Tough Day at the Office: Lupus, Sarcoidosis, and Morphea - Tips for Effective Management

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• Consulting/Ad board: Sanova works, Oakstone institute, L’Oreal, La Roche Posay, Galderma, Amgen, Aveeno, Valeant, Microcures, Nano Bio-Med, Biogen, Pfizer, Nerium, G&W Laboratories, Novartis, Occulus, Intraderm, Encore, Ferndale

• Speaker: Amgen, Valeant

• Grants: Valeant
Agenda

- Lupus Erythematosus
  - Cutaneous
    - Chronic
- Sarcoidosis
- Morphea

Oh my!
I order ANAs all patients with cutaneous lupus

• Agree
• Disagree
Autoantibodies

- Circulating immunoglobulins detected in autoimmune diseases
- Profile contributes to disease phenotype
- Etiology/inciting event not completely understood
Awesome Autoantibodies

- ANA
- SSA (Ro)
- SSB (La)
- dsDNA
- ssDNA
- Sm
- U1RNP
- U2RNP
- Th/To RNP
- Cardiolipin
- B2-glycoprotein
- Histone
- RF
- Ku
- Mi-2
- Jo-1
- Se
- PCNA
- A-fodrin
- PL-7
- PL-12
- OJ/EJ
- PM-Scl
- Centromere
- Scl-70
- Calpastatin
- HMG
- Fer
- Mas
- KJ
- SRP
- C1q
- U3RNP (fibrillarin)
Antinuclear Antibody (ANA)

- Screening tool
  - Good sensitivity (assay-dependent)
  - Low disease specificity
  - False positives
Antinuclear Antibody (ANA)

- Immunofluorescence staining pattern

A: Homogeneous
B: Peripheral
C: Speckled
D: Nucleolar
E: Centromeric

Bolognia et al. *Dermatology*. 2007
## Table IX. ANA patterns and their antigen and disease associations

<table>
<thead>
<tr>
<th>ANA</th>
<th>Predominant antigen</th>
<th>Disease</th>
<th>Reference Nos.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral</td>
<td>nDNA</td>
<td>SLE</td>
<td>10, 14, 161</td>
</tr>
<tr>
<td>Homogeneous</td>
<td>nDNA, histones</td>
<td>SLE</td>
<td>14, 161</td>
</tr>
<tr>
<td>Nucleolar</td>
<td>Nucleolar RNA</td>
<td>SSc, SLE</td>
<td>14, 158, 161</td>
</tr>
<tr>
<td>Centromere</td>
<td>Kinetochore</td>
<td>CREST</td>
<td>14, 159</td>
</tr>
<tr>
<td>Speckled</td>
<td>Various ribonucleoproteins</td>
<td>MCTD, SLE, SSc, Sjögren’s Syndrome</td>
<td>14, 161</td>
</tr>
</tbody>
</table>
False Positives

Table VII. Conditions other than autoimmune CTDs with positive ANA

- Elderly persons$^{12,153}$
- Pregnant women$^{154,155}$
- Relatives of patients with CTD$^{12,156}$
- Other autoimmune diseases (eg, primary biliary cirrhosis, autoimmune thyroiditis)$^{14,196}$
- Drugs (eg, procainamide, hydralazine)$^{68-83,157}$
- Chronic infections$^{10,14}$
- Neoplasms$^{10,14}$
- Healthy persons$^{9,11,12,153}$

Mutasim, et al.  JAAD Feb 2000
“Normal” ANA cut-off < 1:160

<table>
<thead>
<tr>
<th>Titer</th>
<th>Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:40</td>
<td>32%</td>
</tr>
<tr>
<td>1:80</td>
<td>13%</td>
</tr>
<tr>
<td>1:160</td>
<td>5%</td>
</tr>
<tr>
<td>1:320</td>
<td>3%</td>
</tr>
</tbody>
</table>

Mutasim, et al.JAAD Feb 2000
Internal organ involvement was most commonly observed in:

- Ro/SS-A antibody + patients with LE presenting with LE-nonspecific cutaneous manifestations
- Ro/SS-A antibody + patients presenting with acute cutaneous LE and mucosal LE high risk
  - Highest frequency of lupus nephritis and serositis
288 patients, 13.8% had discoid lesions
Renal lesions were more common in those without discoid lesions (p = 0.016), and hemolysis (p < 0.0001) was more common in those with discoid lesions.
Only the anti-RNP ab was more common in those with discoid events (p = 0.04).
  – Only the renal lesions and anti-RNP maintained their associations with discoid manifestations
Autoantibodies and Disease Activity in Patients With Discoid Lupus Erythematosus

