Senior Case

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First admission - chief complaint

70 year old female with PMH of HTN presents with LLQ abdominal pain x1 month and tightness of skin, as well as stiff muscles for several months

Abdominal pain

- LLQ
- Worsening over the last month
- Relapsing and remitting
- Non-radiating
- Associated symptoms include nausea and decreased appetite
- One episode of NBNB vomiting and one episode of watery diarrhea on separate occasions
- Endoscopy and colonoscopy in the last year which were normal

Skin tightness

- Started 4 months ago, progressively worsening
- No difficulty swallowing, however difficulty opening mouth has made it so that she can only eat soup
- No recent dental work or trauma
- Unable to move eyes as well as before, but no changes in vision
- Tightening of skin of chest, back, face and limbs

Medications

- Ferrous sulfate 324/325 daily
- HCTZ 12.5 mg PO daily

Allergies

- NKA

Family History

- Sister - cancer, unspecified
- Father - liver cirrhosis secondary to alcohol abuse
- Sister - DM, HTN, CVA

Social History

- Works as a nursing assistant
- Recently remarried
- Denies tobacco, alcohol or drug use

Vitals

Temp 98.9-99.3

Heart rate: 80-97

Respirations 15-22

SpO2: 99%-100%

Weight 41.7kg (91lb15oz)

Physical Exam

General: alert, cachectic, temporal wasting

Eyes: PERRL. Decreased EOM in all directions. Bilateral ptosis, nonfluctuating. Full visual fields

Mouth: No TMJ tenderness, normal excursion

Neck: Supple, no adenopathy

Lymphatics: No palpable lymphadenopathy

Heart: normal rate, regular rhythm, normal S1, S2, no murmurs rubs or gallops

Physical Exam continued

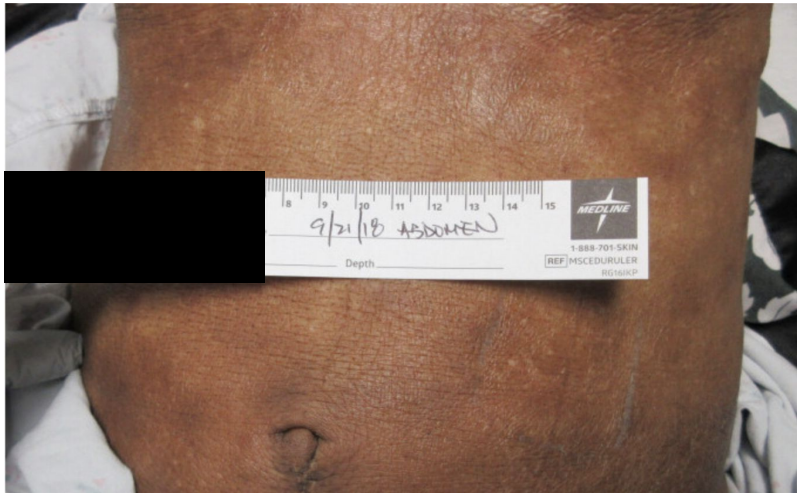
Chest: CTAB, no wheezes rales or rhonchi

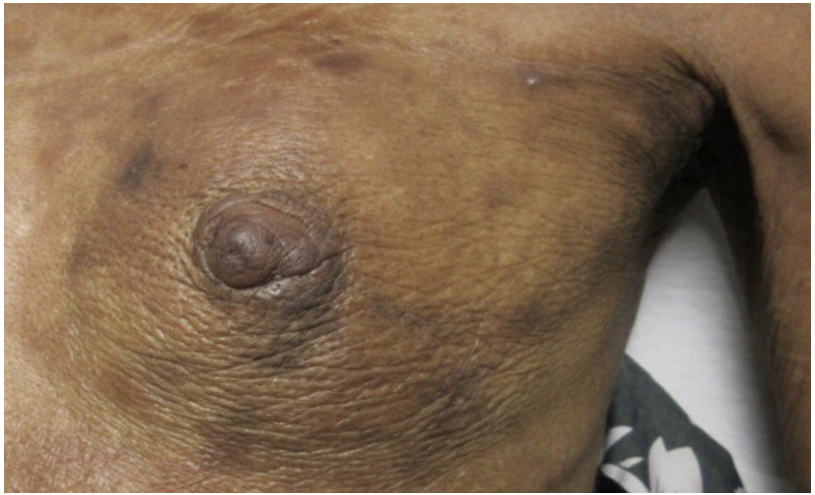
Abdomen: nondistended, tenderness noted to LLQ, no rebound or guarding, tense to palpation

