

Reed's syndrome: A case report and literature review

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ABSTRACT:

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Cutaneous leiomyomas are benign smooth muscle tumors arising from the arrector pili muscle. Uncommonly, they were found coexistence together with uterine fibroids named multiple cutaneous and uterine leiomyomatosis, also known as Reed's syndrome. A small proportion of patients will increase prevalence of renal cell carcinomas a result of the fumarate hydratase genetic defect. Affected women, whose develop uterine leiomyomatosis which are larger, more numerous and earlier onset than those in general populations, maybe predisposed to developing renal cell carcinoma. This report demonstrated a case of Reed's syndrome in 36-year-old Thai female who presented with multiple cutaneous leiomyomas, early onset uterine leiomyomatosis and renal cysts.

Key words: Cutaneous leiomyoma, Piloleiomyoma, Reed's syndrome, Uterine fibroid

บทคัดย่อ:

วราวุฒิ อมรภิญโญ, จรัสศรี พียาพรรณ, วรัญญา บุญชัย รายงานผู้ป่วยโรค REED'S SYNDROME และการทบทวนวารสาร วารสารโรคผิวหนัง 2557; 30: 146-151.

ภาควิชาดจวิทยา คณะแพทยศาสตร์ศิริราชพยาบาล มหาวิทยาลัยมหิดล

โรค Reed's syndrome เป็นกลุ่มอาการที่มีการตรวจพบเนื้องอกผิวหนังพร้อมกับเนื้องอกมดลูก ซึ่งพบได้ไม่บ่อยนัก มีรายงานการเกิดมะเร็งที่ไต (renal cell cancer) เนื่องจากมีความเกี่ยวข้องกับการถ่ายทอดทางพันธุกรรมเด่นในการกลายพันธุ์ของยีนที่ทำให้เกิดความผิดปกติของเอนไซม์ฟูมาเรทไฮเดรเตส (fumarate hydratase enzyme) โดยเฉพาะหากตรวจพบมีเนื้องอกมดลูกที่มีขนาดใหญ่ จำนวนหลายก้อนในหญิงที่อายุน้อยควรมีการตรวจเพิ่มเติมเนื่องจากอาจมีความเสี่ยงต่อการเกิดมะเร็งที่ไตสูงกว่าประชากรทั่วไป รายงานนี้เป็นการนำเสนอผู้ป่วยหญิงอายุ 36 ปี มาพบแพทย์ด้วยเรื่องผื่นผิวหนังกระจายบริเวณหัวไหล่ ร่วมกับตรวจพบเนื้องอกที่มดลูกตั้งแต่อายุน้อยและถุงน้ำที่ไต ซึ่งจากการวินิจฉัยเข้าได้กับโรค Reed's syndrome

คำสำคัญ: โรค Reed's syndrome, เนื้องอกผิวหนัง, เนื้องอกมดลูก

Introduction

Reed's syndrome is an uncommon disease characterized by cutaneous and uterine leiomyomas, establishing an autosomal dominant pattern of inheritance and increase risk of renal cell carcinoma. The diagnosis is based on the morphology of skin lesions with histopathology and immunohistochemical study confirmed.¹ This report demonstrated a case of Reed's syndrome with typical skin lesions, early onset of uterine leiomyomatosis and renal cysts in a young woman.

Case report

A 36-year-old Thai female was presented at dermatologic clinic, Siriraj Hospital with a presenting symptom of multiple, asymptomatic, skin-colored, soft papules located on her left shoulder. Over the past 3

years, the lesions were gradually increased in size and number. The lesions are occasional pain after exposure to pressure and cold. Her past medical history showed uterine leiomyomas that caused pelvic pain. Likewise hysterectomy was performed since 4 years ago. No family history of similar skin lesions and uterine conditions were found.

Physical examination revealed bilateral symmetrical monomorphic brownish papules on both forearms. They were 1 to 2 mm in diameter and distributed on flexural more than extensor surface.

The histopathologic findings of the papule demonstrated well circumscribed, non-encapsulated tumor in the dermis. It was composed of interlacing bundle of smooth muscle cells. The cells were

characterized by elongated, cigar-shaped with blunt-ended nuclei and abundant eosinophilic cytoplasm.

Discussion

Cutaneous leiomyomas are benign smooth muscle tumors classified into 3 categories according to locations where smooth muscle occur; piloleiomyomas from arrector pili muscles, angioleiomyomas from vascular smooth muscle and genital leiomyomas from dartos muscle of the genitalia. Piloleiomyomas is the most common type of cutaneous leiomyomas. The lesions typically present in male, predominance ratio of 2:1, through the age of 20's and 40's.¹

Clinically, leiomyomas appears as firm skin-colored or pink-brown papules or nodules up to 2 cm in diameter with variably distributed as grouped, linear, segmental, and dermatomal pattern. The lesions may be asymptomatic or painful when affected by pressure, stress or cold. The pathogenesis of the pain remains undetermined, anyway it was assumed to be related to local stimulation of peripheral cutaneous nerves or contraction of local smooth muscles. The trunk and upper limbs are the most common site of involvement.²

