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Multiple Cutaneous and Uterine Leiomyomatosis

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Clinical Case

- 36 y.o. healthy female
- One year ago:
  - sudden onset of at least 20 lesions over back, shoulders and upper arms
  - Mildly tender when rubbed
- ROS: non-contributory
- PMH: No skin cancers
- PSH: Hysterectomy age 28 for multiple leiomyomas
Physical Exam

- 4-12mm pink-brown dermal papules
  - Mildly tender with palpation
  - No increase in erythema when rubbed

- DDX:
  - Leiomyomas
  - Mastocytomas
  - Neurofibromas
  - Metastasis
  - Adnexal tumors

Histology:

- Fasicles of fusiform shaped cells
- Eosinophillic cytoplasm
- Cigar-shaped nuclei
  - Perinuclear vacuoles
- S-100 negative
- Actin positive

Leiomyoma
Cutaneous Leiomyomas

- Arise from smooth muscle in arrector pili, genitalia, breast or vasculature
- Equal sex distribution
- Brown-pink dermal papules or nodules
  - Multiple lesions may follow Blaschko’s lines
  - Favor trunk
- Pseudo-Darier’s:
  - Contraction of muscle when rubbed

- Pain: spontaneous or when exposed to cold
  - Unclear mechanism

Family History: Mother of patient
- Hysterectomy age 21
- Diagnosed with metastatic Renal Cell Carcinoma age 42

One brother: no skin/renal disease
- No additional contributory family history
Diagnosis: 
*Multiple Cutaneous and Uterine Leiomyomatosis*

**Associations:**
- Multiple Leiomyomatosis
- Reed’s Syndrome
- Hereditary Leiomyomatosis and Renal Cell Carcinoma (HLRCC)
- Uterine Fibroids
- Family history of early aggressive Renal Cell Ca

**HLRCC**
- 1954: Kloepfer et al. heritable predisposition to develop multiple cutaneous leiomyomas
- 1973: Reed “multiple cutaneous and uterine leiomyomatosis”
- Autosomal Dominant
- 2002: Fumarate Hydratase
  - Kreb’s cycle enzyme converts fumarate to malate
  - Thought to act as a tumor suppressor, but exact mechanism of tumorigenesis is unknown
HLRCC

- **Cutaneous Leiomyomas:**
  - 76% multiple or single
  - 40% 5 or fewer lesions
  - Mean age: 25 (range: 10-47)

- **Uterine Fibroids:**
  - Almost 100% females
  - Numerous/large
  - Mean age: 30 (range: 18-52)
  - Undergo symptomatic hysterectomy or myomectomy younger than general population

  Uterine leiomyosarcoma:
  - Unclear association, No families in North America reported

HLRCC

- **Renal Cell Carcinoma:**
  - 10-16%
  - Median age of detection: 44
  - Unilateral, solitary
    - Most: “type 2 papillary”
      - tubulo-papillary, collecting-duct carcinoma
    - Aggressive: often present with metastatic disease at time of diagnosis
HLRCC

- No genotype-phenotype correlations
  - No correlation between *fumarate hydratase (FH)* mutations and occurrence of skin and uterine lesions or renal cancer
- More than 100 families have been described from various populations
  - Most have missense mutations
- Importance of Genetic Counseling to screen for FH mutations:
  - All patients with leiomyomas with a personal or family history of:
    - Early hysterectomy
    - Renal cancer

Surveillance and Treatment

Leiomyomas:

- Treatment dictated by degree of discomfort
- Surgical excision, cryoablation, CO₂ laser ablation
- Medications:
  - Calcium channel blockers, alpha blockers, nitroglycerin, antidepressents, gabapentin, topical anesthetics
- Full skin exam every 1-2 years:
  - Assess extent of disease
  - Eval for changes suggestive of leiomyosarcoma
Surveillance and Treatment

Uterine Fibroids:
- Gynecology evaluation annually
  - Assess severity of fibroids
  - Evaluate for changes suggestive of leiomyosarcoma
- Most require surgery earlier than general population

Renal Cell Carcinoma:
- Early detection and surgical intervention
  - Consider total nephrectomy for detectable renal masses
- Baseline CT with contrast or MRI
  - Repeat every 2 years if normal
  - PET-CT to ID metabolically active lesions
  - U/S alone may not be sufficient
- Urologic oncology surgery evaluation of tumors
Case

- CT with contrast of Abdomen/Pelvis: NEGATIVE
- Genetic Counseling (pending results)
  - >90% chance of finding a mutation
- Treatment of cutaneous leiomyomas?
  - None desired at this time
- Considerations: patient may desire to have her only child (daughter) also screened for FH mutation

Thank you!

References: