Introduction

- Morphea is a rare fibrosing disease of skin and subcutaneous tissue
  - Females
  - Caucasians
  - 2 peaks of onset
    - Childhood (age 6-8)
    - Mid-40s
- Classification (Laxer and Zulian, Padua Criteria, 2004)
  - Circumscribed (plaque)
    - Superficial
    - Deep
  - Linear
    - Trunk/limb variant
    - Head variant
      - En coup de sabre
      - Parry-Romberg
  - Generalized
  - Pansclerotic
  - Mixed
- Pediatric morphea is different from adult morphea
  - More severe disease
    - Linear morphea most common
    - More likely to have extracutaneous manifestations
  - Longer disease duration
    - 1/3 with active disease >10 years
    - Periods of remission and disease reactivation

Case 1: What extracutaneous manifestations do you have to worry about in children?

- Neurologic manifestations occur in 20-40%
  - Most common with ECDS and PRS
  - Signs and symptoms
    - Seizures
    - Headaches
    - Neuropathy
    - Behavioral changes
    - CNS vascular malformations
    - Asymptomatic MRI abnormalities
  - There is poor correlation between symptoms and MRI findings
    - Children’s Hospital of Wisconsin experience (32 children, 21 with neuroimaging)
      - Only 2 abnormal brain MRI in 9 children with neurologic symptoms
      - Only 2 children had neurologic symptoms out of 4 children with brain MRI abnormalities
    - Mayo Clinic experience (88 adults and children)
      - 72 patients were evaluated by neurology → 40% had neurologic abnormalities
      - 43 had neuroimaging → 44% had abnormal imaging
    - Poor correlation between MRI findings and neurologic symptoms
- 48% of those with neurologic symptoms had normal MRI
- 23% with abnormal MRI had no neurologic symptoms
- Poor correlation with clinical findings
  - Most MRI findings were bilateral
  - No progression with time despite cutaneous progression
- The pathogenesis of neurologic disease is unclear
  - Perivascular lymphocytic infiltrate
  - Infiltration of vessel walls and vessel wall hyalinization
  - Thrombi and calcifications
  - Gliosis
- Musculoskeletal manifestations occur in 20-50%
  - Most common with linear morphea on limbs
  - Signs and symptoms
    - Arthralgias
    - Arthritis
    - Joint contracture
    - Limb length and girth discrepancy
    - Functional limitations
- Ocular manifestations occur in 2-3%
  - Most common with ECDS and PRS
  - Signs and symptoms
    - Anterior uveitis, episcleritis, keratitis
    - Acquired glaucoma
    - Xerophthalmia
    - Strabismus
    - Mydriasis
    - Papilledema
- Linear morphea and early disease onset are risk factors for extracutaneous manifestations

<table>
<thead>
<tr>
<th>Linear morph</th>
<th>Risk of Extracutaneous Manifestations</th>
<th>Odds Ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear morpaea</td>
<td>38%</td>
<td>22.3 (2.8 – 178)</td>
<td>0.0035</td>
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<tr>
<td>Plaque morphea</td>
<td>3%</td>
<td>10.0 (2.1 – 47.6)</td>
<td>0.0036</td>
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<tr>
<td>Onset &lt; 10 years</td>
<td>36%</td>
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<tr>
<td>Onset ≥ 10 years</td>
<td>5%</td>
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Case 2: What work-up should you do upon diagnosing morphea?
- Laboratory work-up
  - ANA and RF have been associated with extracutaneous involvement but not clinically significant
    - ANA positive in 39.5% with skin only and 51.6% with extracutaneous involvement
    - RF positive in 13.2% with skin only and 24.3% with extracutaneous involvement
  - Anti-ssDNA, anti-histone, and anti-chromatin have been associated with disease severity
  - No autoantibodies correlate with disease activity or predict future disease severity
- I perform a work-up on all en coup de sabre and Parry-Romberg patients
  - MRI at diagnosis even if asymptomatic
    - Repeat MRI if symptoms develop or worsen
  - EEG at diagnosis if seizures are suspected
  - Ophthalmology exam if eye complications are suspected
• I perform joint exams on all patients with linear morphea on the limb
  o Joint exam at each visit
    - Physical therapy if functional limitations
    - Leg length x-ray if limb length discrepancy
• I do not perform any serologic screening