It was found on histopathology that smooth muscle fiber bundle composed of eosinophilic cytoplasm with elongated blunt-ended nuclei with little or no waviness are interspersed with collagen within the dermis. Immunohistochemical study disclosure the presence of smooth muscle differentiation marker, such as desmin and actin.¹

Initially, Reed et al defined Reed's syndrome, in 1973, which was an autosomal dominant condition composed of multiple cutaneous and uterine leiomyomas.³ A mutation in gene located on chromosome 1q42.3-43, encoding fumarate hydratase (FH), has been described and reported to have an association with type II papillary renal carcinomas and renal collecting duct cancers about 20-25%.⁴⁻⁵

Uterine leiomyoma was benign smooth muscle tumor of uterus which showed no different clinical presentation as occurred in sporadic cases and Reed's syndrome, which was hereditary leiomyomatosis. Many uterine leiomyomas and larger size of those were observed in hereditary leiomyomatosis. 30's aged was period of diagnostic of hereditary leiomyomatosis and was approximately 10 years in prior of diagnostic in sporadic cases. Affected women, whose develop uterine leiomyomatosis which are larger, more numerous and earlier onset than those in general populations, maybe predisposed to developing renal cell carcinoma.⁶ RCC in HLRCC occurred about 10-16%. The mean age of diagnostic time of renal cell carcinoma in HLRCC is approximately 44 years. The earliest time of patient whose diagnosed renal cell carcinoma is 11 years old.⁷ The NIH recommends screening for occult renal malignancy in all patients whose present with leiomyomatosis. Genetic analysis of the FH gene should be performed in all cases suspected hereditary leiomyomatosis and renal cell cancer (HLRCC). The recommendations for all HLRCC patients, FH

heterozygotes and at-risk family members are minimum annually checkup by full skin examination, gynecologic assessment, evaluating sign and symptoms of renal cancer such as hematuria, flank pain, palpable abdominal mass. Because of the aggressive nature of HLRCC-associated renal cancers, the yearly abdominal CT or MRI are considered starting from the age of 18 for all HLRCC patients and everyone with familial history of HLRCC-associated RCC. Total nephrectomy should be strongly considered as if detectable renal mass. Genetic counseling is important for other family members about planning early pregnancy to avoid infertility conditions from uterine leiomyomatosis.⁸



Figure 1 Multiple, skin-colored, soft papules on the left shoulder. Of note, these lesions were occasional painful to cold and pressure.

This presented patient presented with multiple, asymptomatic cutaneous leiomyomas on her left shoulder and history of early onset uterine leiomyomas supporting diagnosis of Reed's syndrome. Further investigations were performed for screening renal cell carcinoma. The ultrasonography disclosed renal cysts

and urine examination were normal. The test for fumarate hydratase gene was not performed in this patient.

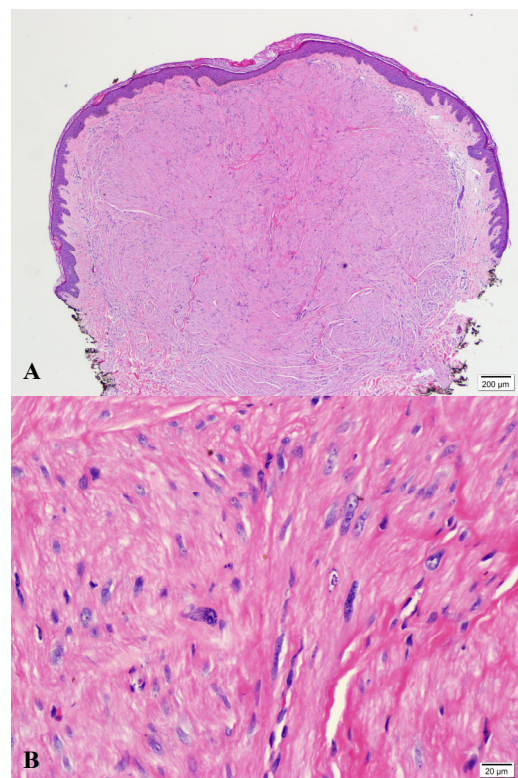


Figure 2A and 2B Microscopic features. A) Scanning magnification revealing well circumscribed, non-encapsulated tumor in the dermis. B) Higher magnification demonstrating interlacing bundle of smooth muscle cells. The cells were characterized by elongated, cigar-shaped with blunt-ended nuclei and abundant eosinophilic cytoplasm.

The treatment of cutaneous leiomyomas is only for improvement of cosmetic and pain relief. Excision is standard of choice for solitary tumor in contrast with high recurrent rate. Multiple extensive lesions can use

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such modalities as electrocoagulation, cryotherapy, and CO₂ laser ablation.^{1, 9} Medications which block smooth muscle contraction, such as nitroglycerine, nifedipine, phenoxybenzamine, and doxazosin, and medications that target the activity of nerve, such as gabapentin, topical analgesic, botulinum toxin type A injection, can be used to treat symptomatic leiomyomas.^{1, 10} For the treatment of this case, because of no intensive pain from the lesions and no cosmetic concern, no any treatment was needed for this patient. She was advised to have regular checkup on renal cysts which had been postulated to represent premalignant lesion of renal cell carcinoma.

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