Comparison of CO2 Laser and Cryotherapy for Clinical Improvement in Vascular Tumor Lesions in Patients with Klippel Trenaunay Syndromes: A Rare Case

Pipim Septiana Bayasar¹, Khairuddin Djawad², Airin R. Nurdin³, Idar Mappangara³, Paskalis Indra Suryajaya¹

¹Department of Dermatology and Venereology, Faculty of Medicine, Hasanuddin University, Makassar, South Sulawesi, Indonesia
²Department of Dermatology and Venereology, Faculty of Medicine, Wahidin Sudirohusodo Hospital, Makassar, South Sulawesi, Indonesia
³Department of Cardiovascular, Faculty of Medicine, Hasanuddin University, Makassar, South Sulawesi, Indonesia.

ABSTRACT
Klippel Trenaunay’s syndrome (KTS) has three main characteristics: (1) varicose veins; (2) hypertrophy (soft tissue, bone); and (3) malformations (veins, capillaries). Hemangioma is a vascular anomaly in the form of endothelial cell tumors accompanied by cell hyperplasia. Vascular doppler examination and MSCT-scan arteriography found venous malformations, soft tissue thickening, capillary malformations and varicose veins which support the diagnosis of KTS syndrome. One case was reported, a 29-year-old male treated with a CO2 Laser (frequency 500; fluence 20ml; energy 63.69 J / cm²), combined Laser CO2 (frequency 500; fluence 20ml; energy 63.69 J / cm²) with Timolol maleate 0.5% every 4 hours occlusive and cryotherapy for hemangioma lesions. Significant improvement in lesions was obtained with the use of cryotherapy with a low recurrence rate compared to the use of CO2 laser.

INTRODUCTION
Klippel-Trenaunay-Syndrome (KTS) is a rare syndrome. This condition involves soft tissue (such as skin and muscles), bones and blood vessels. This disorder has three characteristics, namely varicose veins, abnormal hypertrophy and bone tissue as well as venous and capillary malformations (hemangiomas or port-wine stains). (1) Diagnosis is made if it fulfills 2 of the 3 criteria above.(2) This syndrome is not affected by gender, and few report the incidence of Klippel-Trenaunay Syndrome.(3) There is no difference between the ratio of male and female(4) The most common site of predilection of KTS in the lower extremities, KTS is often associated with the genetic mutation of Phosphatidylinositol-4,5-Bisphosphate 3-Kinase Catalytic Alpha Subunit (PIK3CA) and Angiogenic Factors with G-Patch and FHA Domains 1 (AGIP1) genes.(5) KTS is often mistaken as Parkes Weber’s Syndrome, but if you look closely, even though it has almost the same clinical manifestations, only the etiology and prognosis of these two diseases are different.(6) A multidisciplinary approach to KTS is needed because of the many involved organs. Related sections include orthopedic surgery, vascular surgery, skin and genital specialties, and geneticists.(7) Laser surgery can be the first choice therapy for treating skin vascular lesions.(8) Cryosurgery is a therapeutic modality that can be applied to treat hemangioma lesions in KTS by causing tissue damage. This method is a method that is simple, effective and tends to be easy to do.(9)

CASE HISTORY
A 29-year-old man came to dermatology and venereology clinic of Wahidin Sudirohusodo Hospital with chief complaints of swelling in the left leg that was felt since fifteen years ago, which was felt increasingly growing. Black spots appear more or less since ten years ago initially only appeared on the back of the thigh which is felt increasingly extended to the front area of the thigh. Black spots are recognized by the patient to bleed very easily when exposed to friction. Dermatological examination of the inferior region of the extremity showed efflorescence in the form of edema, purplish-red papules, varicose vein and hyperpigmentation patch. Histopathological examination, the results obtained on pieces of skin tissue obtained epidermis coated with layered squamous epithelium which shows a picture of maturation and contains a core without the atypical sign. In the superficial dermis contains proliferation of blood vessels of varying sizes, which are coated by a layer of endothelial cells, with a flat, round-shaped core without atypical markings. The lumens of blood vessels appear to contain deposits of erythrocytes. On examination of the dermoscopy, red lagoons or lacunae globular structures are found, well-defined, various sizes scattered on a homogeneous colour basis. On examination found both superficial veins and deep compressed deep veins and no description of the thrombus was found in it. In the examination of flow in blood vessel malformations, a slow-flow picture is found indicating the flow of the venous system.
Figure 1. (A, B) In the inferior extremities Sinistra acquired efflorescence of oedema, purplish-red papules, varicose vein and hyperpigmentation patches.

Figure 2. Dermoscopy examination shows a picture of Red lacunae

Figure 3. At histopathology screening (enlargement 20x (a) 10x (b)) with Hematoxylin Eosin staining obtained the proliferation of blood vessels coated with endothelial cells accompanied by an overview of the lumen of blood vessels containing a deposit of erythrocytes.

Figure 4. The depiction of the venous malformations of the Popliteal sinistra area (A), with the characteristic Slow-flow (B), the venous malformations of the Thighbals area of Sinistra (C), with the characteristics of slow-flow (D) and the venous malformations of the area of the dorsum pedis sinistra (E) with a view of thickening of the surrounding soft tissue (sign *)
On examination of the deep veins of the inferior extremities of the sinistra, there were no features of thrombus or venous insufficiency. On examination of the inferior arterial extremity arterial flow, a smooth impression of blood flow was found, with a picture of biphasic flow ranging from as high as the femoral to distal arteries. There were no lesions or plaques found in the arteries.

