therapeutic outcome	Post-laser hyper-pigmentation	Post-laser hypo-pigmentation	Ref.
140/F	QSRL (694 nm, 25 ns)	7-10 (2-4)	1-6 wk	1-6 (2.3)	CC:93.6%	7%	5.7%	7
30/F	QSRL (694 nm, 20 ns)	2.5-3.5 (6)	3-6 mo	1-7 (3.2)	GC:86.7%; CC:40%	30%	6.7%	This study
32/F	QSAL (755 nm, 100 ns)	6.5-8 (3)	7-322 d	2-13 (7.0)	GC:80%; CC:28%	12.5%	50%	8
24	QSAL (755 nm, 50 ns)	4-5 (4)	3 mo	1-6	GC:45.8%	Not mentioned	Not mentioned	9
63/F, 3/M	QSNYL (1064/532 nm, 6-8 ns)	4-6 (3)	3-6 mo	1-7	GC:30.3%	73%	0	10
70/F	QSNYL (1064 nm, 25 ns)	8-10 (2-4)	2-3 wk	2-5 (2.8)	CC:97.1%	50%	0	11
10/F	QSNYL (1064 nm, 5-7 ns)	4.2-9.9 (3)	3 mo	1-5.3 (3.0)	GC:50%	Nearly 100%	Not mentioned	12
29/F	QSNYL (1064 nm, 5-7 ns)	8-9.5 (3)	4-12 wk	1-10 (5.0)	GC:66%	40%	0	13
13/F, 2/M	QSNYL (1064 nm, 5-20 ns)	2.2-2.6 (6); 4-6 (4)	1-2 wk	10-15 (11)	GC:80%	0	0	14

ABNOM: Acquired bilateral naevus of Ota-like macules; F: female; M: male; QSAL: Q-switched alexandrite laser; QSNYL: Q-switched Nd: YAG laser; QSRL: Q-switched ruby laser; CC: complete clearance of lesions; GC: good to excellent (>50%) clearance.

laser dyspigmentations. Besides, Lam et al described that the melanocytes in ABNOM contained less mature melanosomes which might survive the laser irradiation and become activated instead, producing more melanin.⁸ In fact, PLH is fairly common after QS laser treatment of ABNOM.¹⁷ According to Momasawa et al., without any pretreatment bleaching agents, PLH was almost always observed in Japanese patients after one QSRL treatment.¹⁵ Furthermore, ethnic skin types like those of Chinese are considered susceptible to PLHo after QSRL therapy, which may render laser surgeons reluctant to use this device. Despite all that, we found a relatively low incidence of pigmentary complications after QSRL treatment for Chinese patients with ABNOM in our study. Although up to 30% of the patients experienced PLH, it was transient and tended to resolve in months. The long-term influence of PLH on patients was negligible. On the other hand, PLHo was uncommon contrary to popular belief. Compared with naevus of Ota treated by QSRL,¹⁹ the incidence of PLH in ABNOM seems to be higher (30% vs 5.9%) but PLHo lower (6.7% vs 16.8%). The particular reason for this lower rate of PLHo is unknown. We suggest that the mottled distribution of ABNOM lesions may be accountable. Normal, intact skin surrounding the lesions are frequently spared during treatment and may facilitate the restoration of pigmentation in the treated area. Although it persisted for years, PLHo was regarded cosmetically acceptable by the patients in our study. A review of the safety profile of different laser systems suggests that QSRL may be equally safe when compared with other QS lasers for ABNOM (Table 3). Since no split-face study of ABNOM laser treatment is available, direct comparison among different QS lasers is difficult. More prospective controlled studies thus are indeed warranted for optimising treatment protocols and minimising complications.

To eradicate both epidermal and dermal pigmentation in ABNOM, combined therapeutic approaches have also been introduced, such as QS lasers with chemical peels; scanned carbon-

dioxide laser followed by QSRL; 532nm QSNYL followed by 1064nm QSNYL; and intense pulsed light with QSRL.²⁰⁻²³ Combined treatments were reported to have better clinical responses with fewer sessions and complications. However, they are usually more expensive and add to the cost. QSRL-emitted radiation (694 nm) alone is readily absorbed by epidermal melanin while penetrating deep enough into dermis, simultaneously destroying both pigmentations. Therefore it would be more economical than those combined approaches with comparable overall efficacy and safety.

In conclusion, we suggest that QSRL provides a safe and economical treatment modality with an enhanced efficacy for Chinese patients with ABNOM. The risk of complications was relatively low and transient, but hypopigmentation may persist.

Conflict of interest

None.