Case 3: How should we treat pediatric morphea?
• Survey of 224 morphea patients
  o Dermatologists more likely to use topicals than systemic therapy
    - Topical corticosteroid (45%) was most commonly prescribed treatment by dermatologists
    - Methotrexate (38%) was most commonly prescribed treatment by rheumatologists
  o Even for linear and generalized morphea in children, topical corticosteroids were prescribed in 40-45% of cases
• Children more likely to have morphea complications
  o 54% have permanent sequelae of disease
  o Presence of extracutaneous manifestations associated with quality of life
  o Longer disease duration (13.5 years vs 5.8 years)
• Only active disease will respond to treatment
  o Signs of active disease
    - Enlarging size
    - Worsening atrophy
    - Red or violaceous border
    - Firm white sclerosis
  o Manage expectations
    - Halts disease activity
    - Does not reverse scar
• Choice of therapy depends on clinical features
  o Topical therapy for localized superficial lesions
  o Phototherapy for widespread superficial lesions
  o Systemic therapy for deep lesions, linear morphea, and face
• Topical therapy for superficial plaque morphea on the body
  o Class I topical steroid BID for 4-8 weeks
  o Transition to steroid-sparing BID until no signs of clinical activity
• Phototherapy can be a good option for generalized morphea
  o NBUVB: widespread superficial dermal lesions
  o UVA1: widespread deeper dermal lesions
• Methotrexate is the standard treatment for moderate-severe morphea
  o CARRA treatment plans
    - Methotrexate 1 mg/kg/week SQ (max 25 mg)
    - Methotrexate 1 mg/kg/week SQ (max 25 mg) + Methylprednisolone 30 mg/kg/dose IV (max 1000 mg)
      ▪ Methylprednisolone for 3 consecutive daily doses a month for 3 months (my preferred regimen)
      ▪ Methylprednisolone once a week for 12 weeks
    - Methotrexate 1 mg/kg/week SQ (max 25 mg) + prednisone PO
      ▪ Start 2 mg/kg/day divided BID for 2-4 weeks
      ▪ Taper to 1 mg/kg/day by 8 weeks
    - Taper off by 12 months
  o Subcutaneous methotrexate is preferred
- Nurse teaching and first injection in clinic
- Preservative-containing 25 mg/ml solution
- ½ inch, 30-gauge insulin needles
- Topical lidocaine cream
- Both the tablets and injection solution can be given orally to children
  - 2.5 mg tabs
  - 25 mg/ml injection solution can be disguised in orange juice
- Administer on Friday nights to minimize side effects
- Folic acid 1 mg daily
  - 2-5 mg on day of methotrexate if side effects
- Minimize lab draws and confusion for the family
  - Baseline
    - Complete blood count
    - Complete metabolic panel (liver function, renal function)
    - Consider urine pregnancy, HIV, hepatitis B/C
  - No test dose or dose escalation
- 1 months
  - CBC
  - Liver function
- Every 3 months
  - CBC
  - Liver function
- Risks
  - No increased malignancy risk
  - Increased risk of opportunistic infection
- Vaccines
  - Avoid live vaccines
    - Measles, mumps, rubella
    - Varicella
    - Influenza nasal spray
  - Annual influenza vaccine
  - Assess antibody titers after completion of methotrexate course and re-administer if low
- Mycophenolate mofetil is second-line after methotrexate
- Treatment with systemic therapy for 2 years to minimize relapse
  - Relapse is possible even after 2 years of treatment

Please consider supporting the Dermatology Foundation, The Society for Pediatric Dermatology, or the Pediatric Dermatology Research Alliance with a donation!