Beyond Osteomyelitis: An Adult Presentation of CNO/CRMO

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Disclosures

- None

Objectives

- Recognize the clinical and imaging features of adult-onset Chronic Nonbacterial Osteomyelitis (CNO/CRMO), including multifocal sterile bone lesions with negative cultures and biopsies
- Identify the characteristic distribution of CNO/CRMO lesions, including involvement of the clavicle, anterior chest wall, and vertebral bodies, as sites that should prompt early consideration of the diagnosis
- Appreciate the consequences of diagnostic delay in adult CNO/CRMO, including unnecessary procedures, empiric antibiotics, and prolonged patient suffering

HPI: 61 female with iron deficiency anemia, asthma, depression, OSA, elevated BMI presenting to PCP

January 2019

- Had 6 weeks of pain in shoulder blade and went across upper back
- XR with moderate compression fracture of T8, probably subacute
- Started alendronate for osteoporosis
- Thoracic back pain continued for months

May 2019

- Abrupt worsening of thoracic back pain
- Pain is midline and radiates along bilateral sides
- (+)Night sweats
- (-)Fevers/chills
- PCP ordered imaging

Imaging: Thoracic Xray

- Impression
- 1. Stable appearance of the mild T8 compression fracture with mild cortical irregularity along the superior T8 endplate. Progressive bony sclerosis likely due to interval healing.
- 2. New bony sclerosis along the inferior T7 endplate with mild cortical endplate irregularity. Given apparent about findings these may be due to healing fractures, but cannot exclude the possibility of underlying osteomyelitis/discitis given the endplate irregularities and abnormal widening of the paravertebral soft tissue contour. Recommend clinical correlation and dedicated MR Thoracic Spine w/wo contrast to further evaluate.
- 3. New bony sclerosis with cortical endplate irregularity at the T4-T5 disc level concerning for possible additional level of infection related to osteomyelitis/discitis.

Imaging: MRI Thoracic Spine wwo

- At T4-5 and T7-8, fluid in the disc space with associated endplate irregularity and enhancing vertebral body marrow edema is most compatible with multifocal osteomyelitis. Malignancy is not excluded but less likely.
- At T8, there is superior endplate destruction with wedging and mild vertebral body height loss, and associated mild focal kyphosis.
- There is prevertebral phlegmon at these levels without discrete rim-enhancing fluid collection to suggest abscess. No epidural abscess. No thecal sac or neural foraminal stenosis.

Labs (May & June 2019)

CRP normal; ESR 35 (H)

Plt & CMP normal

Labs at Urgent Care May 2019

Underwent IR guided biopsy and further imaging

Labs: CRP 0.52 mg/dL (H)

WBC/diff normal

Hgb 12.2, MCV 78.9 (L)

Plt & CMP normal

SPEP/UPEP normal

Admission OSH June 2019

Imaging: CT Chest Abdomen Pelvis w

- 1. Endplate irregularity and adjacent vertebral body sclerosis most consistent with chronic osteomyelitis-diskitis at T4-T5 and T7-T8.
- 2. Nonspecific 6 mm circumscribed lucent focus in the anterosuperior aspect of T7 vertebral body.
- 3. Probable minimal Schmorl's node formation right superolaterally at L4 vertebral body.
- 4. Tiny scattered sclerotic foci in the bony pelvis bilaterally, likely representing bone islands.
- 5. Multiple liver lesions as described above likely representing cavernous hemangiomata, although assessment is incomplete on this examination. Note that several hyperechoic liver nodules were noted on the 2011 abdominal ultrasound, also compatible with cavernous hemangiomata.
- 6. No other mass is identified in the chest, abdomen, or pelvis. No lymphadenopathy.

Bone Biposy #1 (June 2019)

- Pathology
  - Marrow with scant hematopoietic precursors.
  - Bony trabeculae with no significant abnormality identified.
  - No evidence of acute osteomyelitis identified.
  - No evidence of malignancy identified.
- Bacterial Culture both bone and peripheral blood:
  - No growth at day 5

Illness Course: Mid 2019

ID Outpatient Visit June 2019

Felt less likely to be infection in absence of disease progression without antibiotic therapy

Referred to non-surgical spinal specialist

Physiatrist Outpatient Visit June 2019

Recommended topical treatment

ID Telephone Note June2019

Patient was generally doing well so they ultimately elected to repeat MRI

Repeat MRI (Summer 2019)

- As before, findings consistent with multifocal discitis-osteomyelitis.
- Compared to the examination dated 05/29/19, mild improvement in the abnormality at the T4-T5 level with mildly decreased bone marrow edema and enhancement and decreased prevertebral phlegmon.
- Essentially unchanged involvement of T7-T8. No new levels of involvement.
- No abnormal epidural fluid collection.

Illness Course: Empiric Antibiotics (July-August 2019)

ID Telephone Visit July 2019

Given that MRI remains normal, they felt it was reasonable to trial empiric course of 6 weeks of IV ceftriaxone. Followed by an oral course of antibiotics.

ID Telephone Visit August 2019

After weeks of antibiotics, no clear improvement in her back pain

Plan was to proceed with IV and then oral antibiotics.