- Cross-sectional study of patients with DLE (small N)
- Correlation between anti-RNP antibodies and skin disease activity, both in patients with SLE and in those with DLE.
  - ANA, anti-RNP, and anti-dsDNA correlated with SLE activity index scores
  - These and anti-ssDNA IgG correlated with C3 and C4 levels, the number of SLE criteria
    - Need for oral medications!
- Measuring autoantibodies to predict skin disease activity and associated systemic findings

Kim, A et al. JAMA Dermatol 2014 Apr 30; [EPub Ahead of Print],
Approximately 50% of patients with subacute cutaneous lupus erythematosus (SCLE)

Patients with SCLE/SLE vs SCLE
  - Oral ulcers
  - +anti-dsDNA antibodies
  - + ANA
  - Low complement
Cutaneous Lupus Erythematosus (LE)

• Chronic Cutaneous LE
• Subacute Cutaneous LE
• Acute (systemic) LE
The Lupus Spectrum: God Help Us

- Increased prevalence/severity in black/hispanic pediatrics
- Greater risk of renal disease than adults!
Chronic Cutaneous LE

- CCLE
  - Classic Discoid LE
  - Tumid LE
  - Neonatal LE (sort of)
  - Lupus Panniculitis
  - Chilblain LE
Case 1

• CC: 49 yo M with rash for 2 years.
• HPI: First lesion appeared on the trunk and subsequently spread to the face and scalp.
  – Lesions are generally asymptomatic, but are occasionally itchy.
  – Past tx: topical steroids and hydroquinone 4% cream without improvement
• PMH: DM, HTN
• Meds: Glucophage, Lisinopril, Metoprolol
• Allergies: NKDA
• Social Hx: No tobacco, alcohol, or drug use
• Family Hx: Father hx laryngeal ca
Discoid lupus erythematosus (DLE)

- Can be seen w/o serologic or systemic manifestations of SLE
  - May be early sign of SLE
  - Up to 28% progress!!*
- Follicular plugging*
- Chronic lesions may show hyper/hypopigmentation w/ atrophy
- ? exacerbated by UV light
- m/c head and face
  - Also scalp, extremities, back, chest, abdomen

What about peds?
Spontaneous involution with scarring is common. Rarely BCCs or SCCs may occur in scars. Lower lips with hypopigmented scars. Treatment of localized disease: topical steroids and/or intralesional steroids. Photoprotection + Vit D supplementation. Generalized DLE requires systemic therapy with hydroxychloroquine (Plaquenil) dosed up to 6.5 mg/kg/day. Low dose (50-100 mg /d) seems to work better for acral. If Plaquenil is not effective, add quinacrine (~ 100 mg qd vs bid). MTX, retinoids, dapsone, cellcept also options.
Plaquenil Clinical Pearls

- High affinity for melanin-containing tissue, with a tendency to accumulate in ocular tissues such as the choroids and ciliary body
- < 1% risk of eye damage
- Risk factors:
  - Daily dosage of HCQ exceeding 6.5mg/kg
  - Obesity
  - Duration of use longer than 5 years
    - After year 5, MUST have yearly ophtho exams
  - Renal or hepatic functional impairment.
  - > 60 yrs
- Chloroquine + hydroxychloroquine NO NO
- G6P-deficiency
- ? Pregnancy

ANA went from 1:40 to 1:360 over 6 month period
What now?
• Current smokers had higher median CLASI scores (9.5) than did never (7.0) and past (6.0) smokers ($P=0.02$)
  – Current smokers more likely than nonsmokers to receive combination antimalarial therapies and significantly less likely to improve than never or past smokers
• **4 risk increase was seen for buccal cancer, lymphomas, respiratory cancer and nonmelanoma skin cancer

• 300 patients (DLE, SCLE, LP)
  – 38 of these patients had 2 or more associated cutaneous forms
• Median blood hydroxychloroquine significantly higher in patients with complete remission compared with partial remission and treatment failure ($P = .007$)
  – Thirty patients (10.0%) had very low blood hydroxychloroquine concentrations and considered nonadherent to the treatment regimen
• Prove poor adherence

Frances C et al., *Arch Dermatol* 2012 Apr; 148:479
On the horizon: Alitretinoin for CLE

