An Overview about Treatment Lines of Syringoma

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Abstract

Syringomas are benign adenomas of eccrine or apocrine ducts. They often present as multiple 1–2-mm flesh-colored to yellow, firm papules. Although they can present anywhere, favored locations include the eyelids and face. Scalp involvement may produce a scarring alopecia. Syringomas develop during puberty and are more common in women than men. Familial and eruptive forms exist. Eruptive syringomas are more common in black males and often involve the chest or penis. The diagnosis of syringoma may be favored by the clinical presentation, but histological evaluation is necessary for definitive diagnosis. Syringomas are benign lesions with no true proliferative capacity. Treatment for these potentially disfiguring lesions is often done for cosmetic purposes. Single lesions may be surgically excised. Patients presenting with the eruptive form may be treated with laser ablation. Electrodesiccation with curettage is also useful for the treatment of multiple lesions. Cosmetic concern is the primary reason patients seek treatment for syringomas, although some patients with a large number of lesions may complain of itching, especially after sweating. Various modalities have been used in treating syringomas with variable result.

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Introduction:

Often seen in a periocular distribution, syringomas are benign skin-adnexal tumours of eccrine origin that manifest as little dome-shaped papules and may affect the aesthetic look of the face. It can also be present on the neck, belly, or external genitalia. Syringoma is derived from the Greek word syrinx, which meaning tube. Eccrine duct tumours are benign adnexal tumours based on their histological features. When cells multiply in the duct's lumen, they form spiral structures that restrict the flow of

perspiration and prevent it from exiting the skin (1) . Syringoma affects 0.6% of the population, most commonly affecting girls throughout adolescence, with an age peak between the years 20 and 30 **(1) .** Cosmetic concern is the primary reason patients seek treatment for syringomas, although some patients with a large number of lesions may complain of itching, especially after sweating. Various modalities have been used in treating syringomas with variable result **(1**)

1. **Scissor excision with secondary intention healing:**

Careful surgical excision followed by healing by second intention. Using castroviejo ophthalmological scissors to remove syringoma lesions individually, respecting their limits, after a very small initial incision and raising of the skin with a fine-toothed forceps, the tumor is easily visualized. Carefully, one can detach and remove the whole lesion, which avoids relapse, and without going in too deep, which might lead to depressed scar. It is not shaving, but actual excision, except performed extremely carefully (*2*).

2. **Dermabrasion:**

Dermabrasion consists of sequential planing of the raised skin lesions with electrical and/ or manual abraders and allowing the wound to heal by secondary intention, it gives excellent cosmetic results with safety to the patients. But it may cause persistent hypopigmentation, persistent erythema, milia, hyperpigmentation, exacerbation of acne patients, small deep pitted scars or localised secondary infection as side effects (*3*).

3. CO2 laser:

Treatment with CO_2 laser is likely the most efficacious treatment modality with tolerable side effects. While it does not consistently offer complete resolution and is most commonly associated with dyspigmentation. Combining this traditional therapy with other technqiues such as TCA peels or using CO_2 lasers in vaporization mode, may be the most promising methods to increase efficacy and minimize side effects. But many of the lesions recures following superficial ablation, and hypopigmentation and atrophy can be observed with deeper ablation **(4)**.

4. Electrocautery:

Electrosurgery was mentioned as one of the standard treatment options with intralesional electrodesiccation of syringoma (*5*).

5.Temporary tattooing followed by Q-Switched Alexandrite laser:

First, the surface epithelium of periorbital syringomas are vaporized by CO2 laser. A drop of black ink previously autoclaved and filtered through a sterile syringe filter is directed on to deepithelialized syringoma lesions (black ink used as a kind of photosensitizer for targeting the ductal adenomas). One or two shots of Q-Switched alexandrite laser are applied to black-stained syringoma lesions. It is safe, less painful, with short recovery times and less post-operative erythema. However black ink used as a kind of photosensitizer for targeting the ductal adenomas and it may fail to enter the duct because of CO2 destruction of the ductal opening in the epidermis(*6*).

6. Argon laser:

The nonspecific photothermic effect of the argon laser is suitable for the treatment of small tumors of the skin. The pulses of argon laser are applied in a slightly overlapping fashion in order to cover the

affected areas, the patient tolerates the burning sensation of argon laser without local anesthesia, white spots on the skin surface, similar to second degree burns are observed at treatment sites immediately after therapy (*7*).