Plastic Surgery Visit September 2019

Underwent consultation for breast reduction in hopes that would help her back pain

Illness Course: 2019-2021: Brief Apparent Stability

Doing well at that point

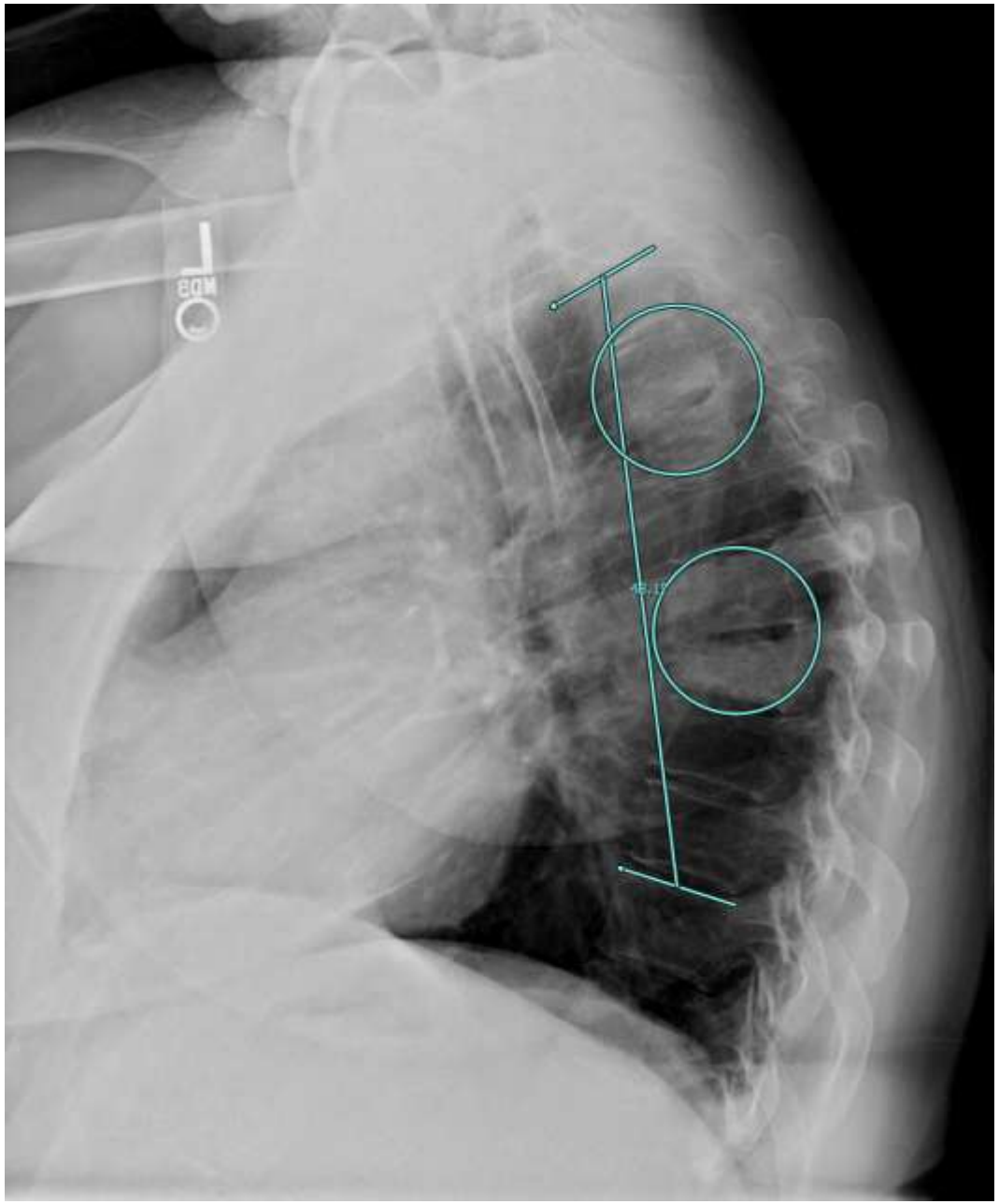
Finished IV CTX now transitioned to oral cephalexin to finish in November 2019

