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THERAPEUTIC HOTLINE: LETTER

DERMATOLOGIC THERAPY WILEY

Treatment of three hereditary leiomyomatosis patients with cryotherapy

Belkız Uyar[1] | Emine M. Acar[2] | Aslı Subaşıoğlu[3]

[1]Department of Dermatology and Venerology, Kırşehir Training and Research Hospital, Ahi Evran University, Medical Faculty, Kırşehir, Turkey

[2]Kırşehir Training and Research Hospital, Kırşehir, Turkey

[3]Department of Medical Genetics, Ataturk Training and Research Hospital, Izmir Katip Celebi University, Izmir, Turkey

Correspondence
Belkız Uyar, Department of Dermatology and Venerology, Ahi Evran University Medical Faculty, Kervansaray District, 2019, Street No 1, 40200 Kırşehir/Turkey.
Email: belkisuyar@gmail.com

Abstract

Hereditary leiomyomatosis and renal cell cancer (HLRCC) syndrome is an autosomal dominant disorder characterized by cutaneous leiomyomas (CLM), uterine leiomyomas, and the increased risk of renal cell carcinoma. Piloleiomyomas develop from the arrectorpili muscle and are usually painful. For 22% of the affected patients, the pain is reported to impair their life quality. Since there are few case reports about cryotherapy for cutaneous leiomyomas in the literature, we have decided to present three patients who had painful cutaneous leiomyomas treated with cryotherapy.

KEYWORDS

hereditary leiomyomatosis, cryotherapy, treatment

1 | INTRODUCTION

Hereditary leiomyomatosis and renal cell cancer (HLRCC OMIM 150800) syndrome is an autosomal dominant disorder characterized by skin leiomyomas (CLM), uterine leiomyomas, and the increased risk of renal cell carcinoma. CLMs develop during puberty or late adulthood, usually with a smooth surface, skin colored or pink-brown papules or nodules with a diameter of 0.2–2.0 cm (Alam et al., 2005; Garman, Blumberg, Ernst, & Raimer, 2003). More than 300 families with heterozygous mutations in the fumarate hydratase (FH) gene and clinical features of HLRCC have been reported (Bhola, Gilpin, Smith, & Graham, 2018).

In HLRCC, 89% of cutaneous leiomyomas are characterized painful lesions in response to cold, trauma, or mild touch. Piloleiomyomas develop from the arrectorpili muscle and are usually painful. For 22% of the affected patients, the pain is reported to impair their life quality (Alam et al., 2005).

2 | CASE REPORTS

Case 1 A 49-year-old female patient presented to our clinic with painful lesions on the skin. The painful lesions developed on her right abdomen region first nearly 15 years ago. Based on her medical history, it was learned that she had undergone total hysterectomy and bilateral salpingo-oophorectomy for uterine myomatosis two years ago. Dermatological examination revealed multiple brown tender papules and nodules of varying in size from 5 mm to 1 cm over the right abdomen and arms. A few tumors were also observed over back.

Although a biopsy was suggested at that time, the patient went to a general surgery specialist, to remove some of the lesions in the abdominal region surgically, and the lesions were sent to pathology.

Histopathology revealed normal epidermis and superficial dermis showing interweaving bundles of spindle-shaped cells of dermal smooth muscle.

Masson trichrome staining was consistent with smooth muscle staining. Immunohistochemically, neoplastic cells were evaluated as s100 (–), SMA (+), desmin (+), CD68 (–). The patient was diagnosed with multiple dermal piloleiomyomatosis.

Case 2 A 28-year-old man, son of the patient in Case 1, presented with painful lesions emerged on his back, which began to develop nearly 6 years ago.

A dermatological examination revealed; erythematous brown nodules on the left arm and left side of the lumbar region. The scars from the previous surgical procedures were also seen on the upper back.

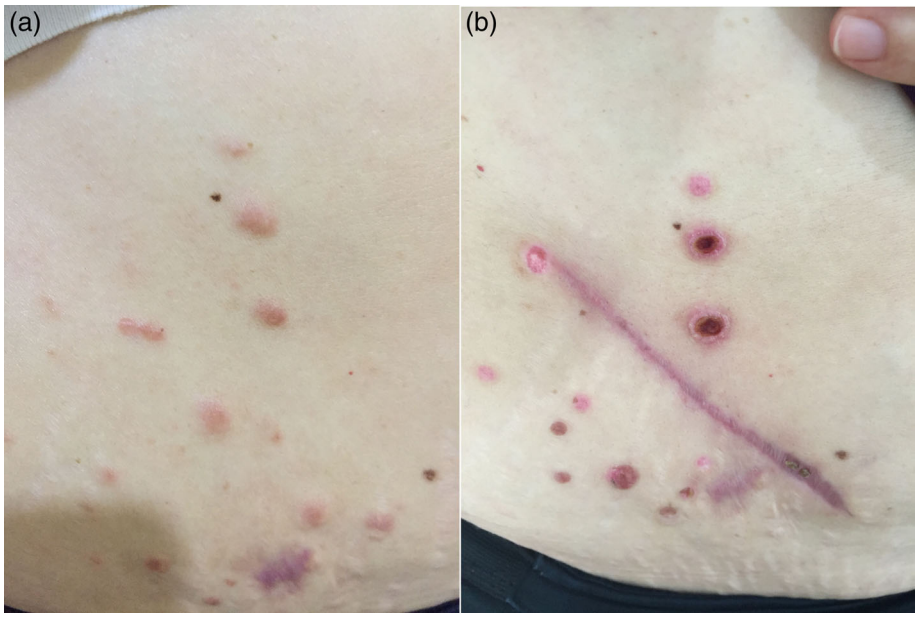

FIGURE 1 (a) Erythematous, brown nodules on the abdomen of the first case (b); appearance of the lesions 15 days after cryotherapy and a scar related to surgical incision

