Dermatology Practical & Conceptual

Efficacy of Long-Pulsed Nd:YAG Laser for Classic Kaposi's Sarcoma: A Dermoscopic Study

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ABSTRACT

Introduction: Classic Kaposi's sarcoma (CKS) is a chronic and indolent skin tumor. Because CKS has a low mortality rate but can have a significant impact on quality of life, it is important to choose safe, long-term treatments with minimal side effects.

Objectives: The aim was to assess the efficacy of long-pulsed Nd:YAG laser therapy in treating CKS based on clinical and dermoscopic observations.

Methods: Forty-two nodular lesions from three CKS patients (stage 4) were treated using a long-pulsed Nd:YAG laser with a spot size ranging from 3 to 7 mm, a fluence of 200–250 j/cm^2, and a pulse duration lasting between 10 and 20 milliseconds in one or two sessions. Patients were photographed clinically and dermoscopically before the procedure, immediately after the procedure, and at 1, 6, and 12 months after the procedure.

Results: All participants displayed significant clinical and dermoscopic improvements, and all lesions healed within 2–3 weeks, resulting in only minor atrophic scars. No instance of recurrence was found among any of the patients during the 1-year follow-up.

Conclusions: Nd:YAG laser therapy may prove to be an effective therapeutic alternative for both early and advanced-stage CKS, specifically in instances of stubborn cutaneous lesions or patients receiving systemic therapy. The treatment results in quick improvement, typically within 2–3 weeks, and is well tolerated. Nd:YAG laser therapy could provide potential benefits for HIV-positive patients as it is free from immunosuppression, easy to apply to recurring lesions, and demonstrates overall effectiveness and safety.

Introduction

Classic Kaposi's sarcoma (CKS) is a chronic indolent angioproliferative skin tumor associated with human herpesvirus 8 (HHV8) and is characterized by violaceous macules, papules, and nodules. The lesions are often located in the lower extremities and include macules, nodules, and plaques, depending on stage of the lesions. CKS predominantly affects males, with a male-to-female ratio of 3:1, with the highest incidence observed in the sixth decade of life [1]. CKS is prevalent in Mediterranean and Eastern European regions, and risk factors are advanced age, immune deficiency, and sexual activity [1]. The definitive diagnosis of CKS relies on histopathological analysis, with clinical and dermoscopic findings playing a crucial role. While CKS has a low mortality rate, it significantly impacts the quality of life of affected individuals [2]. Therefore, it is important to choose a reproducible local treatment that is long-term, fast-acting, and safe and that has minimal side effects in this cutaneous limited disease. Local treatments using various types of lasers have been reported in the literature.

Objective

Here, we aimed to investigate the clinical and dermoscopic features as well as the outcomes of neodymium-doped yttrium-aluminum-garnet (Nd:YAG) laser treatment in three CKS patients.

Methods

We evaluated a total of 42 nodular lesions located in the lower and upper extremities of three CKS patients who visited our clinic between March 2018 and January 2020. The retrospective study protocol was approved by our Ethics Committee (Ethics Committee Approval n. İ10-701-23), and informed consent was obtained from the patients. All of our patients had been diagnosed pathologically with KS prior to enrolling to this study. The patients had no history of immunosuppressive drug use, systemic disease, or organ transplantation, and their medical histories were unremarkable. The complete blood count, complete metabolic panel, and HIV serology were normal for all patients. None of the patients had endemic, epidemic, or iatrogenic KS. All patients were staged using lymph node ultrasound, thoraco-abdominopelvic computed tomography, and endo-colonoscopy. None of the patients had extracutaneous or mucosal involvement, and all patients had stage 4 CKS according to the classification of Brambilla et al. [3]. The study excluded patients who had received systemic treatments for CKS in the previous months and lesions that had previously undergone local treatments. None of the patients included in the study had a history of hypertrophic scars or coagulation disorders.

All 42 nodular lesions, ranging in diameter from 3 to 12 mm, underwent long-pulsed Nd:YAG laser treatment, administered in one or two sessions. The laser parameters employed during treatments were as follows: spot diameter of 3–7 mm; energy density of 200–250 j/cm2; pulse duration of 10–20 msn. A satisfactory treatment outcome was defined by the grey whitening of the nodular lesions accompanied by a significant popping sound. Patients were instructed to report any severe pain or discomfort experienced during the procedure. Local anesthesia was not administered prior to the procedure.

