

IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME (IRIS): AN EASILY OVERLOOKED CONDITION IN ONCOLOGIC RADIOLOGY

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Objective and Method: Case series to review the imaging findings of IRIS

Introduction: Two adolescents with newly diagnosed acute lymphoblastic leukaemia (ALL) were started on chemotherapy, later complicated with neutropenic fever and disseminated invasive candidiasis.

Patient 1

A 14-year-old with good past health is newly diagnosed with acute lymphoblastic leukemia (ALL). He was started on chemotherapy. He developed neutropenic fever on day 15 post-chemotherapy, absolute neutrophil count (ANC) was $0.03 \times 10^9/L$.

MRI hip (Figure 1) found left hip effusion with synovial thickening and hyperenhancement suspicious of septic arthritis.

Arthrotomy found viscous joint fluid and culture yielded *Candida tropicalis*.

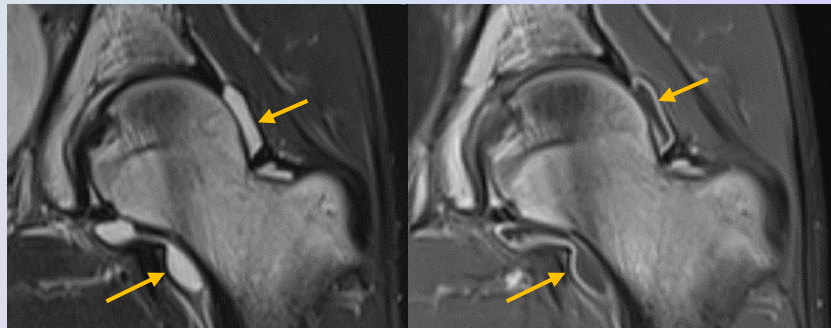


Fig 1a. Coronal T2W MRI left hip showed moderate joint effusion (arrows).

Fig 1b. Coronal T1W post contrast MRI left hip showed synovial enhancement (arrows).

CT abdomen and pelvis (Figure 2) showed multiple small hypoenhancing nodules at bilateral kidneys, also similar lesions at the liver and spleen, suspicious of multiorgan involvement.

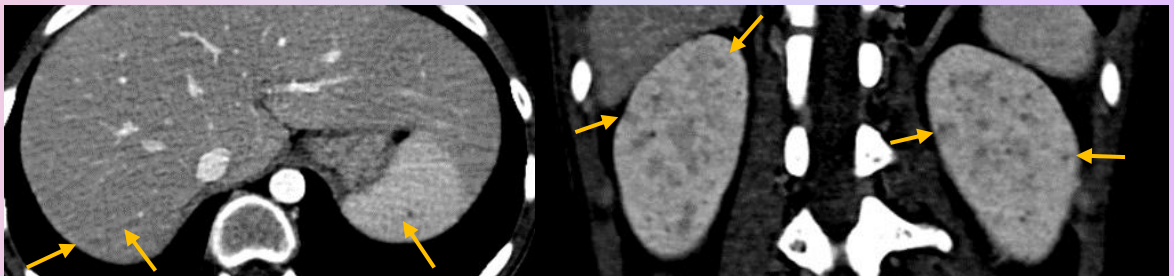


Fig 2a. Axial post-contrast CT abdomen showed hypoenhancing nodules at liver and spleen (arrows).

Fig 2b. Coronal post-contrast CT abdomen showed multiple hypoenhancing nodules at bilateral kidneys (arrows).

He initially responded to antifungal therapy but experienced fever relapse upon normalization of absolute neutrophil count (ANC).

MRI hip (Figure 3) showed hip effusion and enlarging intramuscular abscesses.

He was then treated as IRIS with steroid showing initial good response.

However, symptom relapse with fever and increased in left hip pain during tapering of steroid. Repeat MRI (Figure 4) showed similar left hip effusion and synovial thickening. Repeated arthrotoomy showed no evidence of infection but some cartilage loss at the superolateral femoral head. Follow up MRI (Figure 5) showed thinning of subchondral bone plates and patchy bone marrow edema at the left femoral head, suggestive of bone loss related to IRIS.



Fig 3. Coronal T1W post-contrast MRI left hip and thigh showed multiple small enhancing intramuscular abscesses (arrows).

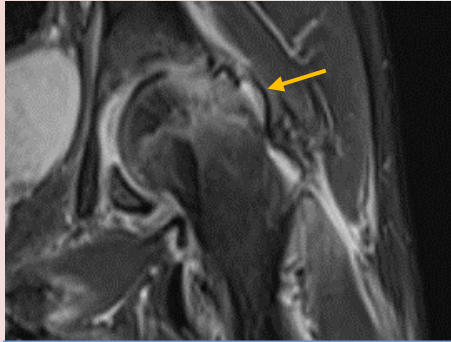


Fig 4. Coronal T2W MRI left hip showed similar hip effusion (arrow) and synovial thickening.

