Reed's syndrome: case report and review of literature

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Post Dermatol Alergol 2012; XXIX, 2: 139–142

Abstract

Leiomyomas are benign tumors that develop from smooth muscle cells. Coexistence of the rare skin manifestations together with uterine leiomyomas is known as the Reed's syndrome (multiple cutaneous and uterine leiomyomatosis – MCUL). The suspicion of Reed's syndrome, which is based on the morphology of the skin lesions (multiple, small, oval, reddish-brown tumors around hair follicle, mostly painful) should be confirmed by the histopathological examination. All patients with cutaneous leiomyomatosis should undergo prophylactic examinations to exclude renal cell cancer. Treatment is limited and based on surgical excision of the lesion, carbon dioxide laser ablation or cryosurgery. We have reported a case of Reed's syndrome with typical occurrence of skin changes, uterine leiomyomas and renal cysts. Regular checkup is required in this group of patients because of the higher risk of development of malignant changes.

Key words: leiomyoma, Reed's syndrome, benign tumour.

Introduction

Leiomyomas are benign tumors that develop from smooth muscle cells. Coexistence of the rare skin manifestations together with uterine leiomyomas is known as the Reed's syndrome (multiple cutaneous and uterine leiomyomatosis – MCUL). The disease inherits autosomal dominant pattern. When the syndrome manifests also with kidney cancer it is known as hereditary leiomyomatosis and renal cell cancer (HLRCC). A mutation of the fumarase gene located on the 1st chromosome seems to be the cause of all the variants of the disease [1, 2].

The suspicion of Reed's syndrome, which is based on the morphology of the skin lesions (multiple, small, oval, reddish-brown tumors around hair follicle, mostly painful) should be confirmed by the histopathological examination. During the diagnosis the lesions should be assigned to one of the three types. The most common piloleiomyomas are believed to arise from the pili muscle, genital leiomyomas – from genital muscularis tunica or muscles of the nipple and angioleiomyomas – from tunica media of the skin veins [3]. Tumors of the first two subtypes are multiple, while in the third type they are most often single and located deeper in the skin. All patients with cutaneous leiomyomatosis should undergo prophylactic examinations to exclude renal cell cancer [4].

Treatment is limited and based on surgical excision of the lesion, carbon dioxide laser ablation or cryosurgery [5]. The effectiveness of tumor pain relieving treatment is limited.

Calcium channel blockers particularly nifedipine, phenoxybenzamine, doxazosin, gabapentin and local treatment with 9% hyoscine hydrobromide or α-adrenoceptor blocker are helpful in alleviating the pain.

Case report

A female patient, aged 59 years, visited the dermatological outpatient clinic because of disseminated nodules located on the trunk and extremities. The skin lesions first occurred 20 years before and demonstrated slow but constant progression. Her past medical history included hysterectomy that was performed because of uterine leiomyomas that caused irregular menstrual bleeding. Her mother had similar lesions but she was never properly diagnosed. The patient has also received treatment for rheumatoid arthritis and hypertension.

During the physical examination, multiple nodules were observed. They were skin-colored to brown, up to 5 mm in diameter, located on the left shoulder and on the left side of the cleavage. A smaller number of lesions were found on the dorsal side of the left forearm and on the medial side of the arm. Local tenderness was observed during strong palpation of the lesions.

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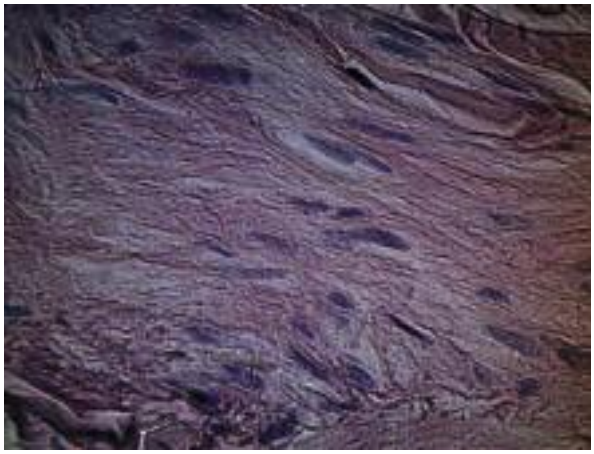
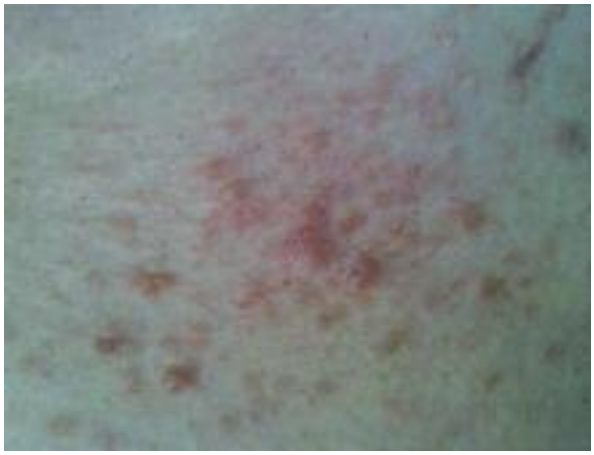


Fig. 1. Histopathological examination of one of the no-dules

Fig. 2. Histopathological examination – SMA positive, VIM positive, S 100 negative