7. Erbium YAG laser:

The use of pulsed erbium YAG laser is an effective method for treatment of different superficial periorbital cutaneous lesions. The erbium laser creates a thin coagulation zone of 20 μm, so it could clear tumor tissue thoroughly and accurately. The tissue removal is easy for isolated lesions. However, for deeper or fusion lesions, more than five treatments are needed, and the long process may be unacceptable for patients **(8).**

8. Systemic therapy:

(a) Isotretinoin:

Oral isotretinoin was reported as a successful treatment in 2 cases and ineffective in other 1 reported case **(9)**

(b) Tranilast:

N-[3,4-dimethoxycinnamoyl]-anthranilic acid (tranilast) inhibits the release of some chemical mediators by mast cells, and is widely used in Japan to treat patients with bronchial asthma, atopic dermatitis, allergic rhinitis, keloid and hyper trophic scar. In addition, some case reports have briefly men tioned that tranilast is also effective for syringoma. Oral tranilast was cited in 2 case reports with good improvement after 3 and 8 months of daily tranilast **(9)**

9. Topical therapy:

(a) Atropine:

One case of topical atropine resulted in significant relief of pruritus with reduction of syringoma lesion size **(10).**

(b) Tretinoin:

Topical tretinoin was reported in treatment of eruptive syringomas resulting in flatter lesions with reduced erythema **(11).**

(c) Trichloroacetic acid (TCA);

The TCA pretreatment removes some bulk of the surface of the lesions before CO2 laser, thereby reducing the number of laser passes required to flatten the remainder of the lesions. It gives good cosmetic results with high clearance, no recurrence rates and no scarring after ablation with CO2 laser **(4).**

Another treatment modality for syringoma is botulinium toxin, Botulinum toxin A (BTXA) is a neurotoxin widely used in dermatology **(12).**

Laser light properties:

Laser light has several unique properties, monochromicity in which laser light contains a single wavelength. So it can be selectively absorbed by specific chromophores such as melanin or hemoglobin, coherence which means that laser radiation waves travel virtually parallel with a minimal degree of divergence. And collimation which means that waves have a high ordered pattern allowing the beam

to be propagated across long distance without spreading and to be focused on a small spot with very high power density **(13)**.

Laser tissue interaction:

The effects of laser on tissue are divided into thermal, mechanical, and chemical effects **(14)**.

• **Thermal effects:**

At temperature below 100°C, macromolecules, proteins, and DNA molecules become denaturated. At temperatures greater than 100°C, intracellular water exceeds its boiling point and vaporization occurs. The steam produced causes damage to cells and blood vessels. Further heating over this temperature leads to desiccation and scarring. When light is absorbed by a target, heat loss occurs immediately, a process known as thermal relaxation. The speed or thermal relaxation varies according to thermal relaxation time (TRT) of the tissue, which is the time taken for a structure to cool to half the temperature to which it has been heated. The extent of thermal damage is influenced first by the degree of the temperature achieved, which determines the damage to the target and second by the length of time the target is at the temperature, which is influenced by the heat conduction. Finally, the extent of the tissue damage is governed by the energy density, pulse duration, and heat conduction **(15)**.

• **Mechanical effects:**

When the pulse duration is less than the TRT, there is a sudden thermo-elastic expansion due to spatially localized heating. This sudden change creates acoustic waves that evidently damage the absorbing tissue **(15)**.

• **Chemical effects:**

Laser technology has been relined to reach perfect selectivity to a specific target, decreasing unwanted side effects such as infections, dermatitis, pigmentation, and scar formation. The use of photosensitizing agents enhances the effect and specificity of laser increasing the therapeutic outcomes in treatment of acne, actinic diseases, and photorejuvenation **(14)**.

Properties of CO_2 laser

The CO_2 laser emits a continuous invisible beam of l0,600 nm wavelength. It can be focused or defocused, depending on its focal point and the distance at which the hand piece is held from the skin surface. The spot size is small when the hand piece is held close to the skin surface forming the focused beam, which allows using the CO_2 as a cutting tool. The de focused beam is made when the spot size gets large by increasing the distance of the hand piece from the skin surface, that permitting using its use as an ablative tool for the superficial skin without damage to the deep structures **(16)**.

CO_2 laser in syringoma

The CO_2 laser is the most widely used ablative laser therapy in syringoma but is usually associated with adverse events. Pinhole and multiple drilling methods using CO_2 laser yielded excellent cosmetic results with minimal adverse effects. Fractional lasers reduced the downtime and complications compared to non-fractionated ones. Non-ablative fractional lasers could be advantageous in terms of easy operation, minimal side effects and moderate recovery period compared with ablative lasers **(17)**.