No plans to reimage unless symptoms persist or worsen

ID Telephone Visit October 2019

Underwent breast reduction in January 2020 and recovered well

Breast Reduction with Plastic Surgery

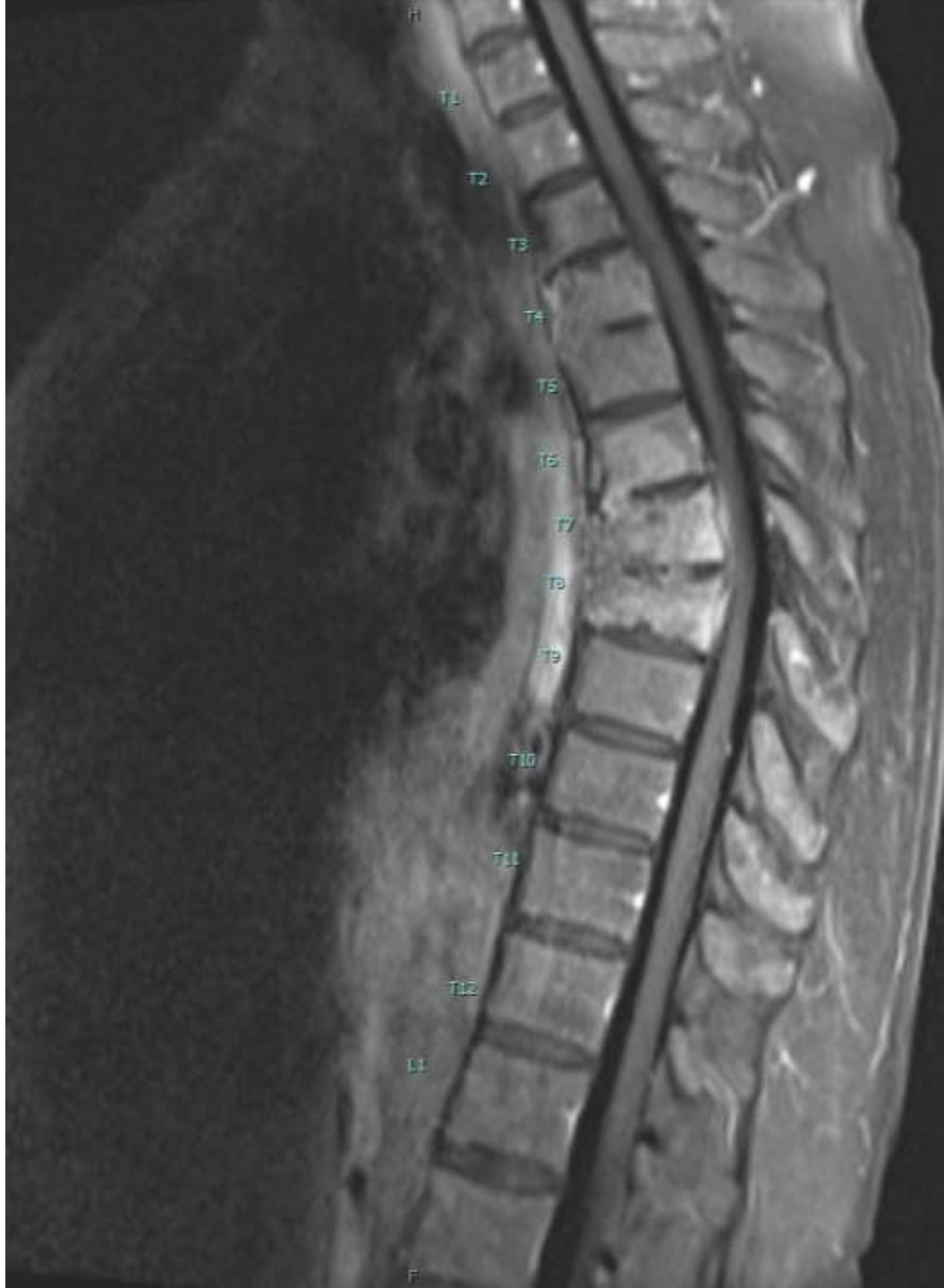


PCP Visit January 2021

- Thoracic back pain; same symptoms
- Xray T Spine: Sequelae of osteomyelitis-discitis redemonstrated at T4-5 and T7-T8. No definite new radiographic bony abnormality.
- Reassured that there wasn't any progression of osteomyeitis
- Taking alendronate regularly

MRI September 2023

- 1. Findings concerning for T4-T5, T6-T7, and T7-T8 discitis osteomyelitis. Subtle mild enhancement involving the T3 inferior endplate is also concerning for possible infection.
- 2. Thin enhancement of the anterior epidural soft tissues from T6 to T8 as well as at the level of T4 with mild thecal sac effacement. Findings are concerning for epidural phlegmon.
- 3. There is associated new minimal to mild height loss involving the T7 vertebral body.
- 4. Chronic T8 vertebral body mild to moderate anterior height loss. Increased severe T4-T5 disc height loss with suggestion of partial bony fusion anteriorly.



Admission September 2023/Biopsy #2

- Expedited workup for MR findings
- CBC w diff/CMP normal; CRP/ESR normal; TB negative; Coccidioides Ab: Negative
- Underwent CT bone biopsy again
- Bone Biopsy Pathology Results
  - Thoracic vertebrae:
    - Scant cortical bone with reactive/remodeling-type changes and focal hematopoietic marrow with crush artifact.
    - No acute osteomyelitis or metastatic carcinoma identified (pan-keratin stain evaluated).
  - Bacterial DNA Detection by PCR: negative
  - Culture: Negative at 5 days; no anaerobes
- Subsequently treated empirically with more IV antibiotics (Ceftriaxone and Daptomycin) x 2 weeks while waiting for cultures to return

Biopsy #3 (November 2023) and Neurosurgery

Decision to repeat bone biopsy with AFB, fungal stain in addition to PCR for bacterial, fungal and AFB

ID Telephone September 2023

Cortical bone with mild fibrosis and reactive/degenerative changes.

Negative for malignancy.

There are no acute inflammatory cell infiltrates, chronic lymphoplasmacytic cellular infiltrates, or necrosis identified.

Definite histologic features of osteomyelitis are not identified.

PCR bacterial, fungal and AFB negative.

AFB, bacterial, fungal cultures negative

Bone Biopsy November 2023

Felt that MRI shows several areas of autofusion and has the appearance of a larger process.

