DELAYED PRESENTATION OF TUBEROUS SCLEROSIS COMPLEX IN AN ADULT WOMAN

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CHIEF COMPLAINT: RIGHT FLANK PAIN

• 27 y/o AAF presents with sudden onset right flank pain.

• Began hours prior to presentation, sharp, unremitting, no radiation, 7/10

• Associated with nausea, dyspnea, and pleuritic pain. No vomiting.

• She was getting out of the shower when the pain occurred.

• Had vague diffuse abdominal pain 3 days prior. No associated constipation or diarrhea.

• Denies any dysuria, fevers, chills, night sweats or recent sexual activity.

• She does report having dark colored urine which she attributes to her menses.
• **SHORTNESS OF BREATH WITH MILD ACTIVITY FOR MANY YEARS.**

• **LESIONS ON FACE AND BACK.**

• **“STARING SPELLS” SINCE CHILDHOOD.**
HISTORIES

• **Past Medical History:**
  - Graves thyrotoxicosis s/p I-131 ablation therapy.
  - HPV infection
  - Anemia
  - Childhood heart murmur
  - Menorrhagia C irregular cycles lasting ~20 days

• **Family History:** mother: thyroid disease (Graves?) s/p partial thyroidectomy; father: unknown

• **Procedure History:** none

• **Social History:** 1-2 cigarettes/day for 2 months; ETOH on occasion; no IVDU. Sexually inactive currently.

• **Allergies:** no known medication allergies

• **Current Medications:** None
VITAL SIGNS ON ADMISSION

- Temp 36.9 C
- HR 78
- RR 18
- BP 150/109
- SaO2 98% on RA
PHYSICAL EXAMINATION

- **Ht:** 5’4”  **WT:** 49.4 KG  **BMI:** 18.7
- **General:** Alert and oriented, No acute distress.
- **Eye:** Pupils are equal, round and reactive to light, Extraocular movements are intact, Normal conjunctiva.
- **HENT:** Normocephalic, Oral mucosa is moist.
- **Neck:** Supple, No carotid bruit, No lymphadenopathy, enlarged thyroid
- **Respiratory:** Lungs are clear to auscultation, Respirations are non-labored, Breath sounds are equal, Symmetrical chest wall expansion, No chest wall tenderness.
- **Cardiovascular:** Normal rate, Regular rhythm, No murmur, Good pulses equal in all extremities, Normal peripheral perfusion, No edema
- **Gastrointestinal:** Soft, Non-tender, Non-distended, Normal bowel sounds, No organomegaly.
PHYSICAL EXAMINATION

• **Genitourinary:** Mild tenderness on deep palpation at the right costovertebral angle, normal on left.

• **Musculoskeletal:** No swelling, no deformity.

• **Neurologic:** Alert, oriented, normal sensory, normal motor function, no focal deficits, cranial nerves II-XII are grossly intact.
LABORATORY

Retic 2.3
MCV 69.1
N 55%
L 26%
M 2%
E 6%
B 1%

Fe 15
Transferrin 312.8
TIBC 407
Fe sat 3.7
Ferritin 30

TP | Alb | TB | AST | AlkP | ALT
---|-----|----|-----|------|-----
8  | 4   | 1.2| 22  | 104  | 11  

GFR 74

UA: clear, yellow, SG 1.005, pH 6.5, blood 250, WBC 6-10, RBC 0-2
few bacteria, sq epith >100, hyal cast 0-2
DIAGNOSIS

• TUBEROUS SCLEROSIS COMPLEX (TSC)
  • PRESENCE OF SIX MAJOR FEATURES (TABLE 1).
INTRODUCTION

• First described by von Recklinghausen in 1862.

• Autosomal dominant disorder characterized by the formation of hamartomatous lesions in multiple organs.

• Results from mutations in one of two genes, TSC1 (hamartin) or TSC2 (tuberin).

• 1/6000 to 1/10,000 live births.

