Sugar or Spice, Siblings are Bitter or Nice!

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Case 1

A 54-year-old male presented with painful nodular skin lesions all over the body for the past 40 years with exacerbation of the lesions over the past 5 years.The lesions were associated with pruritus. On examination, multiple discrete and grouped skin-colored to hyperpigmented macules and nodules with excoriation marks were seen over the back, chest, and bilateral arms, legs, and face. An ultrasound scan of the abdomen showed no abnormality. A punch biopsy was taken from the skin and sent for histopathological examination [Figure 1a-c].

Case 2

A 55-year-old female presented with skin lesions all over the body similar to her sibling (Case 1) associated with pain and pruritus for the past 20 years. On examination hyperpigmented to skin-colored discrete nodules were seen over the back, arms, and trunk. History of uterine fibroid was present, and a hysterectomy had been done. The present ultrasound abdomen showed no other abnormality. A punch biopsy from the skin was sent for histopathological examination [Figure 2a-c].

What is the diagnosis?

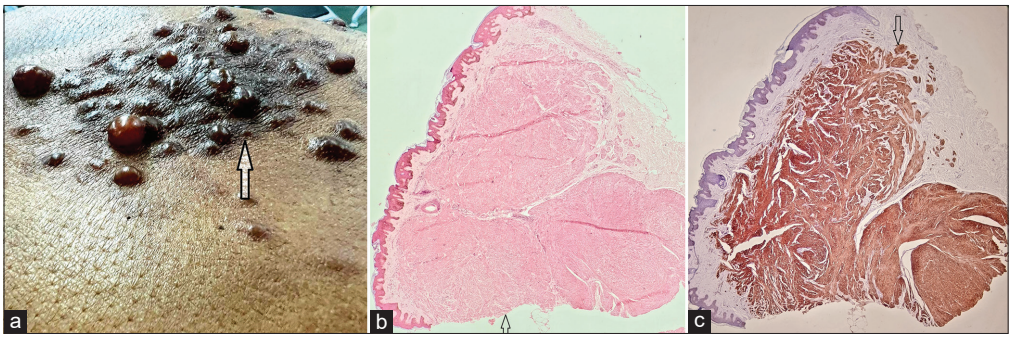

Figure 1: (a) Discrete and grouped hyperpigmented macules and nodules seen over the back. (b) Dermal lesion composed of intersecting fascicle of smooth muscle cells (H and E, 10x). (c) IHC-SMA positive in tumor cells (10x)

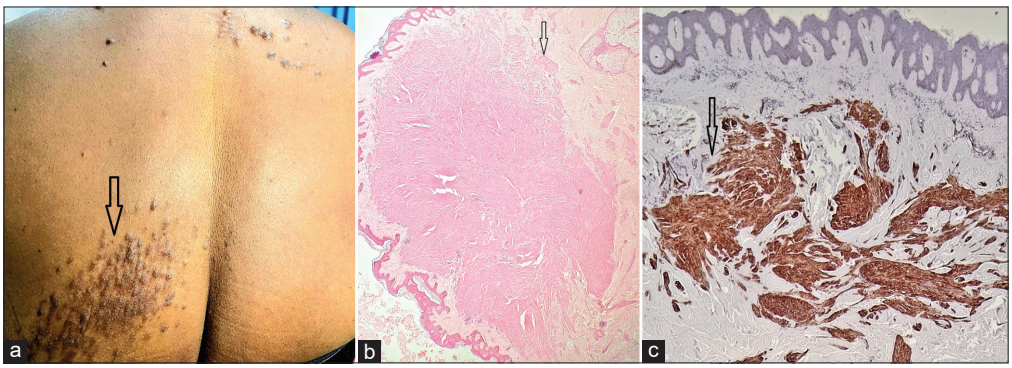

Figure 2: (a) Hyperpigmented to skin colored discrete nodules seen over the trunk. (b) Dermal lesion composed of intersecting fascicle of smooth muscle cells (H and E, 10x). (c) SMA (IHC) positive in tumor cells (10x)

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Access this article online

Website: https://journals.lww.com/idoj

DOI: 10.4103/idoj.idoj_125_23

Quick Response Code:

How to cite this article: Thajudeen AS, Srinivasan S, Raghavan V, Isaac JB. Sugar or spice, siblings are bitter or nice! Indian Dermatol Online J 2024;15:176-7.

Received: 18-Feb-2023. **Revised:** 05-May-2023. **Accepted:** 22-May-2023. **Published:** 05-Oct-2023.

Answer

Cutaneous leiomyomata in siblings.

Discussion

Microscopy of both cases showed a lesion in the dermis composed of intersecting fascicles of smooth muscle cells. No atypia, necrosis, or mitosis were noted. Immunohistochemistry was performed using the marker SMA (Smooth Muscle Actin), and was positive in the tumor cells, which was suggestive of leiomyoma. Leiomyomas are neoplasms of benign nature arising from smooth muscles. Cutaneous leiomyomas arise from the arrector pili muscle.[1] They can be single or multiple. The clinical manifestation of cutaneous leiomyoma can be a papule or nodule with an approximate size of 2 cm, firm in consistency.[2] The most common sites affected are the extensor surface of extremities followed by the trunk, head, and neck region. Features commonly noted with multiple cutaneous leiomyomas are that they arise at a younger age, have a segmental arrangement, and tend to be painful.[3] The pain associated with piloleiomyoma is said to arise because of the pressure exerted by the tumor on the nerves in the skin.[1] The mean age at which the cutaneous leiomyomas, which can be a skin-coloured or purple or reddish papule or nodule, are discovered, is 24 years.[3] This often leads to a clinical differential diagnosis of neurofibroma, glomus tumor, sebaceous cyst, or dermatofibroma.[3] Reeds syndrome (also known as multiple cutaneous and uterine leiomyomatosis, MCUL) and hereditary leiomyomatosis and renal cell cancer (HLRCC) are syndromes that arise due to underlying germline mutations in the fumarate hydratase gene, inherited in an autosomal dominant fashion.[4] Fumarate hydratase is involved in the Krebs cycle. Deficiency of the enzyme can lead to an increase in hypoxia-induced factors that can result in the proliferation of blood vessels and increase growth factors. Fumarate itself can act as an oncogenic metabolite.[5] A UK-based study analyzed 108 affected individuals with multiple cutaneous and uterine leiomyomatosis and found 89% evidence of having germline *FH* mutation. Of the 67 women, 15% had only cutaneous leiomyomas, 69% had MCUL and 9% were clinically normal.[3] Although uterine leiomyomas occur in females with Reeds syndrome, leiomyosarcoma is rare.[3-7] Renal cell carcinoma, as the associated malignancy in familial cutaneous leiomyoma, tends to be more aggressive.[8] It was also noted that type 2 papillary renal cell carcinoma is the variant commonly seen in these individuals.[9] Very rarely these affected individuals may also have multiple endocrine neoplasm type 1 or rheumatoid arthritis.[3] Treatment usually involves excision, electro-dissection, or cryotherapy.[4] The lifetime estimated renal cancer risk is found to be 15% in patients with *FH* mutation carriers. Large cohort studies suggest that screening for renal cancer must be done with an annual abdominal MRI from 20 years of age.[10]

The presence of multiple cutaneous leiomyomas and uterine fibroids should raise the suspicion of the investigator to check for Reed's syndrome, hereditary leiomyomatosis, and renal cell cancer. The importance of the recognition lies in the screening of the individual and family members, and early detection of renal cell carcinoma.

Acknowledgement

Department of Dermatology, Chettinad Hospital, and Research Institute.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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