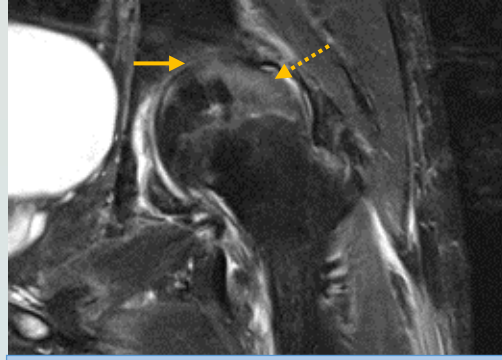
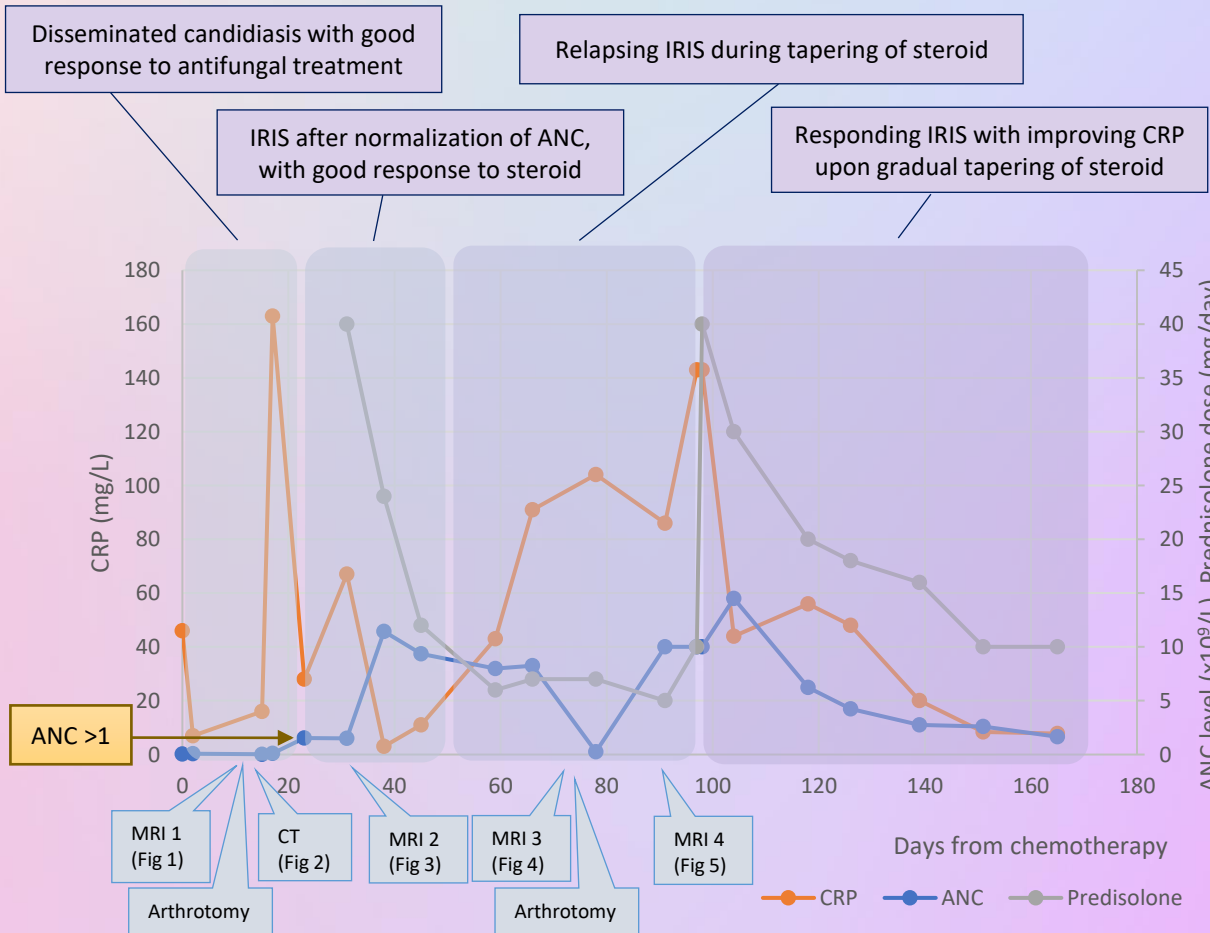


Fig 5. Coronal T2W MRI left hip showed thinning of subchondral plate (arrow) and patchy bone marrow edema (dotted arrow) at the left femoral head.

