Original Research Paper

Volume - 13 | Issue - 02 | February - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Pulmonary Medicine

PONCET'S DISEASE OR INH INDUCED LUPUS ERYTHEMATOSUS? A DIAGNOSTIC DILEMMA

Dr. Pranav Ankur Pandya* 3rd year MD Respiratory Medicine Resident. *corresponding Author

Dr. Pankaj Magar Associate Professor of Respiratory Medicine.

ABSTRACT **INTRODUCTION:** Extra-pulmonary Tuberculosis is defined as infection of organ sites other than lungs. Poncet's disease is a rare, reactive polyarthritis due to active Tuberculosis. INH(drug) induced Lupus Erythematosus (DILE) is a rare idiosyncratic adverse reaction. This case was a diagnostic dilemma between the above two rare possibilities. **CASE HISTORY:** A 42-year-old female, newly diagnosed case of biopsy-proven cervical and abdominal lymph node Extra-pulmonary Tuberculosis. She was started on hepatosafe weight-based HRE regimen because she had developed Pyrazinamide induced hepatitis in 1 week of starting HRZE. She came to the OPD with accelerated hair loss and severe debilitating pain in multiple joints, immediately after the induction of ATT. DIAGNOSTIC WORK-UP: Routine blood investigations showed iron deficiency anaemia and elevated acute phase reactants. Gout, Dengue, Chikungunya and Rheumatoid arthritis were ruled out by serology. ANA by IF was 3+ for cytoplasmic components (nuclei homogenous pattern). ANA Blot showed Scl70+ and Nucleosome positive with dsDNA and Histone negative. Naranjo algorithm and WHO-UMC assessment scores for ADRs were applied for corroborative evidence to reach a diagnosis. **TREATMENT:** Patient responded well to standard weight-based INH, Rifampicin and Ethambutol under cover of oral steroids in tapering doses. **DISCUSSION:** We had a challenging diagnostic dilemma between Poncet's disease and INH induced Lupus Erythematosus, both being rare outcomes. Since INH could not be stopped due to the extent of disease and Pyrazinamide could not be re-introduced due to proven hepatitis, it became necessary to add steroids to the ongoing ATT regimen. **LEARNING POINTS:** Multiple side effects of each drug from the standard ATT regimen are possible. Steroids can mask the immunological effect of each drug. DILE although rare, should be considered and investigated

KEYWORDS : PONCET'S, TUBERCULOSIS, LUPUS, POLYARTHRITIS.

INTRODUCTION:

Extra-pulmonary Tuberculosis is defined as infection of organ sites other than lungs, like pleura, lymph nodes, omentum, intestine, due to haematogenous spread. It is said to be disseminated when 2 or more non-contiguous sites are involved.

Poncet's disease is a rare, sterile, acute-onset, non-destructive reactive polyarthritis due to active Tuberculosis, different from TB osteoarthritis. (1) A vigorous immune response to mycobacteria within joints has been postulated, where mycobacterial antigen-induced activation of T cells leads to their cross-reactivity with cartilage proteoglycans (1). Drug induced Lupus Erythematosus (DILE) is an idiosyncratic adverse reaction. DILE due to Isoniazid is reported only in 1% of cases globally (2). The inhibition of DNA methylation of CD4+ T cells is responsible for overstimulating autoantibody production by interaction with self-class II major histocompatibility complex (MHC) molecules on B-cells and consequent induction of apoptosis in macrophages. The dying cells release the highly antigenic apoptotic chromatin. This, along with autoantibody production, is thought to contribute to the development of lupus-like autoimmunity (3)

CASE HISTORY:

My case is of a 42-year-old female, home-maker, a newly diagnosed case of biopsy proven cervical and abdominal lymph node Extra-pulmonary Tuberculosis.

This lady came to the OPD with
1. Accelerated hair loss since 1 week
2. Bilateral tingling and burning sensation in fingers since 1 week
3. Bilateral knee, ankle, shoulder, elbow joint pain since 3 days
4. 2 episodes of fever with chills and rigors since 2 days

HISTORY OF PRESENTING ILLNESS-

1) Hair loss- insidious onset 6 months ago, accelerated progression since last 1 week. Scalp and eyebrows hair loss with chunks of hair falling off even on combing. No past history of thyroid abnormality or symptoms like palpitation, anxiety, malaise, hypomenorrhea which were suggestive of thyroid dysfunction

2) Fever with chills- Mild, intermittent, insidious onset, non-progressive, evening rise of temperature. Not associated with headache, rhinitis, sore throat, rash, burning micturition, abdominal pain, nausea or vomiting or diarrhea, loss of appetite or weight, no swelling in inguinal area.