MSCT-Scan Arteriography examination, obtained soft tissue impression with bilateral lower extremity capillary malformation, especially the sinistra and varicose vein saphena magna sinistra.

![Figure 5. In the right extremities (subcutis regio cruris thickened; visible capillaries) and left extremities (subcutis regio cruris and the femoral regio appear thickened; seen dilation and tortuous vein saphenous Magna; seen dilation capillaries regio cruris)](image)

From the heart and blood vessels, 2 mg / 24 hour / oral warfarin therapy and compression stockings are given. The first day of the visit, patients were only given 2 different meetings, at location 1 (CO2 laser frequency 500; fluence 20ml; energy 63.69 J / cm2), location 2 (combination of CO2 laser frequency 500; fluence 20ml; energy 63.69 J / cm2 and timolol maleate drop 0.5% every 4 hours ago).

Control a week after the therapy, there was a better improvement in the lesions given combination therapy of CO2 laser and timolol maleate drop 0.5% (location 1) compared to the location of lesions that were only given Laser CO2 (location 2). Patients were given cryotherapy at 3 different locations, whereas at locations 1 and 2 the therapy continued.

![Figure 7. Visit day 7, There is clinical improvement in therapy (A) CO2 laser and (B) combination of CO2 laser and timolol maleate drop 0.5%, added therapy (C) cryotherapy at the third location](image)

Control 1 week after the action of cryotherapy, there are wounds at the location of the lesions performed cryotherapy, then the patient is given additional therapy in the form of gentamycin ointment. The next week the wound improved and there was a significant improvement that only resulted in side effects in the form of hypopigmentation. Whereas at location 1 and location 2, several lesions reappeared after 3 actions per week either a combination of CO2 laser and timolol maleate drop 0.5% or only given a CO2 laser.

**DISCUSSION**

Vascular anomalies are divided into two categories, namely vascular malformations and vascular tumors. In the case of KTS, most often found due to capillary malformations that provide a clinical picture in the form of Port Wine Stain. However, it is not uncommon to find lesions in the form of hemangiomas.(10) Hemangiomas are endothelial cell tumors that are accompanied by cell hyperplasia.(11) The most common location is found in the face area by 60% and rarely found in the extremities around 15%. Superficial hemangioma lesions involving the dermis have clinical manifestations in the form
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Figure 8. Day 14 visit, lesions reappear in patients treated with (A) CO2 Laser and (B) Combination of CO2 Laser and timolol maleate drop 0.5%. Bullae, erosion and excoriation appear at the location performed (C) Cryotherapy

Figure 9. Visiting day 30, hyperpigmented papules accompanied by hypopigmented patches at the location of the laser action

of lobular and reddish, whereas in lesions deeper in the subcutaneous section a lesion in the form of blush nodules may appear.(12)

The process of vasculogenesis and angiogenesis is thought to cause neovascularization in hemangiomas.(13) Dermoscopy is useful for evaluating the distribution or vascular structure of the superficial epidermis in hemangiomas. red lacunae.(14)

On the examination of MSCT-Scan Arteriography, the impression of soft tissue with bilateral lower extremity capillary malformation was obtained, especially the sinistra and varicose vein saphena magna sinistra. Capillary malformations are often characterized by dilation of the vessels in the papillary and upper reticular dermis. If not treated properly, it will develop into soft tissue and bone hypertrophy.(15)

Vascular malformations consist of various subtypes namely capillary, venous, lymphatic and arteriovenous malformations. This vascular malformation is the result of the failure of vessel formation in the embryogenesis stage in the involution stage.(16) Based on the characteristics of the flow vascular malformations are divided into 2 categories: slow flow (capillary, venous and lymphatic malformations) and fast flow (arteriovenous malformations).(17)

In KTS has the characteristics of slow flow, therefore it occurs due to arterial malformations. Capillary malformation (CM) involves capillaries in the papillary dermis and causes lesions to become a purplish pink macula that appears since birth "port wine stain".(18) Venous malformations arise due to stagnancy in blood flow that can cause thrombosis, and clinically it will appear in the form of skin discoloration, pain and excessive tissue growth.(19)

Lymphedema results from accumulation of water, and electrolytes in the interstitial space which results in changes in the lymphatic system, causing a decrease in functional capacity and morphology.(20)

First-line therapy in hemangiomas can be given corticosteroids, but because of the side effects that are avoided, in this case the patient is treated with carbon dioxide laser, topical thymolol and cryotherapy.

Carbon dioxide laser is the gold standard laser for ablative type laser. The target of this type of laser is liquid in intracellular and extracellular, light energy absorbed by tissue containing water will occur evaporation.(21) Because of its high absorption in carbon dioxide laser tissue it is considered an ideal laser for soft tissue surgery. The continuous wave in this laser produces a beam of light producing a thermal photo effect that causes evaporation of tissue and cell damage.(22)

Timolol maleate 0.5% is a beta blocker group.(23) A study of 278 cases of hemangiomas found significant clinical improvement in the use of timolol maleate compared with the use of ultrapotent corticosteroids.(24) The combination with the use of carbon dioxide laser can accelerate the absorption of timolol maleate.(25)
Cryosurgery is a method of using liquid nitrogen with low temperatures which can irreversibly damage cellular metabolism thereby destroying tissue. (26) This method is an easy, fast, cheap and efficient method for hemangioma cases. Klippel Trenaunay’s syndrome has at least 2 of 3 features that are typical on, such as varicose veins, vascular malformations and soft tissue or bone hypertrophy. Several investigations are needed to diagnose KTS such as dermoscopy, doppler vascular, and MSCT arteriography.

REFERENCES
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