• Clinical features of TSC continue to be the principal means of diagnosis, with the inclusion of identification of a pathogenic mutation in TSC1 and TSC2 as an independent diagnostic criterion.
INTRODUCTION

• AFFECTED PATIENTS MAY PRESENT EARLY IN LIFE WITH THE CLASSIC TRIAD
  • SEIZURES, INTELLECTUAL DISABILITY, AND CUTANEOUS ANGIOFIBROMAS
• RENAL ANGIOMYOLIPOMAS AND PULMONARY LYMPHANGIOLEIOMYOMATOSIS (LAM) EMERGE LATER
• THE MOST FREQUENT CAUSE OF DEATH IN PATIENTS WITH TSC IS RENAL COMPLICATION.
DIAGNOSING TSC
Tuberous Sclerosis Complex Diagnostic Criteria Update: Recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference

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Tuberous Sclerosis Complex Surveillance and Management: Recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference

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### Table 1: Updated diagnostic criteria for TSC

#### Genetic diagnostic criteria
The identification of either a TSC1 or TSC2 pathogenic mutation in DNA from normal tissue

#### Clinical diagnostic criteria

<table>
<thead>
<tr>
<th>Major features</th>
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<tbody>
<tr>
<td>1. Hypomelanotic macules (&gt;3, at least 5-mm diameter)</td>
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<tr>
<td>2. Angiofibromas (&gt;3) or fibrous cephalic plaque</td>
</tr>
<tr>
<td>3. Ungal fibromas (&gt;2)</td>
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<tr>
<td>4. Shagreen patch</td>
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<tr>
<td>5. Multiple retinal hamartomas</td>
</tr>
<tr>
<td>6. Cortical dysplasia</td>
</tr>
<tr>
<td>7. Subependymal nodules</td>
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<tr>
<td>8. Subependymal giant cell astrocytoma</td>
</tr>
<tr>
<td>9. Cardiac rhabdomyoma</td>
</tr>
<tr>
<td>10. Lymphangioleiomyomatosis (LAM)</td>
</tr>
<tr>
<td>11. Angiomyolipomas (&gt;2)</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Minor features</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Confetti skin lesions</td>
</tr>
<tr>
<td>2. Dental enamel pits (&gt;3)</td>
</tr>
<tr>
<td>3. Intraoral fibromas (&gt;2)</td>
</tr>
<tr>
<td>4. Retinal achromatic patch</td>
</tr>
<tr>
<td>5. Multiple renal cysts</td>
</tr>
<tr>
<td>6. Nonrenal hamartomas</td>
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**Definite diagnosis:** Two major features or one major feature with ≥2 minor features.  
**Possible diagnosis:** Either one major feature or ≥2 minor features.
RENAL AML

- PREVALENT IN WOMEN, SUGGESTING A HORMONAL COMPONENT TO THE TUMOR GROWTH.
- FOUND IN ABOUT 70-90% OF ADULT PATIENTS.
- TUMORS LARGER THAN 4 CM IN DIAMETER HAVE A GREATER RISK OF SPONTANEOUS OR TRAUMATIC RUPTURE RESULTING IN HEMORRHAGIC COMPLICATIONS
  - MOST COMMON CAUSE OF DEATH IN PATIENTS WITH TSC.
- RENAL CELL CARCINOMA CAN OCCUR IN APPROXIMATELY 2-3% OF ADULTS WITH TSC.
RENAL AML

For asymptomatic, growing lesions >3 cm in diameter, treatment with an mTOR inhibitor is currently recommended in the short term.

For acute hemorrhage, embolization followed by corticosteroids can be considered.

Nephrectomy is generally avoided.
LAM

- **Pulmonary LAM** also predominantly affects women of childbearing age
  - rare in men
  - estrogen is thought to play a role in disease progression since it does not present prior to menarche and only rarely after menopause

- Treatment mainly consists of supportive management.
  - in select patients with moderate-to-severe lung disease or rapid progression, treatment with an mTOR inhibitor may be used to stabilize or improve pulmonary function and quality of life.
  - candidates for lung transplantation
SURVEILLANCE RECOMMENDATIONS

• Optimal care and prevention of secondary complications associated with TSC.

• This requires coordination of care among medical specialties on a regular basis.

• General monitoring guidelines include
  • High-resolution computed tomography of the chest every 2-3 years
  • Annual pulmonary function testing in symptomatic patients
  • Periodic imaging studies of the brain and kidneys
  • Evaluation of other organ systems as indicated by symptoms.
  • Offer genetic testing for family counseling or when TSC is suspected
CLINICAL COURSE

- Managed conservatively in the hospital with intravenous hydration and pain control until resolution of her symptoms.
- TTE noted normal systolic function with mild MR, no rhabdomyoma.
- Genetic testing later confirmed pathogenic mutation in the TSC2 gene.
- Referred to LSU New Orleans for genetic counseling and further management.
- Referred to Ophthalmology for dilated funduscopic exam.
REFERENCES