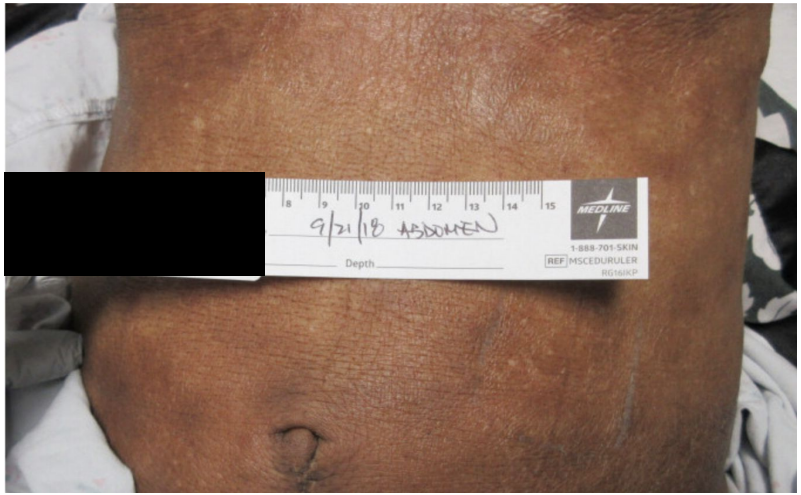
Back exam: Limited range of motion on rotation of back, neck, ~30 degrees either side laterally

Neuro: increased muscle tone of jaw and facial muscles. Normal tone BUE and BLE. No tremors, strength 5/5, reflexes 1+ in lower extremity and upper extremity

Extremities: diffuse tightening of skin on neck, trunk, and abdomen



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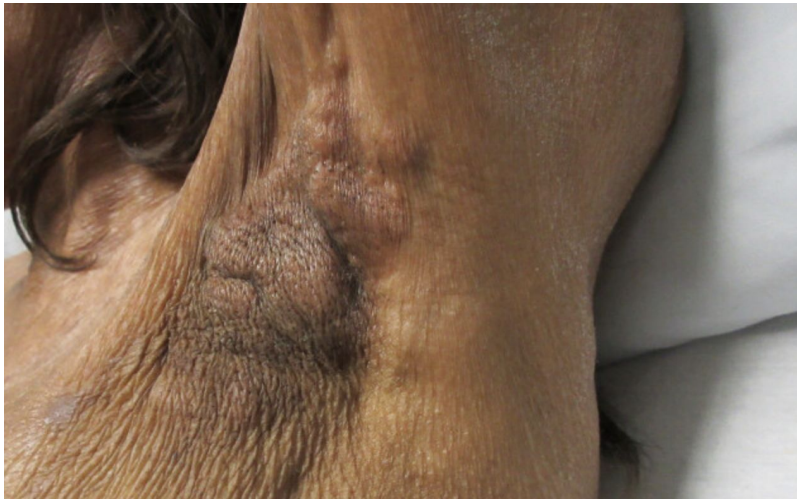
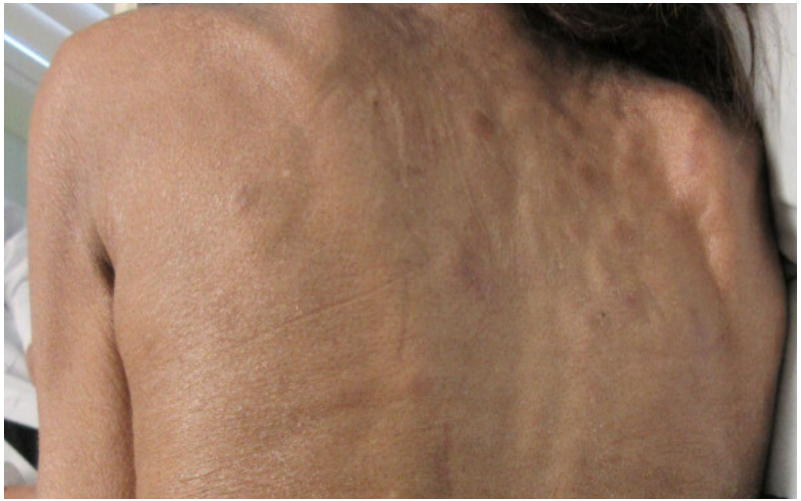




Labs

Recent Labs

Lab	09/16/18 1136	09/16/18 1640	09/16/18 1900
WBC	4.3	4.4	4.0*
HGB	7.2*	5.7*	6.6*
HCT	23.7*	17.6*	20.9*
MCV	77.4*	78.5*	76.8*
PLT	433*	389	409

Lab	09/16/18 1136	09/16/18 1900
NA	138	--
K	4.4	--
CL	106	--
CO2	21	--
ANIONGAP	11.0	--
BUN	50*	--
CREATININE	2.11*	--
CA	8.3*	--
PHOS	--	3.9
TPROT	7.0	--
ALBUMIN	3.2*	--
ALT	12	--
AST	22	--
ALKPHOS	145*	--
TOTALBILI	0.4	--

Summary of presentation:

- Diffuse dermal thickening
- Trismus
- Truncal spasm
- Cachexia
- Ophthalmoplegia
- Absent LE reflexes

Differentials?