- Alitretinoin (9-cis retinoic acid)
  - Approved in Europe as an oral formulation for use in recalcitrant hand eczema,
  - Topical version is approved for Kaposi sarcoma.
- 3 patients with varying types of CLE tx oral alitretinoin at 30 mg/day.
  - 1 severe DLE with SLE
  - 1 hypertrophic LE
  - 1 SCLE.
- Total clearance in 2 patients and nearly complete resolution in the third.
- No serious AE
- 2 patients tapered to 10 mg/day

Kuhn A et al., J Am Acad Dermatol 2012 Sep; 67:e123.
On the horizon: Apremilast for CLE

- Apremilast
  - PDE4 enzyme inhibitor capable of blocking leukocyte production of IL-12, IL-23, TNF-a, INF-γ with subsequent suppression of Th1 and Th17-mediated immune responses
- 1st open label study
- CLASI scores significantly (P<0.05) decrease after 85 days of treatment with apremilast 20 mg twice daily in 8 patients with active discoid lupus.

De Souza A et al., J Drugs Dermatol 2012 Oct; 11:1224
Case 2

- 74 yo M presented with 8 week history progressively enlarging “rash” L eye and mid chest
  - Mildly painful/burning
  - No past episodes
- No family history of similar lesions
- PMH: HTN, High Chol, OA
- Meds: HCTZ, Amlodipine, Simvistatin, Metoprolol
- Otherwise well
### Table 3. Diagnostic Criteria of Lupus Erythematous Tumidus

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Findings in Study Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical</td>
<td>Erythematous, succulent, urticarialike, nonscarring plaques with a smooth surface in sun-exposed areas</td>
</tr>
<tr>
<td>Histological</td>
<td>Perivascular and periadnexal lymphocytic infiltration, interstitial mucin deposition, and, in some cases, scattered neutrophils; no epidermal involvement or alteration of the dermoeipidermal junction</td>
</tr>
<tr>
<td>Phototesting</td>
<td>Reproduction of skin lesions after UV-A and/or UV-B irradiation in 28 patients (70%)</td>
</tr>
</tbody>
</table>

But of course…

Jessner’s

Pseudolymphoma

PMLE
• Antimalarials— up to 90% effective (with rapid resolution of lesions in 1 study)
• Topical steroids/ILK
• Dapsone
• Sun protection

Arch Dermatol 2000;136:1033-1041
Case 3

- Newborn baby boy presents with a red macular facial rash
- PMH: born at 37 wks. Mother had a URI x 2 wks prior to delivery, but otherwise the pregnancy had been going well.
- All: NKDA
- Medications: none
- FH: non-contributory
- SH: has 2 siblings (11 yr old brother, 5 yr old sister)
12/17-28/09:
TORCH panel:
HS Ab (type 1/type 2), Rubella Ab IgM, Toxo Ab IgM/IgG, CMV IgM/IgG: negative, Urine CMV cx negative
Rubella Ab IgG + (?)
Syphilis screen NR

CSF HSV-1/2 DNA negative
CSF VDRL NR
CSF pink WBC 21, RBC 15684, glucose 40, protein 217 (10-40)
CSF culture no growth

Eye cx, viral eye cx, nasal viral cx, rectal viral cx, HS cx: no growth

Anti-SSA (Ro) > 8.0 (< 1.0)
Anti-SSB (La) < 0.2 (< 1.0)            EKG: WNL
6/1/09:
VZ Ab IgG +
Rubella Ab IgG -
Syphilis screen NR

10/30/09:
HIV-1/2 Ab -
• Pt was given ampicillin and gentamicin after a full sepsis work-up, and abx stopped once blood and CSF cultures were negative x 48 hrs.

• Pt was given acyclovir until CSF HSV PCR returned negative

• Pt was discharged on DOL 4 with f/u with PMD, rheumatology, and dermatology
Neonatal Lupus Erythematosus (NLE)
Neonatal Lupus Erythematosus (NLE)

- Caused by maternally transmitted autoantibodies (anti-Ro/SS-A in 95% of cases)
  - Anti-La/SS-B (60%-80%)—mean level higher in mothers of infants with congenital heart block
  - Anti-U1RNP (small subset)

