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Comparative Study

Rendu-Osler's disease: the effectiveness of mixed technology laser (Alexandrite laser combined with Nd:YAG laser)

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ABSTRACT

Rendu-Osler's disease is an autosomal dominant disorder that usually affects the skin and mucous membranes, but also internal organs can be involved. To date, laser treatments have been used only to treat systemic lesions, while diathermocoagulation has been considered the primary treatment for skin lesions. We wished to evaluate the effectiveness of treatment with Alexandrite laser combined with Nd:YAG laser on vascular skin lesions of these patients. Vascular skin damage of 3 patients afflicted with Rendu-Osler's disease was treated with Alexandrite laser combined with Nd laser:YAG laser. After 3 treatments, once a month, we found a remarkable improvement in skin lesions. The cutaneous manifestations of Rendu-Osler's disease do not increase the mortality of these patients but are often the source of psychological discomfort. For this reason, it is necessary to have an effective treatment on hand and the Alexandrite laser combined with Nd:YAG laser represents an excellent therapeutic alternative to the diathermocoagulation.

INTRODUCTION

Rendu-Osler's disease, also called hereditary hemorrhagic telangiectasia (HHT), is an autosomal dominant disease with age-linked penetrative qualities. The incidence is about 1-2 cases per 100,000 annually, which makes this disease rare (1).

Two different genes, located on chromosomes 9 and 12 (2, 3), are known to be responsible for the development of the pathology. These genes encode two transmembrane proteins expressed by endothelial cells: activin receptor-like kinase 1 and endoglin. The first is the transforming growth factor ß (TGF-ß) receptor, which can bind both TGF-ß1 and activin A together. The second has a high affinity for TGF-ß1 and TGF-ß3, both involved in the angiogenesis processes and maturation of blood vessels. These abnormal proteins cause the disappearance of the perivascular support (pericytes, smooth muscle and elastic fibres), leading to the loss of connection between the endothelial cells; this results in vascular fragility, typical of the disease.

Frequent epistaxis might be the only symptom during infancy, but most clinical manifestations usually begin during adolescence; mucocutaneous telangiectasias, which are the hallmark of this disease, usually appear during the 2^{nd}-4^{th} decade of life.

Clinically, telangiectasias appear as macules or papules and tend to be smaller than 3 mm. In some cases, nodular elements and spider angiomas are observed. Any trauma can cause bleeding.

Cutaneous lesions occur symmetrically, potentially on the entire body surface; however, the upper half of the body is the most frequently involved: lips, eyelids, and conjunctivas are the most classical localizations. The hands can also be affected: a typical location is indeed the nail bed. Palmar and plantar regions can be involved as well.

Mucosal lesions are often observed in these patients: the entire oro-pharyngeal tract can be involved, but telangectasias can be found in any tract of the gastroenteric system. Less frequently, the genitourinary tract can be affected as well. Tongue appearance is very characteristic because of the fungiform aspect of the papillae: even a single dilated vessel can cause the expansion of a papilla. The quantity and frequency of bleeding determine the gravity of the disease.

Internal organs can also be affected, particularly the lungs: HHT is one of the most frequent causes of artero-venous pulmonary fistulae. As a result, these patients may complain of dyspnea, and their fingers may appear

cyanotic. Other vascular manifestations may be artero-venous pulmonary anastomosis, artero-venous anastomosis in the liver (which can lead to hepatic cirrhosis), and aneurysms of different vessels, particularly the aortic arc and the splenic artery, while ocular and central nervous system lesions are less frequent.

The biopsy of cutaneous lesions shows irregularly dilated venules and capillaries, whose walls are formed by flattened endothelial cells within the papillary derma. In the most recent lesions, a slight inflammatory infiltration can be observed.

Treating skin lesions is still not codified: diathermocoagulation and laser therapy are possible options. A case series of 3 patients affected by Rendu-Osler's disease treated with Nd laser:Yag 1064 nm λ is presented.

MATERIALS AND METHODS

The subjects were treated with long-pulse Alexandrite 755 nm and long-pulse Nd:YAG 1064 nm emitted with Mixed Technology (Duetto MT and Thunder MT, Quanta System Spa, Samarate, Varese, IT). Both wavelengths have been used in sequential emission: first 755nm Alexandrite, followed by 1064nm Nd:YAG. All subjects released written informed consent for the procedure.