Differentials

Dermatomyositis

Systemic sclerosis

Tetanus

Malignancy

Paraneoplastic syndrome

Scleroderma

Myasthenia Gravis

Polymyositis

Neurology consult: Trismus, Truncal Spasm, Ophthalmoplegia

Cranial nerves:

CN II	PERRL, full visual fields
CN III, IV, VI	Decreased EOM in all directions (restricted ROM but no paresis in a particular direction), oculocephalic demonstrates similar restrictions in horizontal motion. +Bilateral ptosis (nonfluctuating, possibly apparent due to tightening/abnormal appearance of surround facial structures)
CN V	ophthalmic, maxillary, mandibular, intact to LT
CN VII	Limited on examination- eyes close fully to resistance. Symmetric eyebrow raising, eye closure, cheek puffing (weak), lip pursing, smile (restricted)
CN VIII	intact to conversation
CN IX/X	palate equal rise, normal speech, no dysarthria,
CN XI	head rotation, shoulder shrug 5/5 (normal SCM &trapezius strength)
CN XII	normal tongue position and movement

Motor

Pronator drift	+ Left sided pronator drift (mild)
Bulk	Cachectic throughout with wasting noted throughout BUE/BLE
Tone	Increased tone about her bilateral jaw/facial muscles. Normal tone BUE/BLE
Tremor	Absent

	Nerve root	Right	Left
Finger extension	C8	5/5	5/5
Dorsal interosseus	C8T1	5/5	5/5
Wrist extension	C6	5/5	5/5
Wrist flexion	C7	5/5	5/5
Elbow flexion	C5,6	5/5	5/5
Elbow extension	C6,7,8	5/5	5/5
Shoulder abduction	C5,6	5/5	5/5
Hip flexion	T12-L3	5/5	5/5
Knee flexion	L4-S2	5/5	5/5
Knee extension	L2-L4	5/5	5/5
Plantarflexion	S1	5/5	5/5
Dorsiflexion	L4	5/5	5/5

*All muscle groups normal strength

Sensory:

Intact to light touch, vibration bilaterally.

Deep Tendon Reflexes:

	Right	Left
Biceps	2+	2+
Brachioradialis	2+	2+
Triceps	2+	2+
Patellar	1-2	1-2
Achilles	trace	trace
Down going toes bilaterally		
Clonus not present bilaterally		

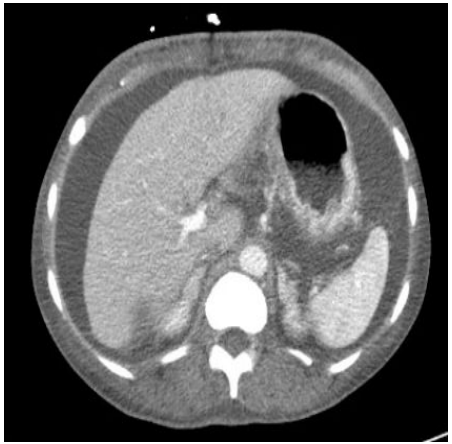
Cerebellar:

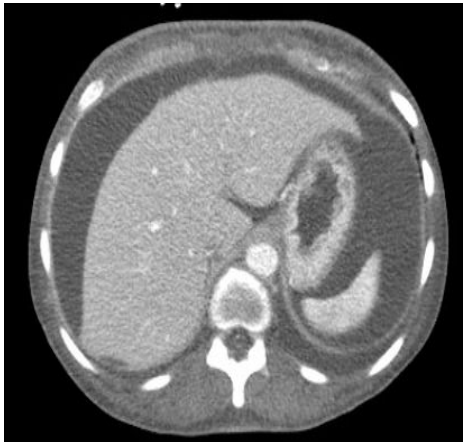
Finger to nose	Intact
Heel to shin	intact
RAM	R=L

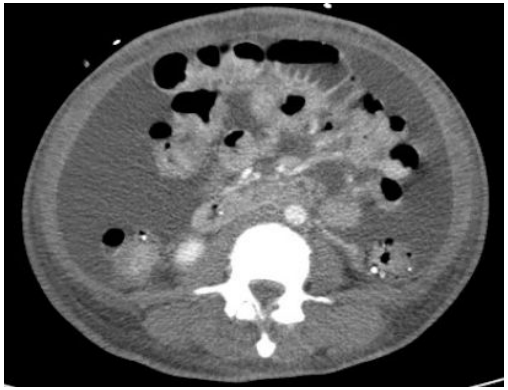
Differentials: Malignancy, Stiff Person Syndrome, Myasthenia Gravis, other rheumatologic cause

Recommendations: Complete malignancy work-up including CTAP, paraneoplastic panel, MRI brain and orbits, CSF panel, rheumatology consult, myasthenia gravis antibody panel

CT Abdomen/Pelvis with IV contrast







CT Abdomen/Pelvis with IV contrast

Findings:

- Soft tissue anasarca
- Large ascites present
- Pancreatic atrophy
- Diffuse sclerosis of the skeletal system suspicious for osseous metastases

Impression:

