61 year old woman with soft tissue calcifications

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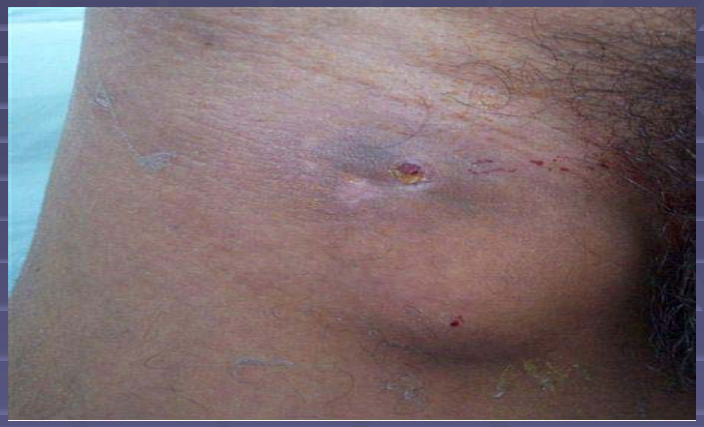
May 2, 2013

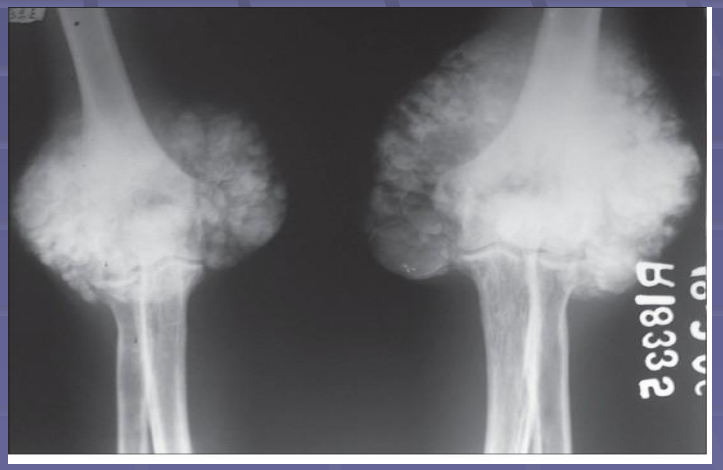
HPI

- Diagnosed with scleroderma in 2000 after presenting with flexion contractures of hands, skin firmness, and reflux
- Later developed Raynaud's symptoms and lung involvement
- Then began to develop soft tissue calcifications in 2009

HPI continued

- Calcifications have grown in size
- Primarily around elbows and forearms
- Significant pain and decreased mobility
- Initial resection of right forearm mass 2/2011 which recurred





PMH

- Scleroderma
  - Diagnosed 2000
  - Prednisone x 3-6 mos in 2001
  - Currently treated with Myfortic and MTX
- Osteoporosis
  - Humerus fracture age 10
  - Low bone mass documented on initial DEXA in 2006 with progressive bone loss despite bisphosphonates
  - 12/2012 BMD LS T -1.3, FN T -2.8

Family and Social History

- Family history
  - 85-year-old mother decreased bone density treated with bisphosphonate, no fractures.
  - Maternal grandmother had osteoporosis related to steroid use
  - Father hypothyroidism, arthritis of hands
- Social history
  - Married with 2 children

Physical Exam

- Constitutional: She is oriented to person, place, and time. She appears well-developed and well-nourished. No distress.
- Head: Normocephalic and atraumatic.
- Mouth/Throat: Oropharynx is clear and moist.
- Eyes: Conjunctivae and EOM are normal.
- Neck: Neck supple. No thyromegaly present.
- Cardiovascular: Normal rate and regular rhythm.
- Pulmonary/Chest: Effort normal and breath sounds normal.
- Musculoskeletal: Mass anterior to R elbow, other golf ball size mass at L elbow, smaller masses R shoulder, L forearm, restricted ROM at b/l elbows
- Skin: Sclerodactyly and tightness of the skin in the fingers, dorsum of the hands, forearms, chest wall, face and feet
- Neurological: She is alert and oriented to person, place, and time.
- Psychiatric: She has a normal mood and affect.

Labs

- Ca 10.09
- PO4 3.39
- Mg 2.29
- U Ca 25 mg/24 hr
- U phosphate 221 mg/24 hr
- PTH 26
- 25OHD 37
- 1,25OHD 48

What Causes Calcinosis?

- Serum calcium and phosphate nl
- Loss of inhibition of calcification
- Pathophysiologic changes
  - Tissue damage
  - Hypovascularity and hypoxemia
  - Structural changes
  - Chronic inflammation and macrophage activity
- Mediators
  - Increased CBAA/GCGA
  - Decreased renal phosphate clearance
  - Increased influx of calcium into cells

How is calcinosis treated?