Decision was made to refer to rheumatology for further evaluation

Neurosurgery Visit December 2023

Neurology Detour (Early 2024)

Outside Rheumatology Visit January 2024

Felt that patient had no evidence of ankylosing spondylitis and felt that metabolic bone disease such as Paget's was unlikely given normal alk phos and no other involvement of skeletal areas

Referred to spine clinic for non-surgical interventions

Physiatry Visit February 2024

(+) Neck Pain

Cervical spine MRI revealed small focus of T2 hyperintensity in the left posterior cervical cord at the C2-3 level, nonspecific but may represent a focus of demyelination or secondary to prior trauma.

Thoracic spine MRI Thoracic spine: Otherwise similar appearance of the thoracic spine MRI.

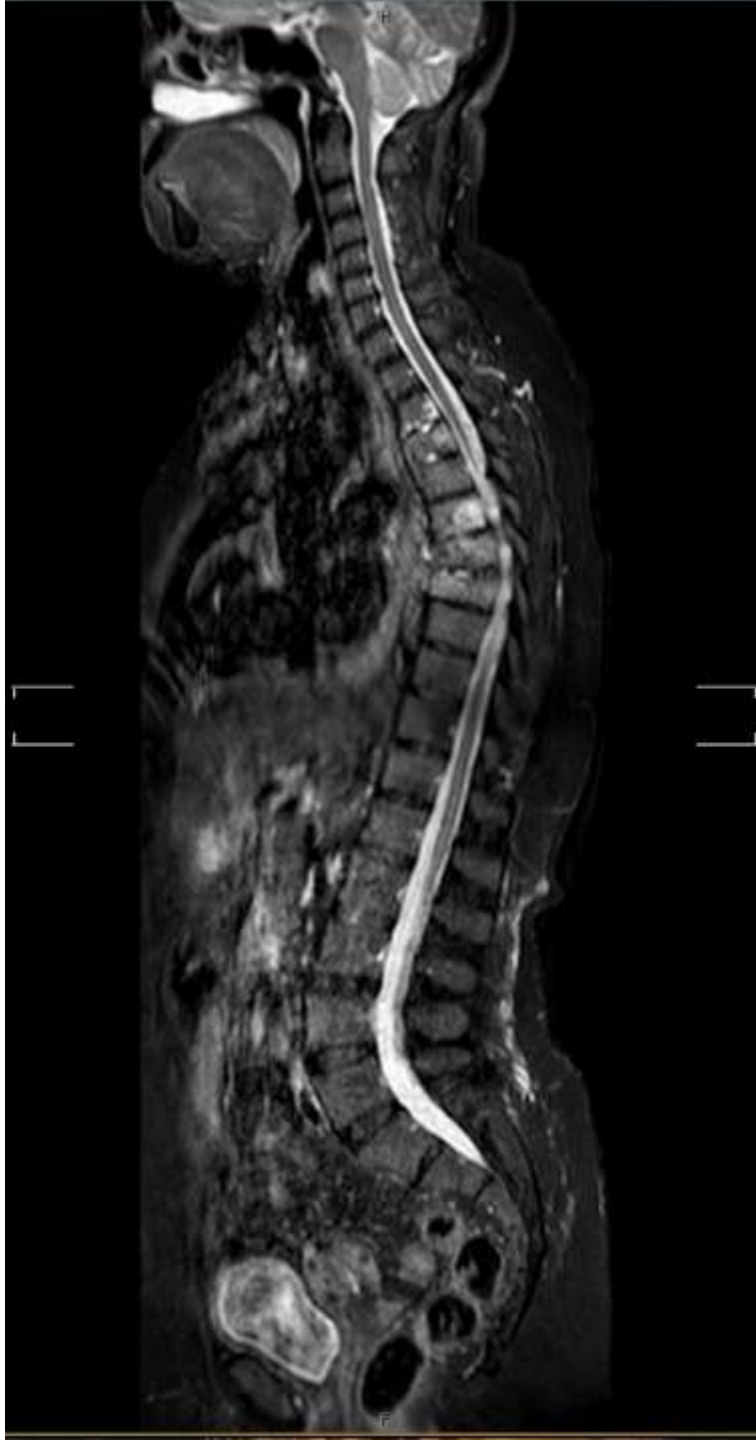
Neurology Visit April 2024

Brain MRI: Revealed 4 small hyperintense FLAIR foci in the right superior posterior frontal lobe, left parietal lobe, right periatrial white matter and right posterior temporal lobe and nonspecific.

Underwent lumbar puncture that was reassuring against MS

The Nuclear Medicine Bone Scan

- IMPRESSION: Increased radiotracer uptake within the medial left clavicle, left anterior first and second ribs, left fifth rib at the costovertebral junction, and the T4-T8 vertebral bodies with associated sclerotic lesions on CT. Given chronicity of spinal findings on correlative imaging, differential considerations include SAPHO syndrome and chronic osteomyelitis.