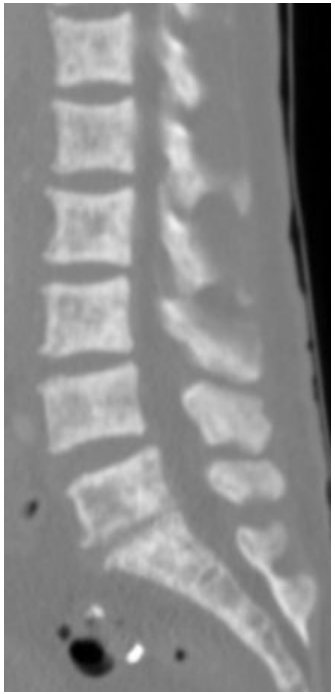
- **Findings consistent with third-spacing**
- **Diffuse osseous metastasis**

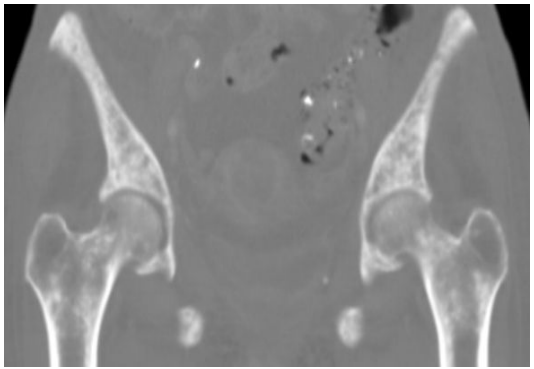
Oncology consult for osseous lesions on CT scan

Oncology did not see patient but did a chart review and dropped a note stating:

“Suspicion for malignancy is low. Most likely it is autoimmune. Consult Rheumatology for autoimmune workup and dermatology for diffuse skin thickening as patient may need biopsy”

Recommendation: Bone scan to evaluate osseous lesions. If concerning, then biopsy





Further workup

ESR 16

CRP 23.1 (H)

CK 32

Vitamin B12 3,314 (H)

Folate 64.7 (H)

Hemoccult Negative

Anti-centromere b antibody: Negative

ANA: Negative

Scl-70 Ab: Negative

CA125 324.7

Hepatitis C: Negative

LDH 220

Haptoglobin 265 (H)