In the literature, the sequential emission of 755nm plus 1064 nm is already present (4). Moreover, Nd: Yag laser in single emission mode has been widely used for the treatment of epistaxis (4-7) or vascular lesions of the oral cavity (4) and gastrointestinal tract (8,9). However, to our knowledge, this specific combination of lasers has never been described for treating cutaneous lesions in HHT.

CLINICAL CASES

Clinical case 1

A 43-year-old male patient came to our attention because of numerous angiomatous lesions scattered all over his body but predominantly affecting his face and hands (Fig. 1). Oral involvement was also noted. Clinically, most lesions were macules, but papular lesions and spider angiomas were also observed. The anamnesis was positive for HHT familiarity. The patient also reported frequent epistaxis during childhood. CBC and coagulation tests were performed, together with liver and kidney function tests, chest radiography, and a faecal occult blood test. No alteration was found.

Fig. 1. *Patient 1: numerous angiomatous lesions localized on the face.*

The cutaneous lesions were disturbing to our patient, as they were in visible areas: medical treatment was then required. Three treatments of mixed technology (755nm- 1064nm) laser were performed once a month for three months.

The result was satisfying for the patient and the physician, as an important reduction of lesions was seen.

Clinical case 2

A 34-year-old female patient affected by Rendu-Osler's disease came to our attention for specific treatment of angiomatous lesions located on the face, upper limbs and oral cavity mucosa. The patient had already been treated with laser therapy because of frequent epistaxis, with good results. However, over the last few years, the involvement of visible skin has progressively increased, becoming a source of psychological uneasiness for the patient. For this reason, she decided to come to our department. Therefore, treatment with mixed technology laser was performed. She underwent three sittings at one-month intervals.

At the end of the third treatment, the patient was very satisfied as her lesions, particularly those on the face, were notably reduced.

Clinical case 3

A 47-year-old male patient affected by Rendu-Osler's disease presented to treat cutaneous lesions (Fig. 2). Previous laser treatments had already been performed because of epistaxis and gastroenteric manifestations. Some cutaneous lesions were previously treated with diathermocoagulation with good results. The physical examination showed numerous purplish papules diffused over the entire body. Even mucous membranes of the oral cavity showed angiomatous lesions. The patient reported bleeding due to trauma of the papular lesions.

Fig. 2. *Patient 3: numerous macules and purplish papules on the hand.*

Once again, treatment with mixed technology laser was performed. After three sittings, lesions were notably reduced (Fig. 3). Unfortunately, three months later, a new increase in lesions was noted. For this reason, two more sittings were performed, with good clinical results.

Fig. 3. *Patient 3: reduction in number of the lesions after three treatments with mixed technology laser.*

DISCUSSION

Rendu-Osler's disease is an autosomal dominant disorder characterized by cutaneous and mucous vascular lesions associated with systemic involvement. Internal organ lesions and artero-venous pulmonary fistulae are the leading cause of mortality and morbidity in these patients.

Even if skin and mucosal lesions do not cause mortality, they can burden these patients and their social life, as the face - fundamental in social interactions – is often affected. For this reason, these subjects often research a medical treatment that effectively deals with cutaneous lesions to obtain the best aesthetical result.

To date, laser treatments have been used for this pathology, especially to treat epistaxis (4-7, 10, 11) and the accessible tracts of the gastroenteric system (8,9). However, in the literature, only a few cases where cutaneous HHT is treated with laser therapy. In most cases, a tunable dye laser was used (12-13). With this case series, we wanted to evaluate the effectiveness of the mix technology laser (Alex 755 nm λ - Nd:YAG 1064 nm λ) for treating HHT skin vascular lesions. The wavelength 1064 nm could be considered useful for treating vascular lesions for two main reasons: its excellent tissue penetration; it corresponds to one of the absorption peaks of haemoglobin.

Our experience shows the effectiveness of 755nm Alexandrite followed by 1064nm Nd:YAG, used sequentially. All 3 patients improved after treatment.

The first shot of Alexandrite turns the haemoglobin into methemoglobin due to the heme component of the blood (14). Therefore, after the first shot, red vessels turn blue. This conversion raises the absorption coefficient of the vessels for the second laser shot provided through Nd:YAG.

Nd:YAG is three times more absorbed by methaemoglobin than Alex (15); this explains the efficacy with lower fluence parameters. Furthermore, mixed technology emission reduces the fluences of the same treatments provided by Nd:Yag alone.

CONCLUSION

The combined use of these two laser technologies increases the advantages of each technique, representing a valid therapeutic option for the treatment of Rendu-Osler's cutaneous manifestations.

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