- The major manifestations of NLE involve which two organ systems, and are the effects transient or permanent in the newborn?
  1) **Dermatologic disease:**
     - transient effects
     - 50% of pts with NLE
  2) **Cardiac disease:**
     - permanent effects
     - responsible for morbidity & mortality of NLE (congenital heart block)
     - 10% of pts with NLE
NLE: Cutaneous Findings

- Develop at a few weeks of age
- ~ SCLE
  - **Papulosquamous variant** (most common)
    - Erythematous, nonindurated scaly plaques
    - No scarring
  - **Annular variant**
    - Annular, more inflammatory plaques
    - Occurs almost exclusively in Japanese
- MC face & scalp, especially periorbital and malar areas ("raccoon eyes" appearance)
- NLE lesions may occur in sun-protected areas
- Transient hypopigmentation & epidermal atrophy may result
- Telangiectasia may be a permanent sequela
• Heart block
  – seen in up to 50%
  – Permanent defect developing in utero
    • Inflammation due to antibody-antigen reaction on conduction system causes scarring
    • Require pacemaker
  – 10% die with cardiac related disease
  – 90% of pts have HLA-DR2, DR3
  – 100% have lupus anticoagulants
Treatment & Prognosis

• Workup:
  – complete physical exam, EKG, CBC, LFTs

• Skin disease treatment:
  – sun protection, topical steroids, PDL for residual telangiectasias

• Congenital heart block treatment:
  – 50% of newborns with complete congenital heart block require pacemaker in neonatal period
  – 15% mortality in neonatal period from complete congenital heart block

• Risks for mothers with anti-Ro or anti-La antibodies:
  – 1%-20% risk of developing infant with NLE
  – 25% risk of recurrence of congenital heart block in subsequent pregnancies
I order ACE levels on all patients with cutaneous sarcoidosis

• Agree
• Disagree
Case 3

- CC: Arm rash and Dry skin
- HPI: 72 Year old woman with a 2 year history of a solitary pruritic plaque on the right upper arm.
  - No previous episodes
- PMH: Bronchiectasis, Gastritis
- PSH: Not Contributory Meds: Flovent  All: NKA  FH: HTN
- SH:
  - Never smoked, no hx of passive exposure
  - No work health hazards; worked as nurses aide for many years
  - One child, grown; No pets; Lives alone
Clinical Data

- **PMH:** Pulmonary Sarcoidosis, Granulomatous gastritis
- **Labs:**
  - ANA: negative; RF: 20 (nrml)  **ACE: 87 (↑)** in 2007
  - Multiple negative PPDs
  - Current: Ca$^{2+}$ 9.7
    - High Ca$^{2+}$; low PTH 2010
- **Imaging:**
  - CXR 7/11: Parenchymal findings of sarcoidosis with apparent improvement from 2010
  - CT Thorax 8/10: Mild splenomegaly, calcified granuloma in the right lower lobe of lung, enlarged bilateral hilar and mediastinal lymph nodes.
Sarcoidosis

- Female preponderance 1.3:1 among all ethnic and racial groups
  - US: increased incidence among black Americans, ranging from 35.5-64.4 per 100,000
    - Peak incidence in black Americans occurs in the fourth decade.
  - Sarcoidosis is also more likely to be chronic and fatal in black Americans
• **Key Clinical Features**
  – Cutaneous disease in 30%
    • Early manifestation
  – Red-brown to purple dermal papules/plaques
  – Atypical presentations include alopecia, atrophic forms, erythrodermic sarcoidosis, hypopigmented, ichthyosiform, and lichenoid forms.
    • Erythema nodosum is predictive of an subacute, transient form of sarcoid
And don’t forget...
Post herpes-zoster scar sarcoidosis with pulmonary involvement

Archana Singal, Amit Vij, and Deepika Pandhi
Sarcoid as a complication of neurotoxins?

Fig 1. Cutaneous sarcoidosis: 53-year-old woman with cutaneous nodules on her forehead distributed in botulinum toxin–like injection scheme.

Fig 2. Dermatopathology of cutaneous sarcoidosis: epithelioid histiocytes and multinucleated giant cells forming noncaseating dermal granulomas.
So what’s going on here?
- **Lofgren’s syndrome:**
  - Erythema nodosum, bilateral hilar/right paratracheal lymphadenopathy, fever, polyarthralgia

- **Heerfordt's syndrome:**
  - Parotid enlargement, uveitis, fever, and facial nerve palsy.