Rheumatology consult

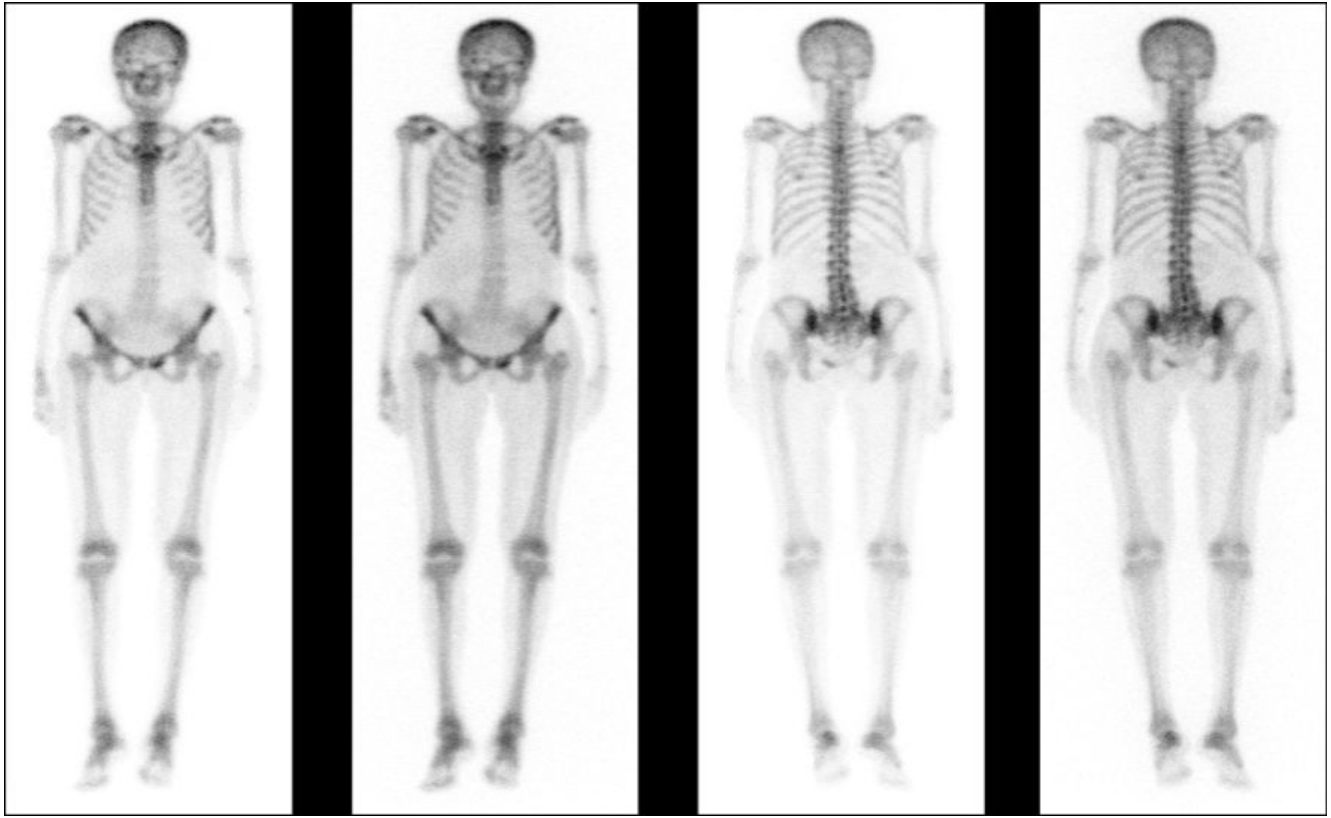
Assessment

- Plaque-like areas of skin thickening around chest, breast, abdomen and thighs. Nature of skin findings along with abrupt onset is atypical for systemic sclerosis.
- Absence of appreciable skin thickening in distal phalanges, absence of Raynaud phenomenon, telangiectasia, or nail fold capillary changes also goes against diagnosis of scleroderma

Recommendations

- Consider CT head for ongoing ophthalmoplegia
- Neurology consult for areflexia/ptosis
- Biopsy of thickened skin and dermatology consult
- Consider malignancy especially in view of bone sclerosis and inflammatory skin changes
- Follow up Scl-70

NM Bone Scan



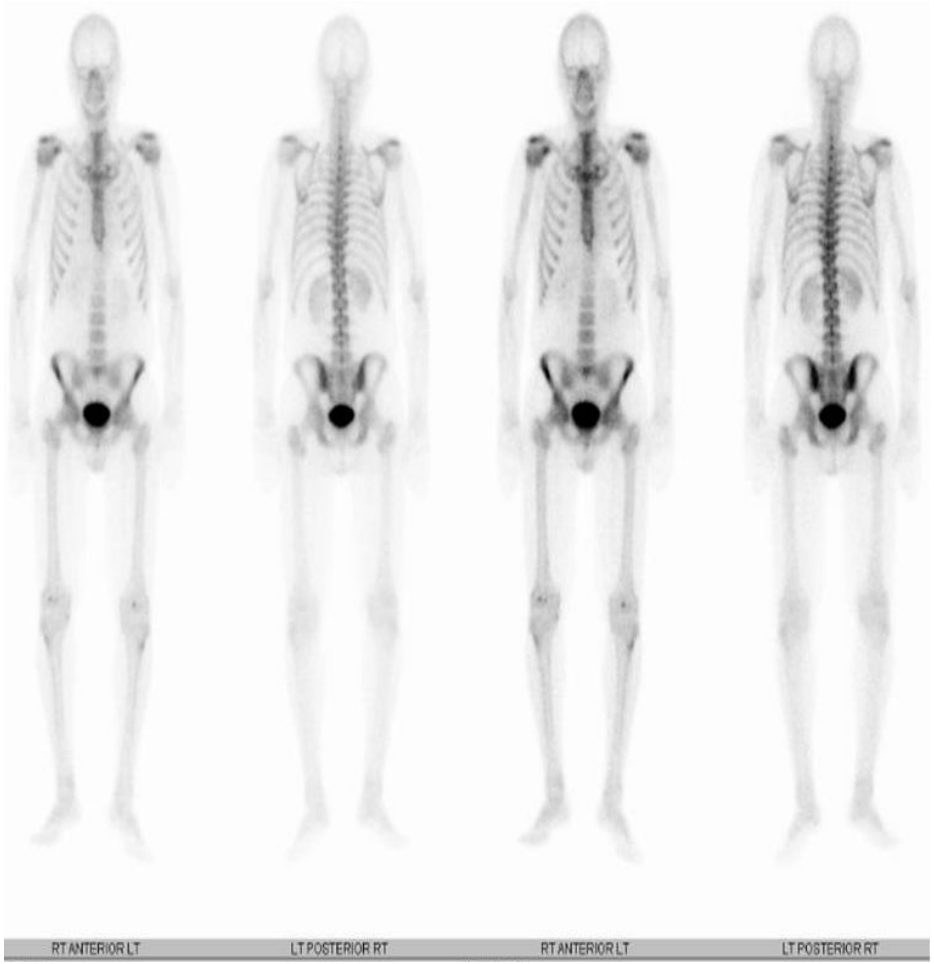
NM Bone Scintigraphy

Technetium-99 injected and taken up by osteoblasts

No purely lytic process will show up on bone scan because tracer only taken up by blasts. Therefore multiple myeloma will not show up on bone scan

What isn't taken up by the bones stored in skin until taken up by kidneys and excreted

A "superscan" demonstrates markedly increased skeletal isotope uptake relative to soft tissues in association with absent or faint renal activity (absent kidney sign)