3) Joint pain- Severe, disturbing sleep at night. Insidious onset and rapidly progressive. Not associated with morning stiffness, swelling, pus/serous exudate from joints. No history of trauma.

PAST HISTORY-

- History of menorrhagia since 9months and dysmenorrhea since 7months. 1-3days bleeding /cycle. 30day cycle. Regular.
- Recently diagnosed Anemia of Chronic disease.
- She was recently started on individual standard weight-based Isoniazid(H) + Rifampicin(R) + Pyrazinamide(Z) + Ethambutol(E) Anti-Tubercular drugs empirically before confirmed microbiological evidence on biopsy.

FAMILY HISTORY- No history of Autoimmune disease in family members.

GENERAL EXAM- She was vitally stable, having a BMI of 28kg/sq m. Pallor was present with palpable bilateral Level-2+3 cervical Lymph Nodes. Otherwise, unremarkable.

SYSTEMIC EXAM- Unremarkable.

SEQUENCE OF EVENTS AFTER DIAGNOSIS

She got ATT induced Hepatitis (Transaminitis)- Drug Induced Liver Injury (DILI) in 1 week of starting HRZE, so we stopped ATT. We did not resume for 1 week, waiting for LFTs to normalize.

She was restarted on hepatosafe Tab INH 300mg + Ethambutol 1000mg once daily. She tolerated these drugs.

Added Tab Rifampicin 600mg once daily. No DILI, but the severe debilitating joint pain was not subsiding so, as a desperate measure, we started her on Tab Prednisolone 20mg twice daily.

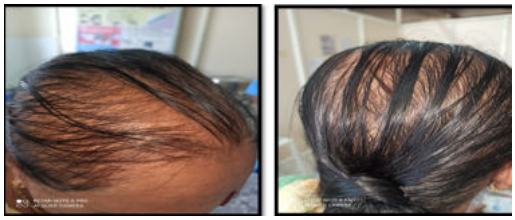

IMAGE-1= Patient's scalp showing diffuse uniform hair loss and receding hairline. Skin punch biopsy revealed Telogen effluvium.

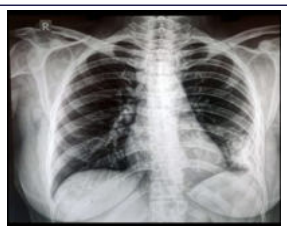

IMAGE-2= Chest Radiograph showing left lower zone pleural calcification and thickening with no parenchymal consolidation.

DIAGNOSTIC WORK-UP

Routine blood investigations showed iron deficiency anaemia and elevated acute phase reactants.

USG(A+P) = Mild hepatosplenomegaly with coarse echotexture of liver with cystitis. Multiple enlarged peri-portal, peripancreatic, para-aortic and iliac Lymph Nodes with loss of fatty hilum, suggestive of necrosis.

CECT Abdomen + Pelvis = Multiple enlarged abdominal Lymph Nodes, largest 3.1 x 2.4 cm with matting and central necrosis, mild terminal Ileo-caecal junction wall thickening, calcified left pleural thickening.

Gene Xpert of Cervical Lymph Node Biopsy = Mycobacterium Tuberculosis bacilli detected low; Rifampicin sensitive.

Histopathology of Cervical Lymph Node Biopsy = Caseous necrosis with epithelioid Langhan's Giant Cell with focal abscess formation with few foci of hyalinization.