- Anti-Inflammatory
  - Colchicine, minocycline, anti-TNF
- Decreased CBAA/GCGA
  - Warfarin, salicylates
- Increased renal phosphate excretion
  - Probenicid, phosphate binders
- Inhibition of calcium influx
  - CCBs, minocycline
- Decreased calcium turnover
  - Bisphosphonates
- Mechanical
  - Surgery, CO2 laser, intralesional steroids

Course

- Had been started on probenicid prior to initial visit
- Phosphate binder lanthanum carbonate added
- Also started on calcitonin and course of Zometa

Follow up

- Repeat surgery 9/2012
- Recurrence
- Urine phosphate 307 mg/24 hr
- 5.7% decrease in femoral neck BMD

Table 1. Characteristics and Prevalence of ACTD Associated With Calcinosis Cutis

Underlying ACTD	Patients, No. (%) (N=78)			Age at Onset of Calcinosis Cutis, Mean (Range), y	Time to Onset of Calcinosis Cutis After Diagnosis of ACTD, Mean (Range), mo
	Female Sex	Male Sex	Total		
Dermatomyositis	23 (77)	7 (23)	**30** (38)	31 (4-75)	65 (3-216)
Classic	11 (73)	4 (27)	**15** (19)	48 (21-75)	94 (12-216)
Amyopathic	1 (100)	0	**1** (1)	52	72
Juvenile	11 (79)	3 (21)	**14** (18)	10 (4-21)	35 (3-84)
Systemic sclerosis with limited cutaneous scleroderma	21 (88)	3 (13)	**24** (31)	54 (28-73)	90 (0-372)[a]
Overlap CTD	5 (83)	1 (17)	**6** (8)[b]	39 (14-55)	128 (2-312)
Undifferentiated CTD	5 (83)	1 (17)	**6** (8)[c]	51 (31-67)	32 (0-84)[d]
Lupus panniculitis	4 (100)	0	**4** (5)	60 (39-74)	58 (5-108)
Mixed CTD	2 (50)	2 (50)	**4** (5)	50 (39-62)	75 (12-92)
SLE	2 (100)	0	**2** (3)	46 (35-57)	258 (228-288)
RA	1 (100)	0	**1** (1)	29	24
Polymyositis	1 (100)	0	**1** (1)	44	108

Abbreviations: ACTD, autoimmune connective tissue disease; CTD, connective tissue disease; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.
[a]Calcinosis cutis preceded the diagnosis of systemic sclerosis in 4 of the 24 patients. When these 4 patients are excluded from the analysis, the mean time to onset of calcinosis cutis in the other 20 patients becomes 109 months (range, 3-372 months).
[b]The 6 patients in this cohort had overlap CTD of the following types: SLE and RA, SLE and systemic sclerosis, SLE and dermatomyositis, systemic sclerosis and dermatomyositis (n = 2), and systemic sclerosis, SLE, and RA.
[c]The 6 patients in this cohort had features of the following ACTDs: dermatomyositis and systemic sclerosis (n = 2), SLE and systemic sclerosis, SLE, dermatomyositis and RA, and SLE and RA.
[d]In 1 of the 6 patients, calcinosis cutis preceded the diagnosis of undifferentiated CTD.

Table 3. Treatment Categories of 78 Patients Who Had Calcinosis Cutis Associated With ACTD

Treatment Category	Best Response, No. (%)				
	CR	NR	PR	Unknown	Total
Medical	1	5	6	7	**19** (24)
Surgical	8	0	3	0	**11** (14)
Medical and surgical	14	1	2	0	**17** (22)
None	0	30	0	0	**30** (38)
Unknown	0	0	0	1	**1** (1)

Abbreviations: ACTD, autoimmune connective tissue disease; CR, complete response; NR, no response; PR, partial response.

Use of Etidronate

- 2012 JBMR case report
- Etidronate 800 mg daily x 3 mos every 6 mos for 3 yrs
- Significant improvement in both OP and calcinosis
  - LS BMD 0.830->0.997, FN 0.403->0.639
- Inhibition of hydroxyapatite crystal growth
  - Less specific for bone than newer BPs
- Anti-inflammatory

Plan

- Continued phosphate binder
- Stopped calcitonin
- Planned to start course of etidronate but high risk of worsening reflux
- Follow up later this month

References

- Balin SJ et al. Calcinosis cutis occurring in association with autoimmune connective tissue disease. *Arch Dermatol*. 2012: 455-62.
- Boulzman N et al. Calcinosis in rheumatic diseases. *Semin Arthritis Rheum*. 2005: 805-12.
- Mori H et al. Marked improvement of calcinosis in adult dermatomyositis with etidronate therapy. *J Bone Miner Metab*. 2012: 114-8.