What is CNO? Disease Overview

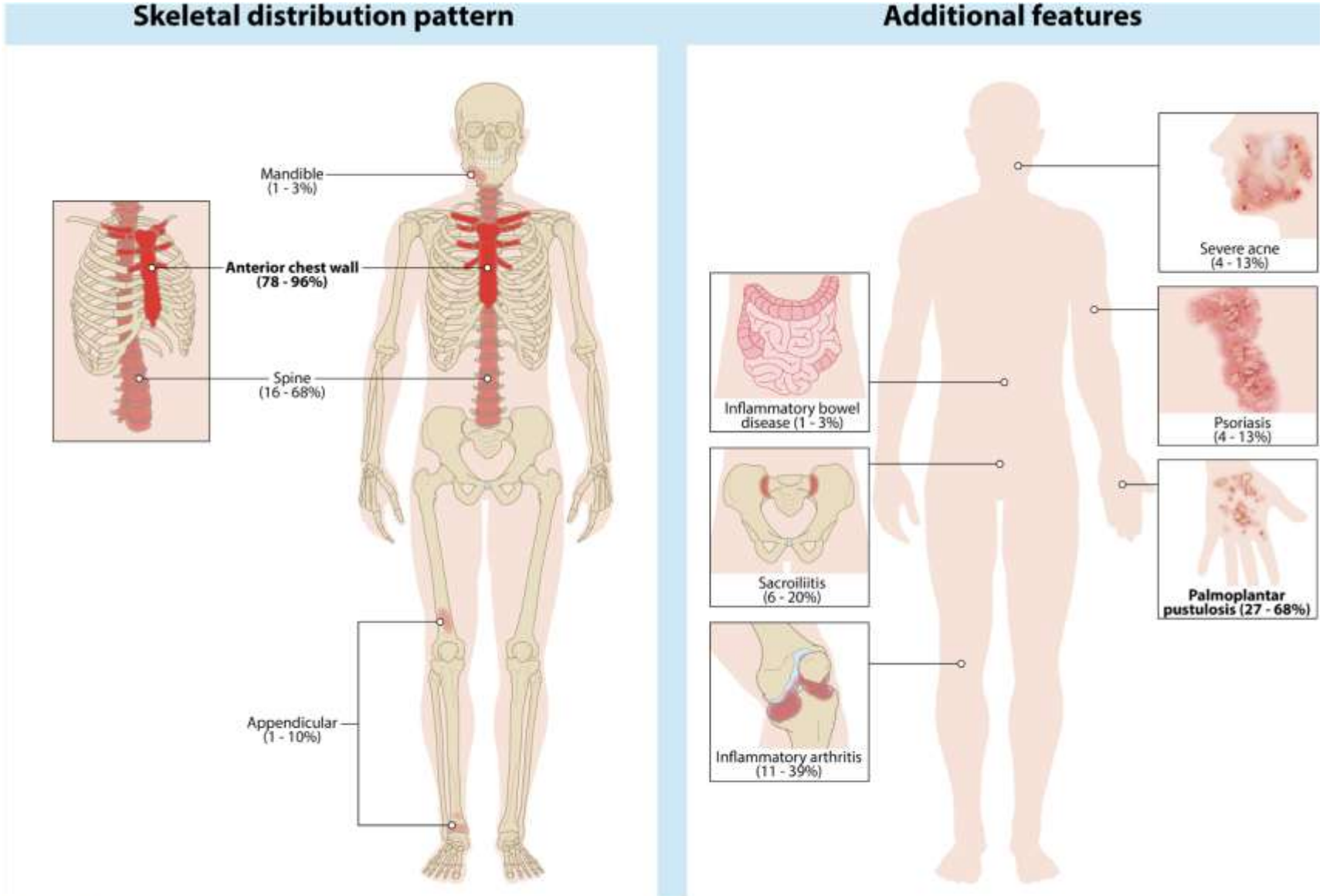
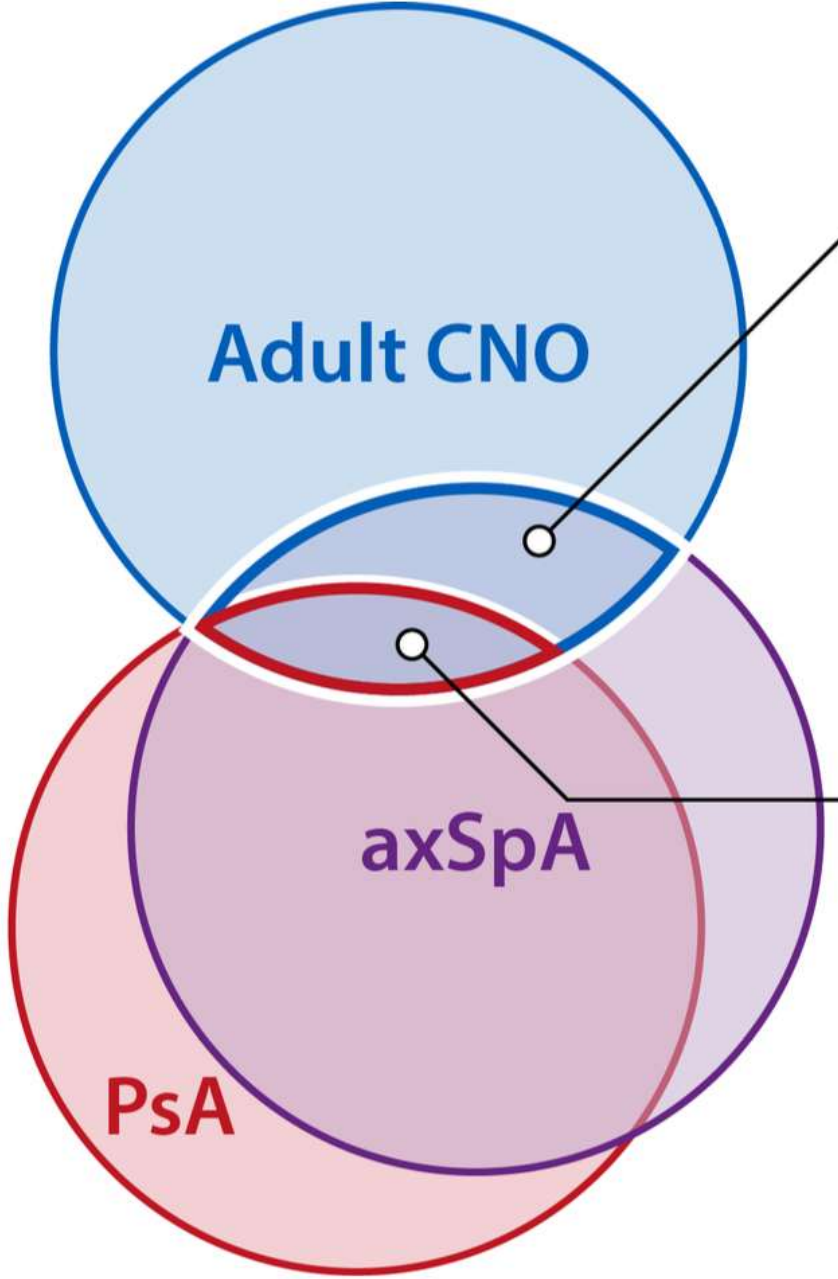