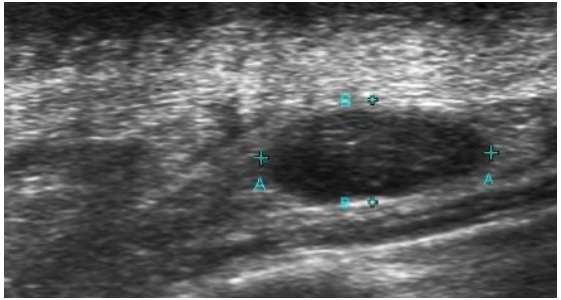


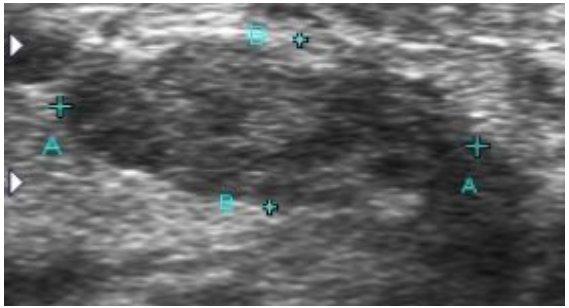
Working differential: Malignancy

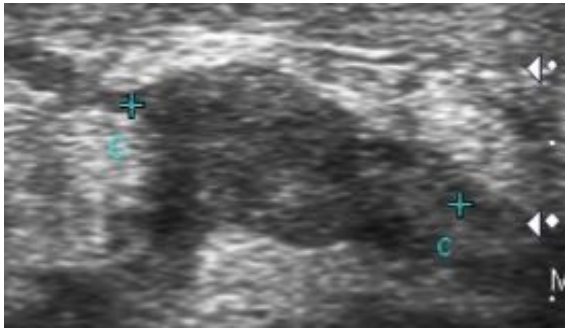
- After discussing Superscan with radiology, they made recommendation to obtain mammogram to rule out breast cancer as primary cancer
- Mammography attempted on day prior to discharge however due to skin changes and cachexia, it could not be completed.

Breast workup

- US bilateral breasts were done with the following findings:
  - 2 masses in left breast including dilated ectatic ducts: BI-RADS 5
  - Multiple prominent lymph nodes within left axilla with thickened cortex: BI-RADS 4







Breast Biopsy

Left breast mass:

Invasive mammary carcinoma with lobular features

Adjacent intraductal papilloma with ductal hyperplasia

Left axillary lymph node:

Positive for metastatic carcinoma

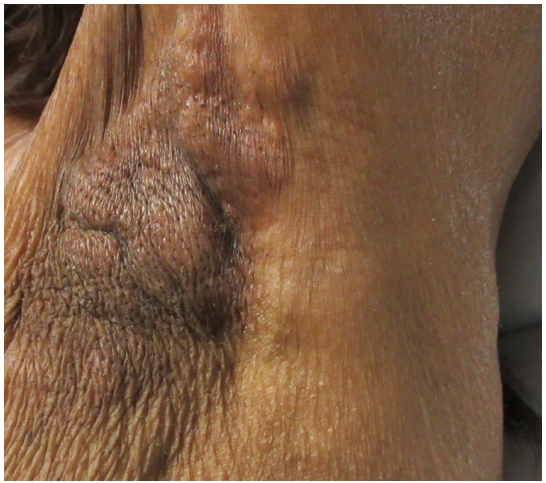
“Lymph node was almost completely replaced by metastatic carcinoma which shows similar lobular features of left breast cancer. Surrounding fibrous adipose tissue also contains tumor cells with lobular features”