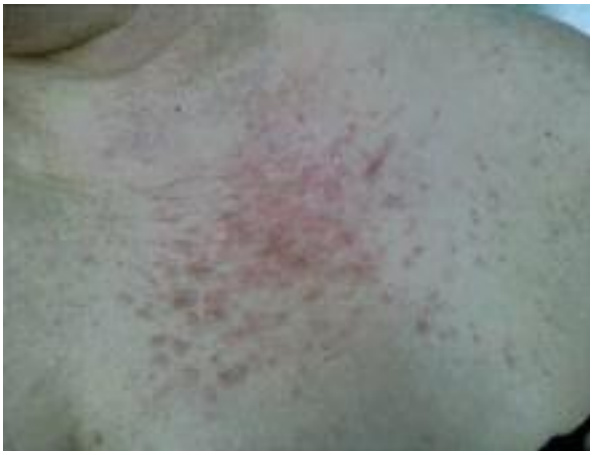


Fig. 3 A-B. Female, aged 59 years, multiple, small, oval, reddish-brown tumors around hair follicle

The histopathological examination of one of the nodules confirmed the diagnosis of leiomyoma cutis, SMA positive, VIM positive, S 100 negative (Figures 1-4).

In 2010, the patient was admitted to the Dermatological Department of our University, where detailed diagnostic procedures were performed in order to exclude any systemic changes (e.g. kidney tumor). Based on the clinical manifestations, past medical history (hysterectomy) and histopathological findings, the diagnosis of the multiple cutaneous and uterine leiomyomatosis (Reed's syndrome) was made.

Laboratory tests, which included FBC, biochemical and enzymatic tests, coagulogram, Latex-R, Waaler-Rose's reactionand urine analysis, did not reveal any abnormalities. The ECG and chest X-ray were normal. During the abdominal ultrasound, two cysts were found – one (47 mm in diameter) in the superior pole of the right kidney and one in the cortex of the left kidney (18 mm in diameter). Neurological and gynecological consultations did not reveal any abnormalities.

Bigger nodular lesions were surgically excised and other were treated with contact cryosurgery with liquid nitrogen. Because of rheumatoid arthritis the patient received steroid therapy (methylprednisolone 4 mg daily) and methotrexate (10 mg once a week).

The patient is under medical supervision of the dermatology outpatient clinic in Katowice (because of the skin lesions) and internal disease outpatient clinic due to kidney lesion and also the rheumatological clinic.

Discussion

In 1854, Virchow first described cutaneous leiomyomas as a rare condition characterized by the presence of tumors, inherited in the autosomal dominant pattern. The gene defect affects the fumarate hydratase – one of

the enzymes of the Krebs cycle. The mutation of the fumarate hydratase gene results in an increased risk of development of breast cancer, urinary bladder cancer, kidney cysts and adrenal adenomas [6].

It is postulated that two types of segmental manifestation of autosomal dominant inherited diseases coexist. The first type of the disease is characterized by a nonmosaic phenotype, in the second type – the homo- or hemizygosity manifests by occurrence of lesions in the affected segment [7, 8]. The lesions with these configurations often can incorrectly suggest the diagnosis of herpes zoster [9].

Toro *et al.* [10] and Wei *et al.* [11] reported a family incidence of leiomyomatosis and renal cell cancer. Our patient's mother had similar skin lesions, but detailed diagnosis was not established. Duś *et al.* [12] described the occurrence of skin lesions with breast cancer in their patient and only skin changes in the patient's brother, mother and grandmother. Calcifications can occur in the lesions [13], but that was not observed in our patient.

The lesions occur equally in men and women and in 50%, the first lesions appear before 20 years of age. The mean age of patients seeking medical assistance because of skin lesions is 35 years (18-60 years) [14]. In our patient, skin lesions occurred at the age of 39, but due to lack of accompanying discomforts she visited the dermatology outpatient clinic when she was 59 years.

The most common locations of the skin leiomyomas include the chest, the dorsal side of the left forearm and the lateral side of the neck. Skin lesions can also appear on the lower extremities. Different locations were reported rarely. Boutayeb *et al.* [15] described a case of a patient aged 70 with leiomyoma on the right index finger. In this case, the surgical excision gave good results. Hachisuga *et al.* [16] reported 562 cases of leiomyomas, 200 of them were located on the calf and the ankle, and also on the head and the hand (around 10%). Janas *et al.* [17] reported two cases of patients with lesions on the floor of the mouth treated by CO_2 laser ablation.

The lesions located on the hand are painful more frequently (80%) than in any other locations. In our case, the lesions located on the left shoulder and on the left side of the cleavage were painless. The pain associated with leiomyomas often gradually increases with time and it is absent in the beginning.

The pathogenesis of the pain remains unknown. It is suggested that the pain results from local stimulation of the peripheral cutaneous nerves or by ischemia caused by contraction of local smooth muscles [18, 19].

Lesions similar to leiomyomas can be malignant. Barbetakis *et al.* [20] reported a case of a patient with metastatic nodules of leiomyosarcoma on the skin of the scalp. The patient underwent radical hysterectomy because of leiomyosarcoma two years before the skin changes occurred. Typical leiomyomas do not give metastases and the recurrence after surgical excision occurs rarely.

The therapy of leiomyomas includes surgical excision, cryosurgery and carbon dioxide laser ablation. In our patient, surgical excision together with cryosurgery was performed with good cosmetic effects. The pain associated with the lesions was not intensive and therefore did not require any treatment.

Smith *et al.* [21] reported a case of a patient with multiple, painful skin leiomyomas. In this case, the initial therapy with nifedipine and gabapentin did not give any effects, so the patient decided to have surgical excision of the lesions. Kostopanagiotou *et al.* [22] described successful treatment of pain by a combination of pregabalin with duloxetine.

We have reported a case of Reed's syndrome with typical occurrence of skin changes, uterine leiomyomas and renal cysts. Regular checkup is required in this group of patients because of the higher risk of development of malignant changes.

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