Figure 2 Visual representation of disease definition of adult CNO; skeletal distribution pattern of osteitis (left) and additional (extra)-skeletal features (right). Reported as 95% CI.

Overlap with Spondy



CNO and axSpA:

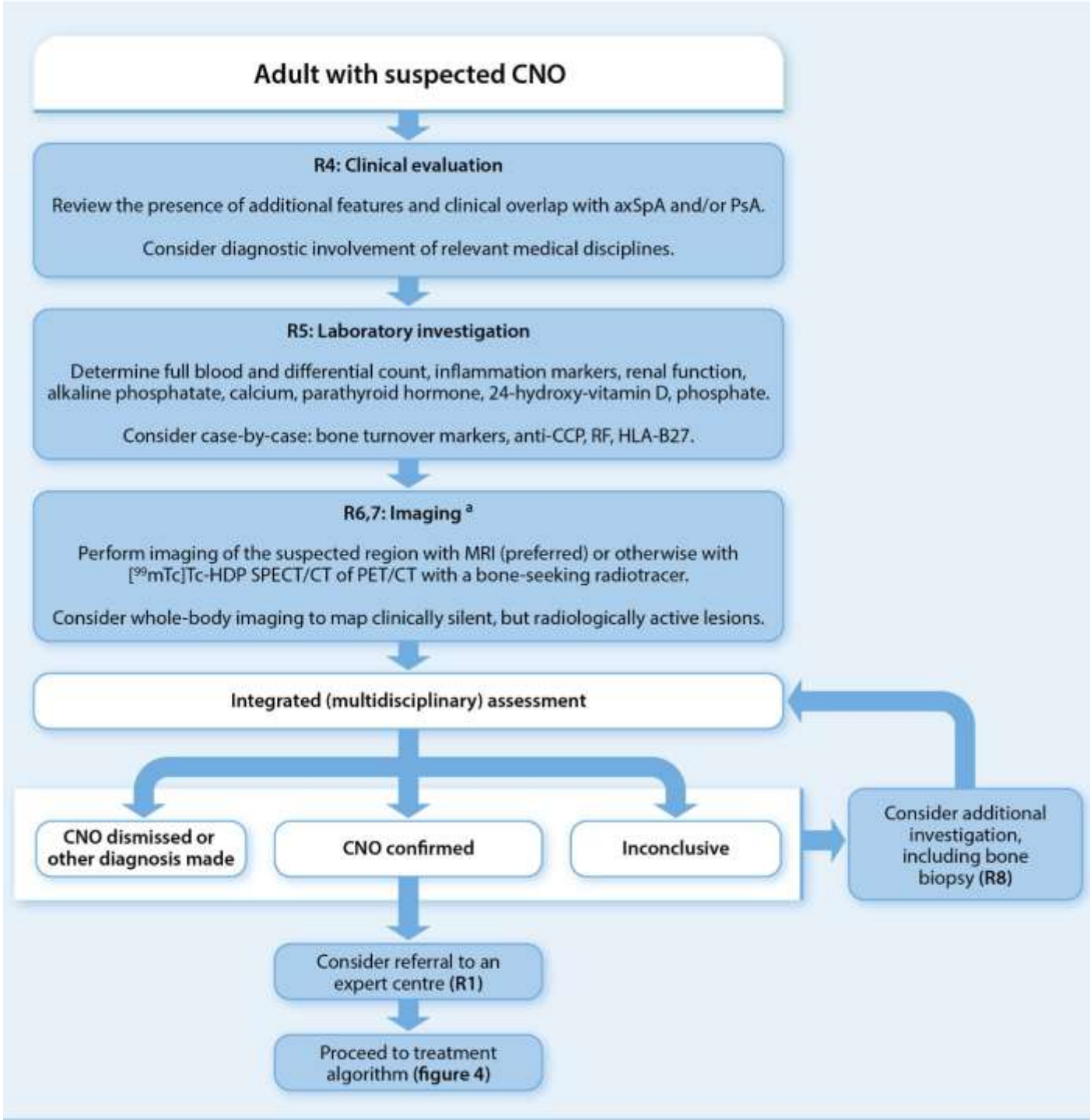
- Axial skeletal involvement
- Sacroiliitis
- Uveitis
- Inflammatory bowel disease
- Symptoms responsive to NSAIDs/COXIBs