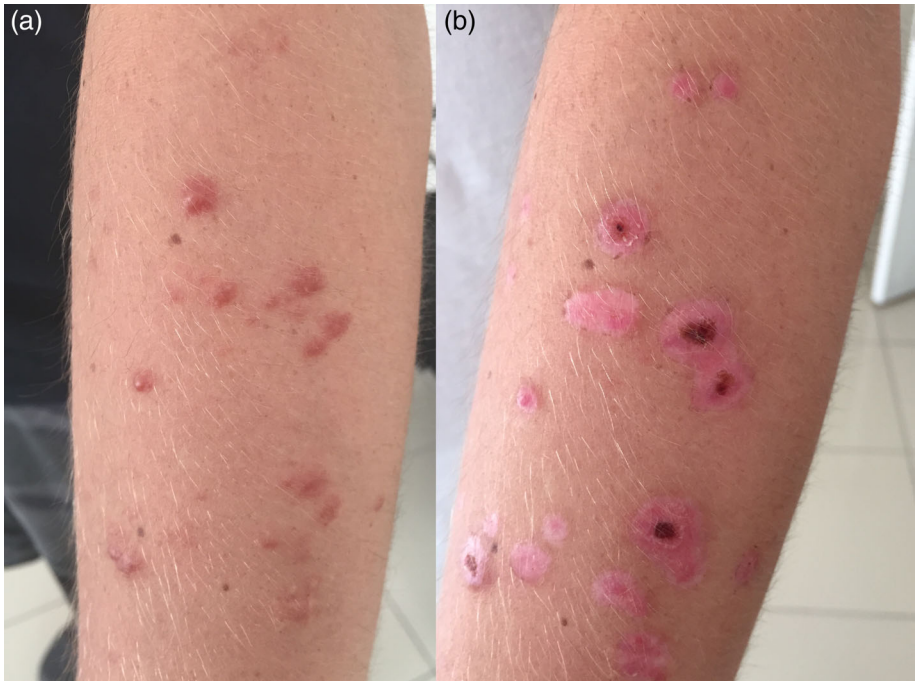

FIGURE 2 (a) Erythematous, brown nodules on the arm of the second case, (b); 15 days after cryotherapy

DNA sequencing showed a heterozygous mutation c.404A > G resulting in p.H135R in the exon 4 of FH gene, in both of the patients.

The identified nucleotide change was not found in the healthy brother of the Case 2.

Case 3 A 54-year-old male patient presented to our clinic with painful lesions that have existed for 35 years. A dermatologic examination revealed multiple skin-colored, pink or brown tender papules and nodules on his left arm, left chest, and back. Dermatopathology confirmed cutaneous leiomyomata.

He stated that although the lesion on his left chest, which had been very painful, had been surgically removed 2 years ago, the pain had not resolved. There was no significant feature in his family history.

The abdominal IV contrast computed tomography (CT) results were normal in all three patients.

We performed a cryotherapy session for the treatment of the lesions in the form of a double freeze–thaw cycle for 20–45 s in all three cases.

At 15 days postcryotherapy, some of the lesions had completely disappeared, leaving atrophic scars, and some had decreased in size (Figures 1 and 2). The patients reported complete resolution of pain in healing lesions and shrinking lesions. For all patients, there was no recurrence of pain one year after treatment.

3 | DISCUSSIONS

For early diagnosis of aggressive renal tumors, intravenous contrast-enhanced renal MRI or CT scans are recommended, which have higher diagnostic accuracy and greater benefit than renal ultrasound (Toro, et al., 2003). No abnormalities were observed as a result of the abdominal CTs with IV contrast in all three cases.

Since cutaneous leiomyomas do not resolve spontaneously, treatment is required especially in painful lesions.

Painful lesions can be excised; however, this treatment may be impractical due to the high rate of recurrence, leaving unwanted scars, and because leiomyomas are often grouped as a "school of fish". Destructive methods such as electrodessication, radiotherapy, and carbon dioxide laser ablation have been used with varying results (Basendwh, Fatani, & Baltow, 2016).

Pharmacological treatments have been reported in small studies and case reports. Drugs that block smooth muscle contractions, such as nifedipine, phenoxybenzamine, nitroglycerin doxazosin, and drugs that target nerve activity such as gabapentin, topical analgesics, have been used (Basendwh, Fatani, & Baltow, 2016). Botulinum toxin injections may be effective by inhibiting the release of certain neuropeptides, such as substance P and glutamate, which reduces central pain signals (Basendwh, Fatani, & Baltow, 2016).

Cryotherapy is an alternative to invasive surgical techniques. There are few published case reports on the efficacy of cryotherapy as a treatment modality for a large number of painful leiomyomas (Archer, Whittaker, & Greaves, 1988; Basendwh, Fatani, & Baltow, 2016). Archer et al. assumed that cryotherapy reduces pain by destroying nerve cells rather than destroying tumor cells (Archer, Whittaker, & Greaves, 1988). We agree with this assumption because, all three patients reported that their pain complaints disappeared completely after the cryotherapy even for the lesions that were reduced in size instead of completely disappearing.

In the light of the literature and the results of our cases, we can assert that cryotherapy is an effective method of treatment for achieving acceptable cosmetic results and relieving the pain in cutaneous leiomyomas.

CONFLICTS OF INTEREST

The authors declare no potential conflict of interest.

ORCID

Belkız Uyar https://orcid.org/0000-0003-3687-6760

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