Skin Biopsy

Punch biopsy of R superior lateral back

Skin with dermal scarring and sparse interstitial lymphocytic infiltrate

No evidence of malignancy

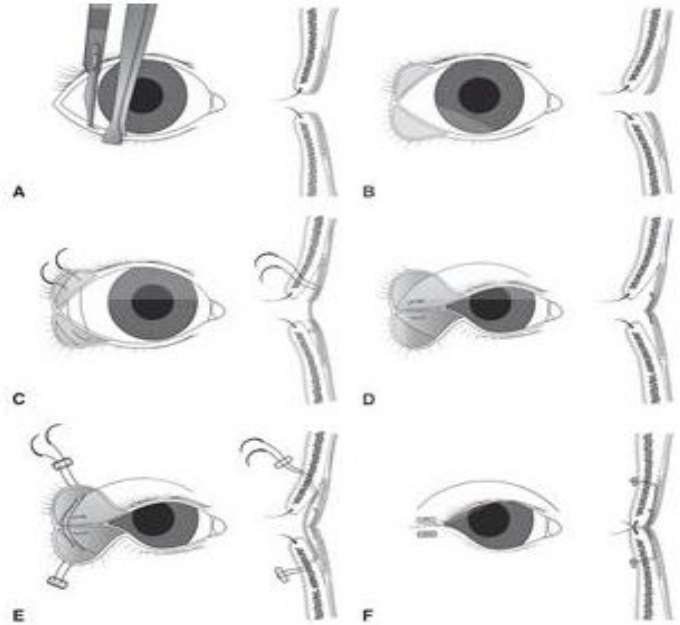


Readmission - 2 weeks after discharge

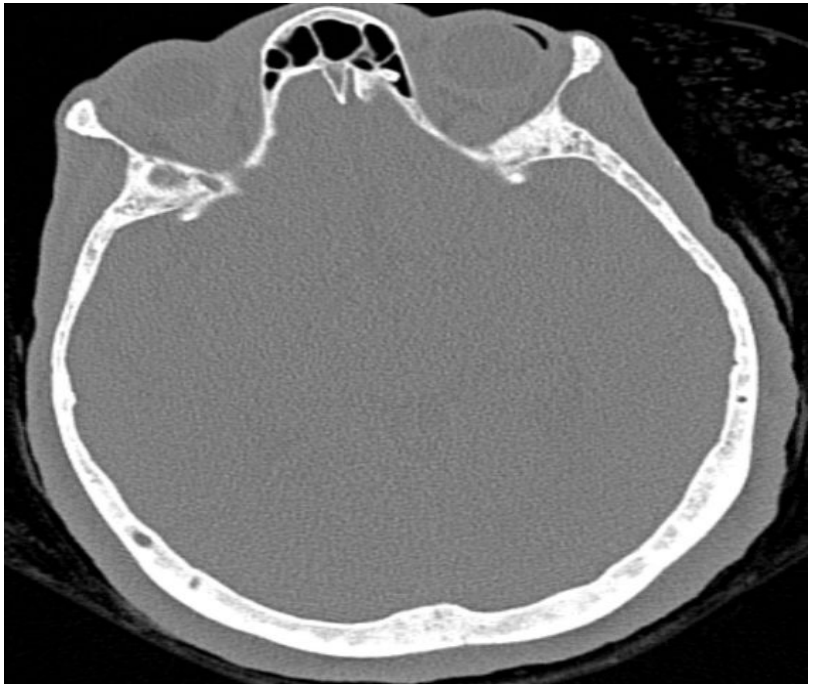
- Presented to ED with acute pain and worsening of vision in right eye
- Evaluated by ophthalmology who found corneal ulcer with uncertain bacterial vs viral etiology
- Corneal cultures obtained and she was started on empiric antibiotics

Corneal Ulcer

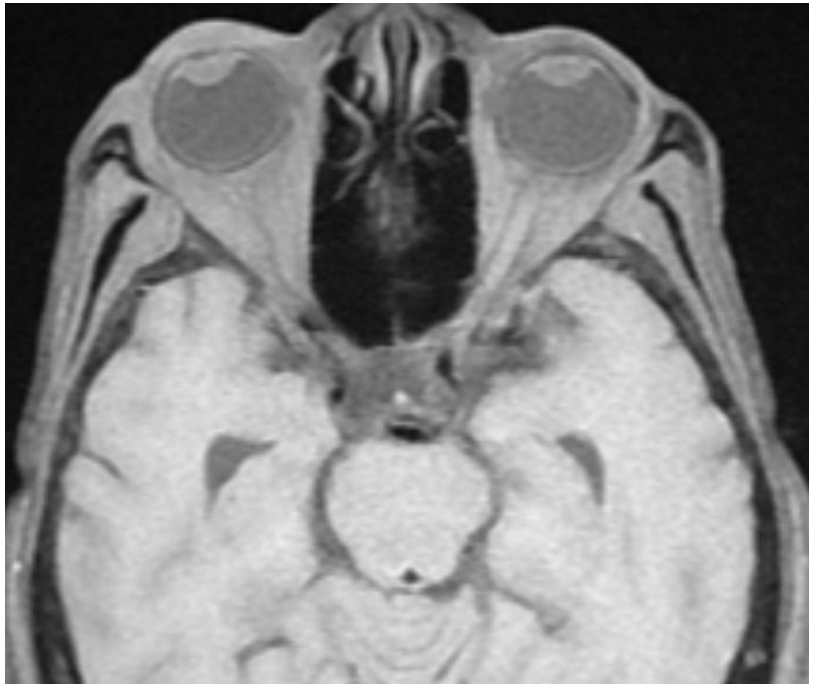
- MRI of brain and orbit significant for heterogenous low signal throughout calvarium representing osteoblastic metastatic disease
- Generalized enlargement of bilateral extraocular muscles
- Ophthalmology saw patient daily and recommended tarsorrhaphy however patient refused



MRI Brain



MRI Orbits



Paraneoplastic Syndromes

Paraneoplastic Neurologic Syndromes

- Group of conditions that affect the nervous system (brain, spinal cord, nerves and/or muscles) in patients with cancer
- Different manifestations
  - Encephalitis
  - Ataxia
  - Neuropathy
  - Myoclonus/opsoclonus
  - Myasthenia Gravis
- PNS can frequently appear to affect only one part of the nervous system but over time other areas can become affected
- Can develop rapidly over the course of a few days or weeks, or they may develop slowly
- In 60% of patients with PNS, symptoms occur before the diagnosis of cancer is made