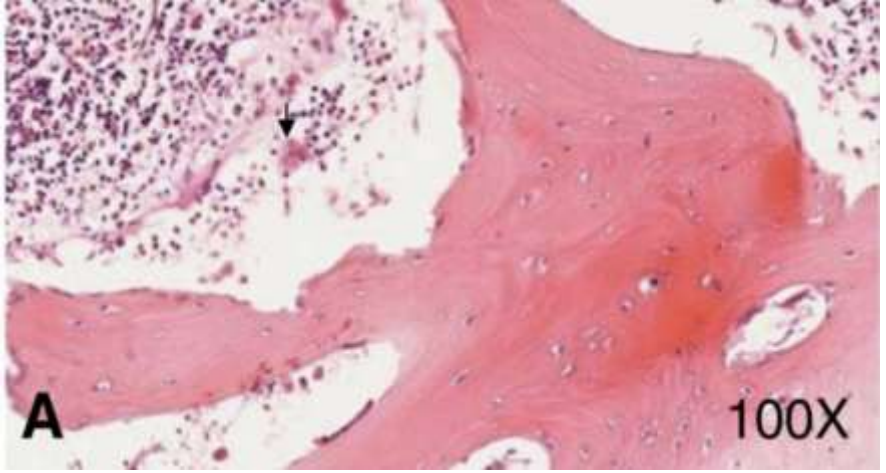
PsA, CNO and axSpA:

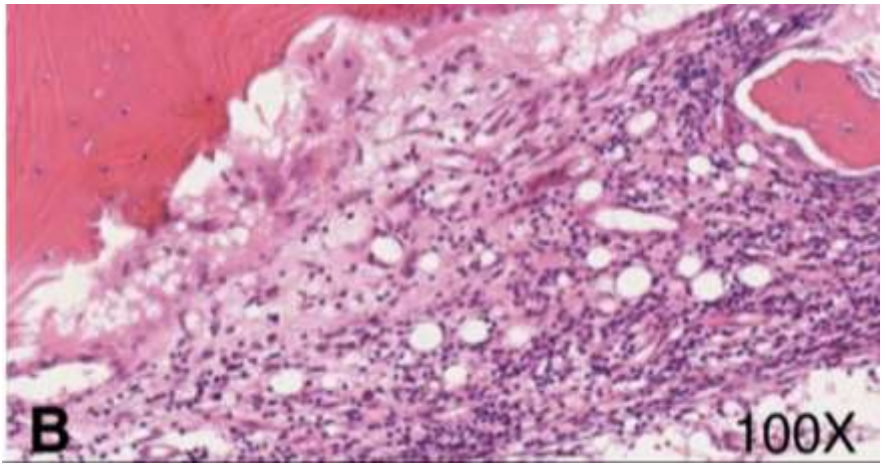
- Enthesitis
- Dactylitis
- Psoriasis
- Inflammatory arthritis
- New bone formation

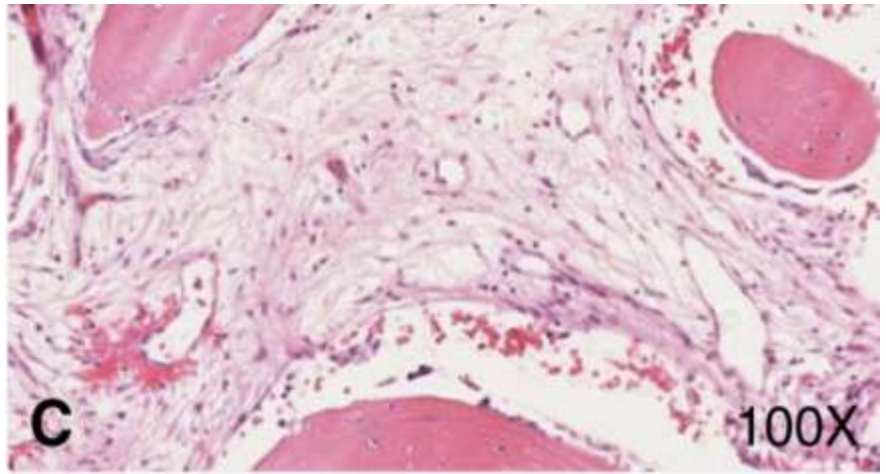
Figure 3 Venn diagram displaying conceptual overlap between adult chronic non-bacterial osteitis (CNO) and axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) based on features seen in the multiple conditions. COXIB, cyclooxygenase-2 inhibitor; NSAID, non-steroidal anti-inflammatory drug.