- **Darier-Roussy Disease:**
  - Subcutaneous sarcoidosis
    - Keep in your ddx with RA nodule and Subq GA
• **Diagnosis of exclusion**
  – Chest radiograph evidence, accompanied by non-necrotizing granuloma on biopsy and supportive clinical history

• Radiologic findings: paratracheal or hilar adenopathy +/- infiltration
  – PFTs: restrictive ventilatory dysfunction

• Ophthalmologic: Uveitis

• CBC, Ca\(^{2+}\), LFTs; ↑ANA in 30%; ↑ serum ACE in 60%, and check for ↑ESR, anemia, eosinophilia, lymphopenia, and hypercalcemia
Treatment of Cutaneous Sarcoidosis

- Corticosteroids
  - Topical, intralesional, and systemic*
- **Tetracycline Abx** (minocycline 100 mg BID)
- **Antimalarials**
  - Hydroxychloroquine (200-400 mg daily) for 12 weeks
- Methotrexate (10-25 mg weekly)
- **TNF-α antagonists**
  - Inflixumab
  - Thalidomide
A randomized, placebo-controlled, single-masked trial on 30 patients – 22 patients biopsy-proven cutaneous disease; 8 had biopsy-proven pulmonary disease with dermatologic lesions

8-week regimen consisted of:
- levofloxacin, 750 mg on day 1, followed by 500 mg/d
- ethambutol, 25 mg/kg/d up to a maximum dosage of 1200 mg/d
- azithromycin, 500 mg on day 1, followed by 250 mg/d
- rifampin, 10 mg/kg/d up to a maximum dosage of 300 mg/d
  - The placebo regimen consisted of riboflavin (in place of rifampin) and lactose (in place of the other 3 drugs).
  - 6 patients withdrew due to AE
  
- Observed improvement with the 8-week CLEAR regimen was still present 180 days after baseline
**Sarcoidosis Appearing During Anti-Tumor Necrosis Factor α Therapy: A New “Class Effect” Paradoxical Phenomenon. Two Case Reports and Literature Review**

Alfonso Massara, MD,* Luigi Cavazzini, MD,† Renato La Corte, MD,*
and Francesco Trotta, MD*

**BRIEF REPORT**

Development of sarcoidosis during adalimumab therapy for chronic plaque psoriasis

Stefanie Marcella,¹ Belinda Welsh² and Peter Foley¹²,³

¹Skin and Cancer Foundation, ²Department of Dermatology, St Vincent’s Hospital Melbourne and ³The University of Melbourne, Melbourne, Victoria, Australia

**Sarcoid Intermediate Uveitis Following Etanercept Treatment: A Case Report and Review of the Literature**

Alex Fonollosa¹, Joseba Artaraz¹, Iñigo Les², Agustín Martínez-Berriotxo², Julio Pérez Izquierdo³, Alberto Saiz Lopez², Jesús Gardeazabal⁵, Barbara Berasategui⁶, and Nerea Martínez-Alday⁶
Safety of Intravenous Infusion of Human Placenta-Derived Cells (PDA001) for the Treatment of Adults With Stage II or III Pulmonary Sarcoidosis

This study is currently recruiting participants.
Verified September 2011 by Celgene Corporation

Assigned Interventions

Biological: Human Placenta-Derived Cells [PDA001 (cenplacel-L)]

1 unit PDA001 (approximately 200 x 106 cells) IV on Days 1 & 8 OR 4 units PDA001 (approximately 800 x 106 cells) IV on Days 1 & 8

Other Names:
- Human Placenta-Derived Cells
- PDA001 (cenplacel-L)
Imaging studies can be prudent in the setting of morphea

- Agree
- Disagree
Case 4

- 9 yo AA girl presented with asx, progressively enlarging rash on RLE x 1 year
  - Began distally → progressed proximally
  - No past episodes
  - No associated symptoms
- Pmhx
  - PPD+ s/p tx with INH
  - Asthma
- NKA
- Meds
  - Albuterol
  - INH
- Family hx
  - Unremarkable
Square BX
• ANA: 1:80 speckled
• ANA-ENA: -
• Anti-centromere: -
• ESR: 6
• Lyme titer: .2 (wnl)
• CBC: wnl
• 0.4 - 2.7 per 100,000 people
• Female predominance of 2.4 to 4.2:1 has been reported
• Etiology:
  – Autoantibodies? Environmental (L-tryptophan, bleomycin), infection (viral)?, vaccination (bcg)?
  – Fibroblasts produce increased collagen
  – Abnormal collagen production due to instruction from surrounding T cells
  – Is morphea a TH1 or TH2 response pattern?
    • TH2 - specifically IL-4 and TGF-beta enhance collagen I, II, III production
Morpheea - Linear