For selected thick nodular lesions, a second session of long-pulse Nd:YAG laser treatment administered at 4–week intervals. Nikon 1 AW1 camera Apple iPad mini retina were used to image the lesions clinically, and a DermLite DL3N and DermLite DL4 coupled to a Nikon 1 AW1 camera was used for dermoscopic imaging before the procedure, immediately after the procedure, and at 1, 6, and 12 months after the procedure.

Results

The demographic characteristics, skin type, and clinical characteristics of the patients are presented in Table 1. The mean age of the patients was 70 (57–78) years, and the mean disease duration was 6.6 (5–8) years. The clinical findings of the patients before and after treatment are shown in Figure 1, and the dermoscopic findings are shown in Figure 2. All three patients had multiple, slowly progressive, nodular lesions located in the lower and upper extremities, and the patients were considered to have stage 4 disease. Among the patients included in the study, one exhibited lymphedema associated with CKS in the lower extremities (Figure 1, C and D). All patients had previously undergone treatment for their extensive lesions with interferon α-2a, along with local radiation therapy and surgery. However, in the three months before, during, and one year after laser treatment, none of the patients received any systemic or local treatment.

Long-pulsed Nd:YAG laser treatment was successfully administered to a total of 42 nodular lesions, located in the lower and upper extremities, with diameters ranging from 3 to 12 mm. Throughout the treatment sessions, a consistent popping sound was noted, and no bleeding was observed. Following the treatment, a crust formed in the treated area, which subsequently healed with scarring (Figures 1 and 2) within 2–3 weeks. Additionally, a notable clinical improvement in lymphedema was observed in one patient with lymphedema associated with KS. The procedure was well tolerated by the patients, as none reported pain requiring

Table 1. Characteristics of Patients.

Patient	Age	Sex	Skin Type	Localization / Number of Nodules	Mucous/Lymph Node/Visceral	CKS Stage *	Disease Duration/ Previous Treatments**
1	57	F	2	lower-upper extremity / 18	–	4	5 years / excision, radiotherapy, interferon α-2a
2	78	M	4	lower-upper extremity / 20	- / lymphedema	4	7 years / excision, radiotherapy, interferon α-2a
3	76	M	4	lower-upper extremity /14	–	4	8 years / excision, radiotherapy, interferon α-2a

* Classic Kaposi's sarcoma staging was performed according to the classification of Brambilla et al. [3].
** In the three months prior, during, and one year after laser treatment, none of the patients received any systemic or local treatment. CKS = classic Kaposi's sarcoma