DIFFERENTIAL DIAGNOSES	INVESTIGATIONS
? Pyrazinamide induced gout	Sr. uric acid= 5(within normal limits)
? Rheumatoid Arthritis*	RA Factor= Negative Anti CCP Abs#- Negative (0.6U/ml, minimum significant titers required are 5U/ml) CRP= 18.3, ESR= 54
? INH induced Alopecia	Telogen effluvium on scalp biopsy
? Dengue fever	Dengue NS-1 Ag, IgG, IgM= All Non-Reactive
? Chikungunya virus fever	Chikungunya IgM= Non-Reactive
? Leptospirosis	Leptospira IgM= Non-Reactive
? Hypothyroidism	TSH= 3.69(within normal limits), Microsomal Thyro-Peroxidase Abs-Negative
? DILE	ANA by IF= Abs against cytoplasmic components 3+ with nuclei homogenous pattern of >1:1000 titres s/o Lupus ANA BLOT= Scl-70+ and Nucleosome+ with dsDNA and Histone negative confirming Drug induced Lupus Erythematosus(4)
?TB reactive polyarthritis aka Poncet's disease	Diagnosis of exclusion

* TB arthritis can be confused easily with RA due to the same radiologic features including periarticular osteopenia and marginal erosions. (5)

Anti-CCP is no more specific to RA and frequently seen in patients with active TB. (6)

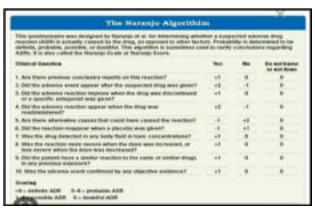
The Naranjo Algorithm

IMAGE-3= Patients' score came to be 5, so probable Adverse Drug Reaction (ADR).

DIAGNOSIS= Extra-Pulmonary Tuberculosis with INH induced Lupus Erythematosus (DILE).

TREATMENT

- Weight based individual (Hepatosafe) INH, Rifampicin and Ethambutol once daily dosing regimen was continued.
- Pyridoxine 100mg orally for INH-induced peripheral neuropathy was continued.
- Gamma linolenic acid for local application over scalp for telogen effluvium.
- Patient was discharged on Tab. Prednisolone 40mg once daily and tapering by 5mg every 10days.

She remains asymptomatic.

DISCUSSION:

We had a challenging diagnostic dilemma between Poncet's disease and INH induced Lupus Erythematosus, both being rare outcomes. We had to apply ADR scores, using the 'Naranjo Algorithm' (7) and 'WHO-UMC causality criteria' (8) as corroborative evidence tools to determine whether the suspected ADR is actually caused by a drug, as opposed to other factors.

Till date, over 100 drugs from more than 10 drug categories have been implicated in DILE(9, 2). The most common drugs causing systemic DILE are hydralazine (high risk), procainamide (high risk), isoniazid (moderate risk), minocycline (very low risk) and more recently reported tumour necrosis factor-α (TNF-α) inhibitors (very low risk) (2, 10)

3 varieties of DILE are reported in literature:-
1. Systemic DILE- characterized by mild arthralgia, myalgia, serositis and constitutional symptoms (11)

2. Drug-induced subacute cutaneous lupus erythematosus (DISCLE)- most common subtype with predominant skin involvement and is more frequently seen in older female patients (12).

3. Chronic cutaneous DILE.
To diagnose DILE five criteria are necessary:-

i. Clinical features must be absent before the administration of the drug.
ii. The drug must be known to be able to cause a lupus-like syndrome.
iii. Symptoms must be reversible upon discontinuation of the molecule in question.
iv. ANA positivity plus at least one clinical feature of SLE.
v. The reappearance of pathological manifestations if ever the drug is reintroduced, which, for obvious reasons, is never purposely tested.

Pyrazinamide could not be re-introduced due to the proven DILI and at the same time INH could not be withdrawn from the regimen due to the extent of disease and because it is an important bactericidal drug, critical to cause rapid clearance of the bacilli from the system in the intensive phase.

Poncet's disease was ruled out since we found a positive investigation for the alternative differential diagnosis and Poncet's disease is usually a diagnosis of exclusion and it disappears with initiation of Anti Tubercular treatment. Whereas, our patient's symptoms flared up after ATT induction.

Osteoarticular TB should ideally be ruled out by identification of mycobacteria in synovial aspirate (13) before the diagnosis of Poncet's can be established, but osteoarticular TB rarely involves more than one joint [14, 15] and responds rather slowly to ATT. (16)

LEARNING POINTS: Multiple side effects of each drug from the standard ATT regimen are possible. Steroids can mask the immunological effect of all the drugs involved, hence making the differentiation between two already rare outcomes, even more difficult. DILE although rare, should be considered and investigated in a similar syndromic presentation.