Diagnostic Approach





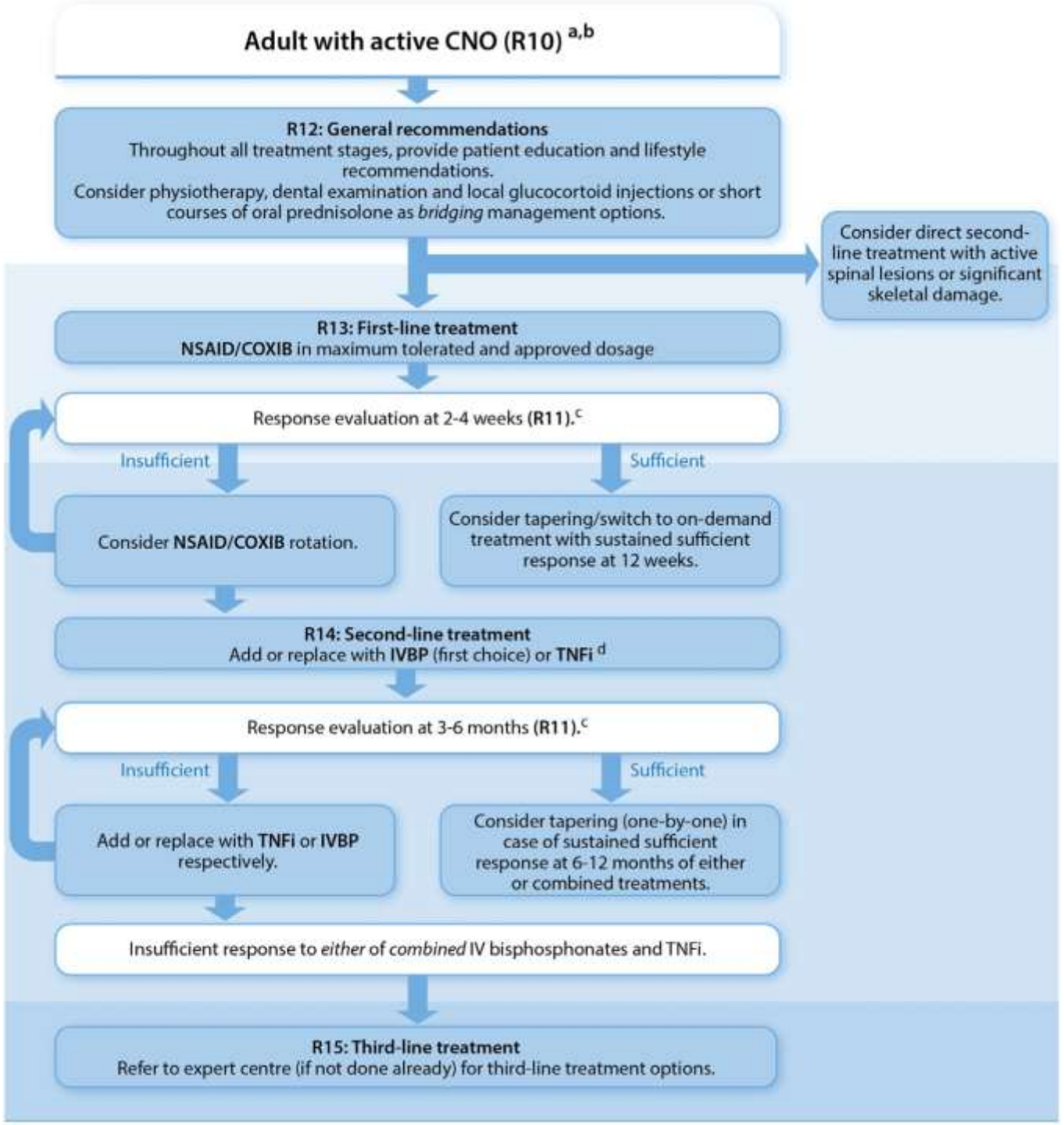




Bone Biopsy

- Destruction of normal bone structure and presence of neutrophils, monocytes, lymphocytes, and plasma cells during early phases
- Predominance of fibrosis and sparse immune cells during later phases
- Mixture of fibrosis and inflammation as well as normal bone has been reported

Treatment


Adult with active CNO (R10) a,b
R12: General recommendations
Throughout all treatment stages, provide patient education and lifestyle recommendations.
Consider physiotherapy, dental examination and local glucocortoid injections or short courses of oral prednisolone as bridging management options.
Consider direct second-line treatment with active spinal lesions or significant skeletal damage.
R13: First-line treatment
NSAID/COXIB in maximum tolerated and approved dosage
Response evaluation at 2-4 weeks (R11).c
Insufficient
Sufficient
Consider NSAID/COXIB rotation.
Consider tapering/switch to on-demand treatment with sustained sufficient response at 12 weeks.
R14: Second-line treatment
Add or replace with IVBP (first choice) or TNFi d
Response evaluation at 3-6 months (R11).c
Insufficient
Sufficient
Add or replace with TNFi or IVBP respectively.
Consider tapering (one-by-one) in case of sustained sufficient response at 6-12 months of either or combined treatments.
Insufficient response to either of combined IV bisphosphonates and TNFi.
R15: Third-line treatment
Refer to expert centre (if not done already) for third-line treatment options.

Treatment Goals and Long Term Follow Up

- Primary Goal:
  - Relieve symptoms (bone pain) and regain function
- Secondary Goals:
  - Reduce inflammation (edema on MRI) and prevent structural damage
- Follow-Up:
  - Long-term follow-up is recommended (3-6 months initially, then every 12-24 months)

Summary

- Consider CNO in adults with sterile multifocal bone lesions
- Bone scan can be diagnostic (hypermetabolic lesions at characteristic sites)
- Treatment:
  - NSAIDs
  - Bisphosphonates
  - TNFi
- Multidisciplinary approach prevents diagnostic delays