References

1. Hori Y, Kawashima M, Oohara K, Kukita A. Acquired bilateral nevus of Ota-like macules. *J Am Acad Dermatol* 1984;10:961-4.
2. Sun CC, Lu YC, Lee EF, Nakagawa H. Nevus fusco-caeruleus zygomaticus. *Br J Dermatol* 1987;117:545-53.
3. Ee HL, Wong HC, Goh CL, Ang P. Characteristics of Hori naevus: a prospective analysis. *Br J Dermatol* 2006; 154:50-3.
4. Kuroki T, Noda H, Ichinose M, Yoshimoto S, Nakajima T. Review of patients with acquired bilateral nevus of Ota-like macules. *J Jpn Soc Aesthetic Plast Surg* 1999; 21:29-37.
5. Wang BQ, Shen ZY, Fei Y, Li H, Liu JH, Xu H, et al. A population-based study of acquired bilateral nevus-of-Ota-like macules in Shanghai, China. *J Invest Dermatol* 2011;131:358-62.
6. Polder KD, Landau JM, Vergilis-Kalner IJ, Goldberg LH, Friedman PM, Bruce S. Laser eradication of pigmented lesions: a review. *Dermatol Surg* 2011;37:572-95.
7. Kunachak S, Leelaudomniti P, Sirikulchayanonta V. Q-Switched ruby laser therapy of acquired bilateral nevus

- of Ota-like macules. *Dermatol Surg* 1999;25:938-41.
8. Lam AY, Wong DS, Lam LK, Ho WS, Chan HH. A retrospective study on the efficacy and complications of Q-switched alexandrite laser in the treatment of acquired bilateral nevus of Ota-like macules. *Dermatol Surg* 2001;27:937-41.
 9. Kagami S, Asahina A, Watanabe R, Mimura Y, Shirai A, Hattori N, et al. Treatment of 153 Japanese patients with Q-switched alexandrite laser. *Lasers Med Sci* 2007;22:159-63.
 10. Polnikorn N, Tanrattanakorn S, Goldberg DJ. Treatment of Hori's nevus with the Q-switched Nd:YAG laser. *Dermatol Surg* 2000;26:477-80.
 11. Kunachak S, Leelaudomlipi P. Q-switched Nd:YAG laser treatment for acquired bilateral nevus of Ota-like maculae: a long-term follow-up. *Lasers Surg Med* 2000;26:376-9.
 12. Suh DH, Han KH, Chung JH. Clinical use of the Q-switched Nd:YAG laser for the treatment of acquired bilateral nevus of Ota-like macules (ABNOMs) in Koreans. *J Dermatol Treat* 2001;12:163-6.
 13. Lee WJ, Han SS, Chang SE, Lee MW, Choi JH, Moon KC, et al. Q-Switched Nd: YAG Laser Therapy of Acquired Bilateral Nevus of Ota-like Macules. *Ann Dermatol* 2009;21:255-60.
 14. Cho SB, Park SJ, Kim MJ, Bu TS. Treatment of acquired bilateral nevus of Ota-like macules (Hori's nevus) using 1064-nm Q-switched Nd:YAG laser with low fluence. *Int J Dermatol* 2009;48:1308-12.
 15. Momosawa A, Yoshimura K, Uchida G, Sato K, Aiba E, Matsumoto D, et al. Combined therapy using Q-switched ruby laser and bleaching treatment with tretinoin and hydroquinone for acquired dermal melanocytosis. *Dermatol Surg* 2003;29:1001-7.
 16. Manuskiatti W, Fitzpatrick RE, Goldman MP. Treatment of facial skin using combinations of CO₂, Q-switched alexandrite, flashlamp-pumped pulsed dye, and Er:YAG lasers in the same treatment session. *Dermatol Surg* 2000;26:114-20.
 17. Park JM, Tsao H, Tsao S. Acquired bilateral nevus of Ota-like macules (Hori nevus): etiologic and therapeutic considerations. *J Am Acad Dermatol* 2009;61:88-93.
 18. Lee B, Kim YC, Kang WH, Lee ES. Comparison of characteristics of acquired bilateral nevus of Ota-like macules and nevus of Ota according to therapeutic outcome. *J Korean Med Sci* 2004;19:554-9.
 19. Kono T, Nozaki M, Chan HH, Mikashima Y. A retrospective study looking at the long-term complications of Q-switched ruby laser in the treatment of nevus of Ota. *Lasers Surg Med* 2001;29:156-9.
 20. Lee GY, Kim HJ, Whang KK. The effect of combination treatment of the recalcitrant pigmentary disorders with pigmented laser and chemical peeling. *Dermatol Surg* 2002;28:1120-3.
 21. Manuskiatti W, Sivayathorn A, Leelaudomlipi P, Fitzpatrick RE. Treatment of acquired bilateral nevus of Ota-like macules (Hori's nevus) using a combination of scanned carbon dioxide laser followed by Q-switched ruby laser. *J Am Acad Dermatol* 2003;48:584-91.
 22. Ee HL, Goh CL, Khoo LS, Chan ES, Ang P. Treatment of acquired bilateral nevus of Ota-like macules (Hori's nevus) with a combination of the 532 nm Q-switched Nd:YAG laser followed by the 1,064 nm Q-switched Nd:YAG is more effective: prospective study. *Dermatol Surg* 2006;32:34-40.
 23. Park JM, Tsao H, Tsao S. Combined use of intense pulsed light and Q-switched ruby laser for complex dyspigmentation among Asian patients. *Lasers Surg Med* 2008;40:128-33.