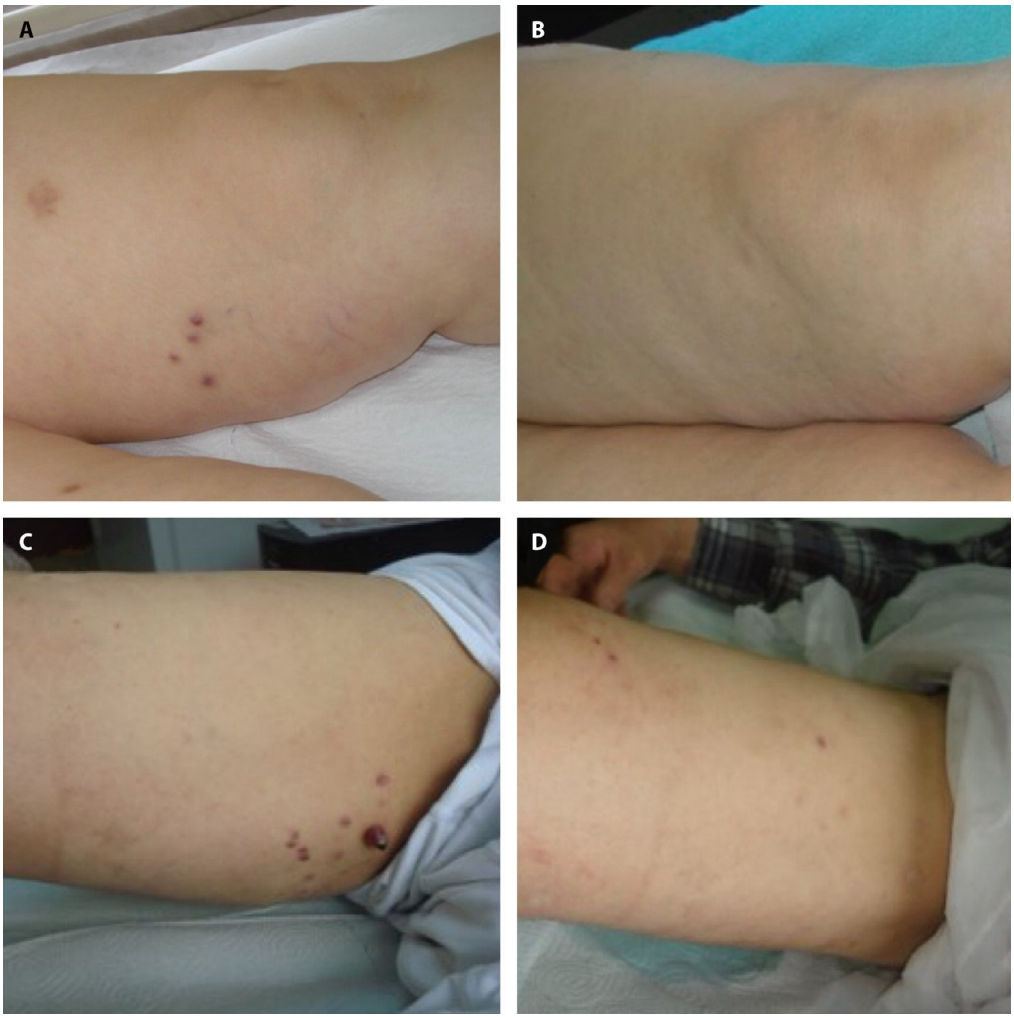

Figure 1. Clinical manifestations of lesions before and after treatment: (A, B) Regression of multiple red-purple papules with atrophic scar on left upper leg after treatment; (C, D) Regression of red-purple nodules and papules on the right upper leg with atrophic scarring after treatment.