REFERENCES

1. Pugh, M.T., & Southwood, T.R. (1993). Poncet's tuberculous rheumatism: a sterile

controversy? [Tuberculous rheumatism, Poncet disease: a sterile controversy?]. Revue du rhumatisme (French edition: 1993), 60(12), 855–860
2. Vasoo S. (2006). Drug-induced lupus: an update. Lupus, 15(11), 757–761. https://doi.org/10.1177/0961203306070000
3. Pan, Q., Guo, Y., Guo, L., Liao, S., Zhao, C., Wang, S., & Liu, H. F. (2020). Mechanistic Insights of Chemicals and Drugs as Risk Factors for Systemic Lupus Erythematosus. Current medicinal chemistry, 27(31), 5175–5188. https://doi.org/10.2174/0929867326666190404140658
4. Kumar, Y., Bhatia, A., & Minz, R. W. (2009). Antinuclear antibodies and their detection methods in diagnosis of connective tissue diseases: a journey revisited. Diagnostic pathology, 4, 1. https://doi.org/10.1186/1746-1596-4-1
5. Hugosson, C., Nyman, R. S., Brismar, J., Larsson, S. G., Lindahl, S., & Lundstedt, C. (1996). Imaging of tuberculosis. V. Peripheral osteoarticular and soft-tissue tuberculosis. Acta radiologica (Stockholm, Sweden : 1987), 37(4), 512–516
6. Kakumanu, P., Yamagata, H., Sobel, E. S., Reeves, W. H., Chan, E. K., & Satoh, M. (2008). Patients with pulmonary tuberculosis are frequently positive for anti-cyclic citrullinated peptide antibodies, but their sera also react with unmodified arginine-containing peptide. Arthritis and rheumatism, 58(6), 1576–1581. https://doi.org/10.1002/art.23514
7. Naranjo, C. A., Busto, U., Sellers, E. M., Sandor, P., Ruiz, I., Roberts, E. A., Janecek, E., Domecq, C., & Greenblatt, D. J. (1981). A method for estimating the probability of adverse drug reactions. Clinical pharmacology and therapeutics, 30(2), 239–245. https://doi.org/10.1038/clpt.1981.154
8. Uppsala Monitoring Center. Why causality assessment? In: The use of the WHO-UMC system for standardised case causality assessment. https://www.who.int/medicines/areas/quality_safety/safety_efficacy/WHOcausality_assessment.pdf. Accessed 19 Feb 2019
9. Chang, C., & Gershwin, M. E. (2011). Drug-induced lupus erythematosus: incidence, management and prevention. Drug safety, 34(5), 357–374. https://doi.org/10.2165/11588500-000000000-00000
10. Aguirre Zamorano, M. A., López Pedrera, R., & Cuadrado Lozano, M. J. (2010). Lupus inducido por fármacos [Drug-induced lupus]. Medicina clinica, 135(3), 124–129. https://doi.org/10.1016/j.medcli.2009.04.035
11. He, Y., & Sawalha, A. H. (2018). Drug-induced lupus erythematosus: an update on drugs and mechanisms. Current opinion in rheumatology, 30(5), 490–497. https://doi.org/10.1097/BOR.0000000000000522
12. Lowe, G. C., Henderson, C. L., Grau, R. H., Hansen, C. B., & Sontheimer, R. D. (2011). A systematic review of drug-induced subacute cutaneous lupus erythematosus. The British journal of dermatology, 164(3), 465–472. https://doi.org/10.1111/j.1365-2133.2010.10110.x
13. Kowalski, M., & Seitz, M. (1999). Tuberculosis manifestations in the musculoskeletal system exemplified by Poncet's disease. Swiss medical weekly, 129(47), 1839-1842
14. Linares, L. F., Valcarcel, A., Mesa Del Castillo, J., Saiz, E., Bermudez, A., & Castellon, P. (1991). Tuberculous arthritis with multiple joint involvement. The Journal of rheumatology, 18(4), 635–636
15. Ideguchi, H., Ohno, S., Takase, K., Tsukahara, T., Kaneko, T., & Ishigatsubo, Y. (2009). A case of Poncet's disease (tuberculous rheumatism). Rheumatology international, 29(9), 1097–1099. https://doi.org/10.1007/s00296-008-0795-1
16. Malaviya, A. N., & Kotwal, P. P. (2003). Arthritis associated with tuberculosis. Best practice & research. Clinical rheumatology, 17(2), 319–343. https://doi.org/10.1016/s1521-6942(02)00126-2