Stiff-person Syndrome

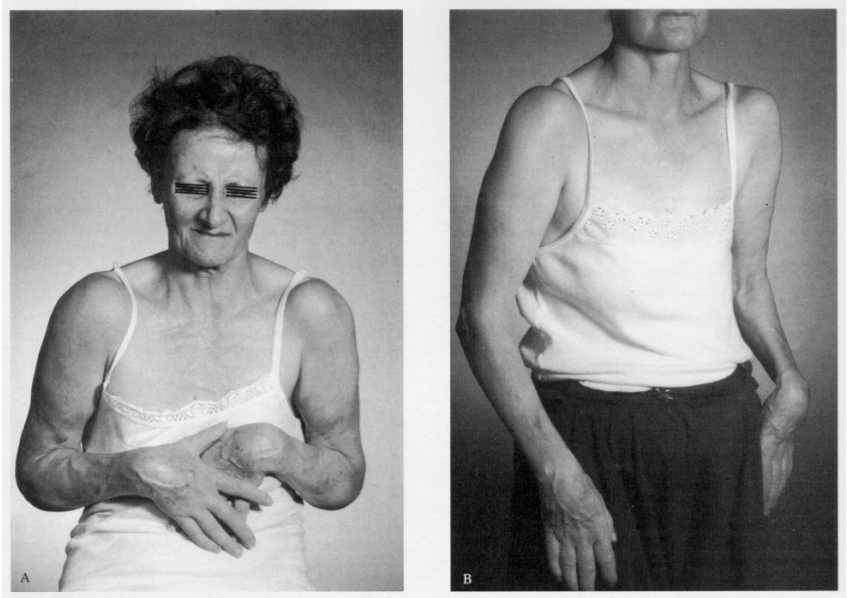
- Disorder characterized by muscle stiffness, rigidity and spasm
- Caused by increased muscle activity due to decreased inhibition of the CNS that results from blockade of glutamic acid decarboxylase (GAD) - the enzyme critical for maintaining inhibitory pathways.
- This results in decline in levels of GABA in the CNS which causes a loss of neural inhibition
- Usually autoimmune
- Association with T1DM
    - Seen in 30% of patients with SPS
- Women affected 2-3x more than men

Stiff-Person Syndrome

- Classic SPS
  - Truncal stiffness, generalized rigidity, frequent muscle spasms resulting in awkward, wide-based gait. 70-80 percent of patients with SPS present this way
- Partial SPS
  - Also called “stiff-limb syndrome”, patients have marked difficulty with ambulation due to stiffness and lack of mobility affecting one limb. Other localized forms may include abdominal or chest wall involvement, severe painful spasms or ocular symptoms
- Paraneoplastic SPS
  - Clinically indistinguishable from classic SPS
  - GAD antibody negative
  - Antibodies targeting specific proteins such as amphiphysin have been detected (<2% of patients with SPS)

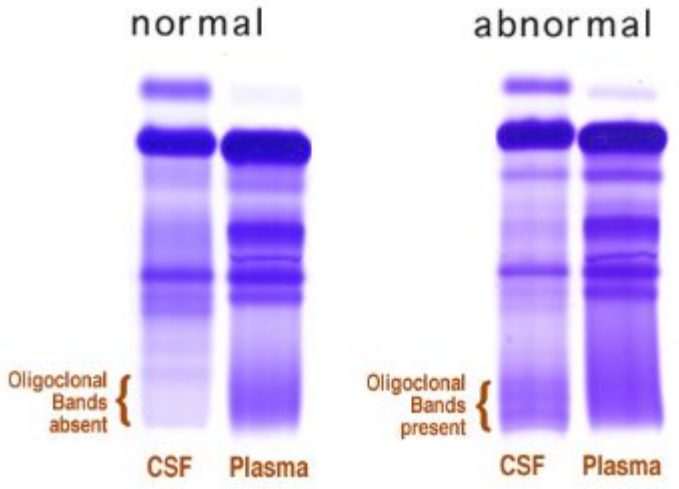
Paraneoplastic SPS

- Classic features of SPS
- Anti-GAD antibody negative
- Concurrent features of an underlying neoplasm such as anorexia, weight loss, or suspicious mass
- <1-2% of patients with SPS
- Most commonly seen in breast cancer, lung cancer, and Hodgkin Lymphoma
- Remission of neurologic symptoms following tumor excision and treatment with glucocorticoids
- Functional rather than structural changes in the CNS



Paraneoplastic SPS - Laboratory Workup

- General lab studies
  - Normal CBC and inflammatory markers such as CRP and ESR
  - CK and Aldolase are normal or slightly elevated
  - Given association with T1DM, HgbA1c may be elevated
- Antibodies
  - Anti-GAD antibodies in 60-80% of patients with classic SPS
  - Oligoclonal banding in CSF
  - Antithyroid, thyroid peroxidase, thyroglobulin, and anti-gastric parietal antibodies have also been noted



Treatment

- Benzodiazepines (Diazepam most effective)
- Baclofen - GABA modulating drug
- IVIG
    - Rituximab if no response
- Plasma exchange

Take away points

1. Early suspicion for paraneoplastic syndrome especially when they present along with symptoms concerning for malignancy such as weight loss and missed cancer screening
2. Association of certain malignancies as higher risk for PNS
3. Advocacy and education to patient population in regards to screening for cancer

References

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