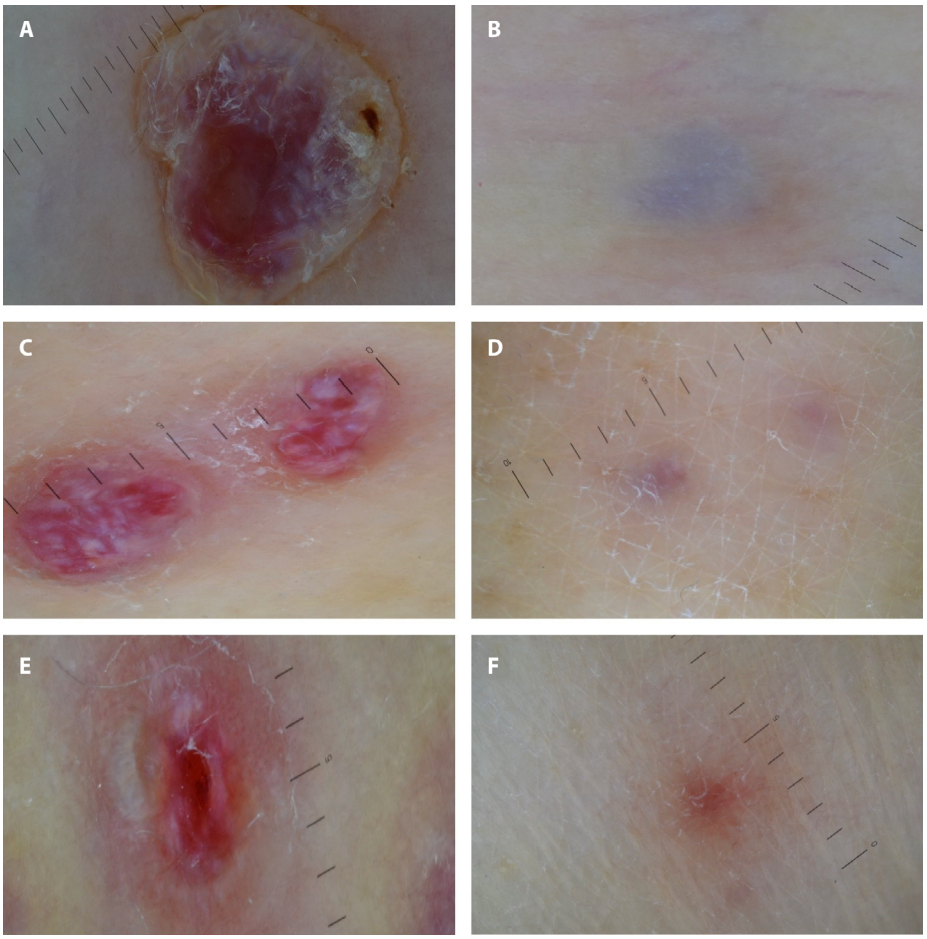

Figure 2. Dermoscopic findings of lesions before and after treatment: (A, B) Regression of nodular lesion with scale consisting of white-blue-pink areas with a polychromatic rainbow pattern and surrounded by a sharply circumscribed brown collarette after treatment; (C) Irregular white clods and a rainbow pattern in a nodular lesion with a pink-white-red polychromatic discoloration surrounded by a yellow-brown color; (D) Atrophic scarring of this lesion after treatment; (E) White clods consisting of white-red-pink areas surrounded by a polychromatic collarette around the hemorrhagic ulcerated area in the central areas of irregular white lines with scale; (F) Mild atrophic scarring of this lesion after treatment.

interruption or termination of the treatment. None of the patients experienced any treatment-related complications, including local wound infections, hypertrophic scarring/keloids, pigmentation, or hemorrhage at the treatment site. No recurrence was detected in any of the patients during the 1-year follow-up.

Discussion

KS, which originates from vascular and lymphatic endothelial structures, is a multisystem disease with prominent skin involvement. Four subtypes of KS have been defined: classic, endemic, iatrogenic, and AIDS-related. In these subtypes, in which systemic involvement is seen at different rates, the prognoses also vary. CKS is characterized by chronic blue-, red-, and purple-colored macular papules, nodules, and plaques in elderly patients, and ulceration, bleeding, and hyperkeratosis can be seen in nodular lesions [2]. Lymphedema is observed in 20% of patients with CKS starting from early-stage disease, and it impairs quality of life [4]. Skin lesions are usually located on the lower extremities, less frequently on the upper extremities, head, and body [3]. Oral, genital, and conjunctival mucosal involvement can be seen, and lymph node and gastrointestinal involvement can be detected in advanced CKS [3]. Along with clinical findings, dermoscopic findings are also very important in the diagnosis and follow-up of the disease [5]. Dermoscopic findings such as blue, purple, and red areas, rainbow pattern, squam on the surface, collar sign, small brown globules, white lines, white globules, and polychromatic discoloration with dotted, coiled, and curved vessels and polychromatic discoloration are very helpful in the diagnosis [5]. During pathological examination, detection of HHV8 + atypical endothelial cell proliferation in dilated

vascular structures and spindle-cell infiltration in the dermis is diagnostic [6].

HHV8, which is responsible for the pathogenesis of CKS, remains in endothelial cells in the latent phase after infection, passes into the lytic phase in certain cases, such as hypoxia, viral infection, and immunosuppression, causing clinical findings of KS [7]. Currently, there is no curative treatment for KS as there is no treatment to eliminate HHV8 infection, and there is no randomized controlled trial for treatment. In the selection of treatment, the individual's KS subtype, clinical features/extent of lesions, immune system, comorbidities, and symptoms should be considered [2].