His symptoms improve once again treated as IRIS with steroid.



Patient 2

A 17-year-old girl with ALL suffered candidaemia due to *Candida tropicalis* during post-chemotherapy neutropenic phase (ANC $0.01 \times 10^9/L$). She initially responded to antifungal treatment but developed relapse of neutropenic fever on D8 into antifungal treatment. Fever persisted despite addition of antibiotics and antifungals, and her ANC recovered to $>0.5 \times 10^9/L$ two days after fever relapse.

CT showed bilateral hypoenhancing thyroid lesions.

USG of thyroid showed multiple hypoechoic lesions with fine internal echoes, suspicious of abscesses.

Aspirate from thyroid abscesses was culture negative while D2 rDNA Fungal PCR and sequencing reveal evidence of *Candida tropicalis* (MicroSEQ® Applied Biosystems, Foster City, CA).

PET/CT found multiple lesions in the subcutaneous tissue, intramuscular region, liver and thyroid gland.

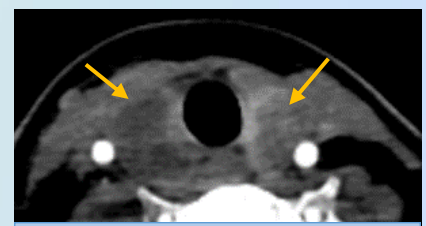


Fig 6. Axial post-contrast CT neck showed hypoenhancing thyroid lesions (arrows).

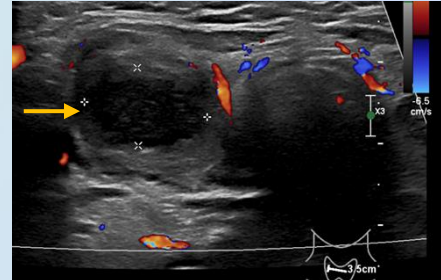


Fig 7. Ultrasound thyroid showed hypoechoic lesions with fine internal echoes (arrow).

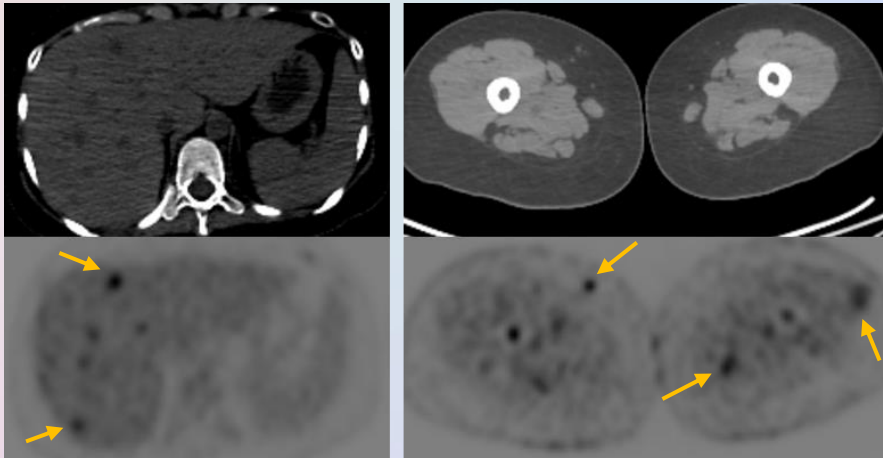


Fig 8. PET/CT showed multiple hypermetabolic lesions in the liver (arrows) and bilateral thigh intramuscular regions (arrows).

IRIS was suspected and patient was started on steroid with good response.

Discussion: IRIS is classically described in HIV patient on anti-retroviral therapy. It is commonly defined as worsening or unmasking infection during recovery of the immune deficiency. Postulated pathogenesis is related to T-cell activation and systemic inflammation. IRIS is a diagnosis by exclusion. Steroid is the mainstay of treatment.

There are case reports on IRIS among leukaemia patient on chemotherapy with disseminated candidiasis. The appearance of new lesions and fever around immune reconstitution raises the suspicion of IRIS. Early and accurate diagnosis of IRIS can prevent unnecessary operation or invasive workup and allow early resumption of oncologic treatment.

Conclusion: IRIS is an important entity to consider in leukaemia patients on chemotherapy having paradoxical worsened imaging finding upon recovery of neutrophil count. Accurate diagnosis of IRIS can influence the direction of management.