CO_2 laser safety:

Chlorhexidine skin preparation should be avoided; as it can be vaporized by the laser and binds irreversibly to the cornea leading to eye opacity. Alcohol should not be used due to its flammability. If desired, preparation of the skin with betadine appears to be safe during CO_2 laser surgery. All reflective jewelry should be removed from the laser field to reduce the risk of unintended laser beam reflection, resulting in injury to the patient or the operator. Operative instruments should ideally be blackened or roughened so as to eliminate reflections and should be kept distant from the immediate treatment site. The patient and all other persons present in the laser room must wear appropriate laser safety glasses or goggles specific for CO_2 lasers. Although the laser beam is filtered by conventional glasses which are made of glass, it is safer to use specific laser safety glasses that have side shields to protect from wandering side impacts of the laser beam **(18)**.

CO_2 laser plume contains carbonized particles as well as cell and tissue fragments. This laser plume is more carcinogenic than cigarette smoke so the smoke evacuator tube should be held as close as possible to the laser impact site, ideally no more than 1 cm away **(18)**.

Complications of CO_2 laser:

Although the rate of serious complications with CO_2 laser is low with experienced operators, there is considerable risk from this procedure due to poor technique, inappropriate patient selection and inadequate pre and post-operative care **(19)**.

The complications that can be observed with CO_2 laser can be classified into minor, serious and severe:

Minor complications are post-inflammatory hyperpigmentation or erythema over the treated area which is common in colored skin and causes anxiety to patients. However, this is temporary lasting for only about six weeks and gradually improves. Serious complications are localized viral, bacterial or candidial infection, delayed hypopigmentation, persistent erythema, and prolonged healing. The most severe complications are hypertrophic scarring, disseminated infection, and ectropion **(19)**.

Botulinium toxin

Botulinium toxin is one of treatment modalities for syringoma, Botulinum toxin A (BTXA) is a neurotoxin widely used in dermatology **(12).**

The exact mechanism of how BTX-A works on syringomas is unknown; it could be explained by the blockade of the cholinergic terminals by the inhibition of the SNAP-25 (synaptosome-associated protein of 25 kd) of the SNARE complex, therefore inhibiting the release of acetylcholine from cytoplasmic vesicles of the nerve ending. The result could be chemo-dennervation of cholinergic nerves, thus targeting the autonomic control of eccrine sweat glands. Given that the syringoma is a tumor derived from these glands, this could explain the clinical result obtained from BTXA **(20).**

Botulinum neurotoxins produced by the gram-positive, anaerobic Clostrridium botulinum are the most potent toxins **(21).**

In the 1920s, a crude form of BTX-A was isolated and the first attempt at purification was done. Pure BTX-A was isolated in crystalline form in 1946 **(22).**

The first insights into the mechanism of action of the toxin came in the 1950s where it was shown to block the release of acetylcholine from motor nerve endings **(18)**.

Botulinium toxin use in the field of dermatology began in the early 1990s when improvement of facial wrinkling was observed, on treating patients with hemifacial spasm with BTX-A **(22)**.

The bacterium C. botulinum produces eight serologically distinct toxins, which are designated as types A, B, C1, C2, D, E, F and G. Only seven of these have been associated with muscle paralysis and could be used for therapy. The similarity of effect of the clostridium toxins at the nerve terminals is a result of a closely related protein structure. The toxin is synthesized in the bacterial cytosol, where it is released in the culture medium only after bacterial lysis **(22)**.

Botulinum toxin A is a safe and effective treatment. Knowledge of the pharmacologic basis of therapy will be useful for achieving consistent therapeutic results. The human nervous system is susceptible to five toxin serotypes (BTX-A, B, E, F, G) and unaffected by two (BTX-C. D). BTX does not affect the synthesis or storage of acetylcholine (Ach), but rather it acts by blocking the release of Ach vesicles bound from the presynaptic terminal of the neuromuscular junction (NMK) **(21)**

Intradermal injection of the diluted botulinum toxin type A by using an insulin syringe 100u (1ml), the dose per injection site is 1 to 2 U into the lesion with a distance between injection sites of 1 cm2 in the periocular area **(23)**

Side effects: hematoma or Eyelid ptosis which can be avoided by injecting superficially with posterior directionality **(24).**

Conclusion

Among ablative lasers, fractional laser modality has been shown to be the safest option. Despite its usefulness in combating Syringoma, the drug is not without side effects. The Er:YAG laser when combined with botulinum toxin A for the treatment of syringoma could be safer and more effective treatment than traditional treatment methods.

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