Pegylated liposomal doxorubicin, paclitaxel, pomalidomide, etoposide, vinblastine or vincristine, bleomycin, gemcitabine, rapamycin, and antiangiogenic agents are systemic treatments that can be used in the presence of rapidly progressive, visceral involvement, widespread involvement of most of the extremities, and severe lymphedema. However, the use of systemic treatments is limited because of their side effects, and these aggressive treatments should not be given to patients in the early stage with limited skin disease [2, 7]. The primary treatment goals for CKS should be to pursue a palliative approach to alleviate lymphedema, reduce the size of cutaneous lesions, and stop or delay disease progression. For this purpose, local treatments, such as elastocompression, surgical excision, cryotherapy, radiotherapy, and intralesional chemotherapies, should be preferred [3]. Elastocompression can prevent lymphedema and new lesion emergence, and surgical excision can be performed on selected well-circumscribed lesions, but it is not recommended for multiple large lesions with unclear borders, and care should be taken to minimize scarring after the procedure [3, 6, 7]. Minimal surgery such as curettage may be preferred for the treatment of exophytic, oozing, or hemorrhagic multiple nodular lesions [8]. Among local treatments, 6–40 Gy radiotherapy, intralesional bleomycin, doxorubicin, vincristine, and interferon alpha-2a injections can be administered [3]. Intralesional vincristine is notably effective and generally less painful than bleomycin [2, 3]. However, it is important to note potential side effects such as pain, pigmentation changes, and edema. Additionally, less common side effects like infection and necrosis can occur. Furthermore, systemic toxicity may develop, particularly in patients with multiple lesions [2, 3]. Local treatments for CKS include the use of CO2, argon, Q-switched 755-nm Alexandrite, pulsed-dye, and Nd:YAG lasers [9, 10].

The Nd:YAG laser operates at a wavelength of 1064 nm, selectively targeting hemoglobin and deoxyhemoglobin in CKS lesions [11]. By emitting light at this specific wavelength, the laser is able of penetrating deep vascular structures with minimal damage to surrounding tissues, effectively destroying the vascular lesions associated with CKS [9, 11]. Nd:YAG laser represents a safe and effective option for patients with multiple widespread lesions who are unable to undergo systemic treatment. It may even be considered the primary choice for disseminated disease [9].

Our study demonstrated both dermoscopic and clinical evidence of the rapid, effective, and safe outcomes achieved with Nd:YAG laser treatment. In our cohort of three patients with stage 4 CKS, 42 nodular lesions were treated with the Nd:YAG laser in one or two sessions. Aside from mild atrophic scarring, no other side effect was observed in the patients, and there were no recurrences during the 1-year follow-up period. These findings are consistent with studies conducted by Özdemir et al. and Nasca et al., where Nd:YAG laser treatment resulted in healing with mild atrophic scarring, no other side effects, and no recurrence in follow-up periods of six months and one year, respectively [9, 12].

Another study by Silvestri et al. explored the efficacy of Nd:YAG laser treatment in patients with stage 1–2 CKS skin lesions and AIDS-related KS lesions (epidemic form) receiving antiretroviral therapy [10]. The treatment was effective in 80% of the patients, with minimal side effects such as post-inflammatory hyperpigmentation and mild hypotrophic scars [10]. Similar to our findings, Nd:YAG laser therapy was deemed a safe and effective treatment option.

Notably, a reduction in lymphedema has been reported in the literature in two CKS patients following Nd:YAG laser therapy [9, 13]. Consistent with these reports, our study also observed a decrease in lymphedema in one patient. However, it is important to note that the small sample size of our study represents a limitation. This effect may be attributed to the modulation of cytokine balance and increased lymphatic circulation, mediated by tissue hypoxia-induced elevation of VEGF levels [14].

Conclusions

In summary, our study, along with previous literature, supports the use of Nd:YAG laser therapy as a rapid, effective, and safe treatment option for CKS. The treatment demonstrates favorable outcomes, with minimal side effects and no recurrence. Additionally, Nd:YAG laser therapy may contribute to reducing lymphedema in CKS patients through its impact on cytokine balance and increased lymphatic circulation [13].

Our study provides evidence of the effectiveness and safety of Nd:YAG laser therapy for stage 4 CKS, supported by dermoscopic findings. Nd:YAG laser treatment can be a valuable therapeutic option for both early- and advanced-stage CKS, particularly in cases of resistant skin lesions or patients

receiving systemic therapy. The treatment is well tolerated, yielding rapid improvement within 2–3 weeks. Nd:YAG laser therapy may also be beneficial for HIV+ patients due to its immunosuppression-free nature, ease of application for recurrent lesions, and overall effectiveness and safety.

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