- Most common subtype in children, affecting 41.8% to 67%
- Tends to involve the underlying fascia, muscle and tendons
- Primary type of morphea to cause disability
- Variants?
  - “en coup de sabre’
  - Parry - Romberg
- + anti-ssDNA abs
- **Melorheostosis**
- ? Assoc with spina bifida
Morphea - Linear

• Initially harmless looking but…

  – Muscle weakness
  – Shortens muscles
  – Immobilizes joint
  – Growth retardation in kids
- Progressive hemifacial atrophy
- May affect what Trigeminal nerve distribution
En Coup de Sabre

- Unilateral
- Forehead to scalp
- Paramedian m/c
- Can involve underlying muscle and bone and rarely meningies and brain causing seizures
### Treatments: Level of Evidence

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Effective/ineffective</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weekly photodynamic therapy(^{[1]})</td>
<td>Ineffective</td>
<td>1</td>
</tr>
<tr>
<td>Twice-weekly intrasional subcutaneous interferon gamma(^{[2]})</td>
<td>Ineffective</td>
<td>1</td>
</tr>
<tr>
<td>Oral calcitriol(^{[3]})</td>
<td>Ineffective</td>
<td>1</td>
</tr>
<tr>
<td>Twice-daily topical 0.1% tacrolimus(^{[4]})</td>
<td>Effective</td>
<td>1</td>
</tr>
<tr>
<td>Low-dose UVA1, medium-dose UVA1, narrow-band UVB(^{[5]})</td>
<td>Effective</td>
<td>1</td>
</tr>
<tr>
<td>Weekly methotrexate and taper of oral prednisone(^{[6]})</td>
<td>Effective</td>
<td>1</td>
</tr>
<tr>
<td>Three times a week topical imiquimod(^{[7]})</td>
<td>Effective</td>
<td>2</td>
</tr>
<tr>
<td>Calcipotriol and betamethasone dipropionate twice-daily(^{[8]})</td>
<td>Effective</td>
<td>2</td>
</tr>
<tr>
<td>Twice-daily occluded calcipotriene(^{[9]})</td>
<td>Effective</td>
<td>2</td>
</tr>
<tr>
<td>UVA(^{[10-18]})</td>
<td>Effective</td>
<td>2</td>
</tr>
<tr>
<td>PUVA(^{[19,20]})</td>
<td>Effective</td>
<td>2</td>
</tr>
<tr>
<td>Broadband UVA without psoralen(^{[21,22]})</td>
<td>Effective</td>
<td>2</td>
</tr>
<tr>
<td>Weekly methotrexate and taper of systemic steroids(^{[23-29]})</td>
<td>Effective</td>
<td>2</td>
</tr>
<tr>
<td>Mycophenolate mofetil(^{[26]})</td>
<td>Effective</td>
<td>2</td>
</tr>
</tbody>
</table>

*United States Preventive Services Task Force quality of evidence rating system\(^{[27]}\)*

*NB-UVB equivalent to low-dose (800 J/cm\(^2\), but not medium (2000 J/cm\(^2\)) UVA*
Generalized morphea without joint contractures

- Phototherapy*
  - UVA1, NB-UVB, PUVA, UVA
  - Better side effect profile than Methotrexate

- No response after 8 weeks

- Methotrexate and systemic steroids

- No response after 8 weeks

- Change therapy to mycophenolate mofetil
Treatment with pirfenidone was three times daily for 6 months.
Successful Combination Treatment of a Patient with Progressive Juvenile Localized Scleroderma (Morphea) Using Imatinib, Corticosteroids, and Methotrexate

Yasuji Inamo, M.D., Ph.D.,* and Toyoko Ochiai, M.D., Ph.D.†

• Prednisolone (1 mg/kg/day) and methotrexate (MTX; 9.5 mg/m² once a week) were started.
  – So severe - treatment with imatinib
    • Imatinib was started at a dosage of 235 mg/ m²/day
• Imatinib was continued at the same dosage for 1 year, and the prednisolone dosage was gradually decreased until it was stopped after 3 months
• MTX was continued at the same dose regimen for 4 years as maintenance therapy.
At the first visit

After 1 year of imatinib treatment
Thank you for your attention