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RESEARCH ARTICLE

A DIAGNOSTIC ODYSSEY: NON-HODGKIN LYMPHOMA MASQUERADING AS RECURRENT TYPHOID FEVER AND NEPHROLITHIASIS — A 14-MONTH DELAY IN DIAGNOSIS AND COMPREHENSIVE TREATMENT OUTCOME

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Abstract

Background: Diagnostic delay in haematological malignancy remains a significant clinical problem, particularly when concurrent endemic infections and benign structural pathology provide plausible alternative explanations for constitutional symptoms. Non-Hodgkin Lymphoma presenting alongside confirmed typhoid fever and nephrolithiasis poses an exceptionally challenging diagnostic scenario.

Objective: To document the clinical, diagnostic, and treatment journey of a 38-year-old male patient with Stage IIIB Diffuse Large B-Cell Lymphoma (DLBCL) whose diagnosis was delayed by 14 months due to concurrent Salmonella typhi infections and bilateral nephrolithiasis, and to describe the complete treatment response to dose-dense R-CHOP-15 followed by Rituximab maintenance.

Case Summary: A 38-year-old non-smoking, non-alcoholic male experienced 14 months of relapsing fever, progressive 18-kg weight loss, and recurrent right flank pain. Three episodes of Salmonella typhi infection and concurrently identified bilateral nephrolithiasis directed clinical attention away from an underlying haematological malignancy. A unique complication was that right ureteric obstruction, attributed entirely to a 9 mm calculus, was in fact caused by extrinsic compression from a 6.8 cm para-aortic lymph node mass — identified only on contrast-enhanced MRI at Month 14. Excisional biopsy confirmed DLBCL Non-GCB subtype with Ki-67 proliferation index of 88%. The patient completed dose-dense R-CHOP-15 every 15 days for 6 months followed by Rituximab maintenance monthly for 4 months, achieving complete metabolic remission on end-of-treatment PET-CT (Deauville Score 1).

A further complication encountered during treatment was the development of peripheral thrombophlebitis during the first three chemotherapy cycles administered through peripheral intravenous cannulae, necessitating Doppler evaluation and subsequent insertion of a PICC line for safe continuation of therapy.

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Conclusion: This case illustrates how anchoring bias, concurrent benign diagnoses, and lymphoma-facilitated immunosuppression collectively delayed a cancer diagnosis by over one year. Early integration of cross-sectional imaging, systematic evaluation of persistent B symptoms as a unified syndrome, and proactive vascular access planning in patients on prolonged cytotoxic therapy are essential clinical lessons from this case.

Introduction:-

Non-Hodgkin Lymphoma (NHL) comprises a heterogeneous group of lymphoid malignancies with diverse clinical presentations. Diffuse Large B-Cell Lymphoma (DLBCL) is the most common and aggressive subtype, accounting for approximately 30 to 40% of all NHL cases, with an estimated 150,000 new cases diagnosed annually worldwide [1]. Constitutional symptoms of DLBCL — persistent fever, night sweats, and significant weight loss — overlap substantially with those of systemic infections and inflammatory conditions, presenting a diagnostic challenge that is compounded in tropical and endemic settings [2].Typhoid fever, caused by Salmonella enterica serovar Typhi, continues to cause an estimated 11 to 21 million illnesses and 130,000 to 160,000 deaths annually, with the highest burden in South and Southeast Asia [3]. Recurrent typhoid, occurring in 5 to 10% of treated patients, is conventionally attributed to premature antibiotic cessation, inadequate drug selection, or bacterial persistence in the gallbladder [4]. However, recurrent typhoidal bacteraemia in an apparently immunocompetent adult warrants investigation for an underlying immunosuppressive condition, a consideration not always made in clinical practice.
Nephrolithiasis affects approximately 10 to 12% of men during their lifetime and is characterised by acute flank pain, haematuria, and obstructive uropathy on imaging [5]. When identified on abdominal ultrasound in the context of flank pain and fever, kidney stones frequently dominate the clinical narrative, potentially obscuring retroperitoneal pathology not visualised on standard ultrasound.

Published case series have documented lymphoma presenting as pyrexia of unknown origin or mimicking infectious illness in tropical settings. Bleeker-Rovers et al., in a structured prospective multicenter study, found that haematological malignancies constituted a significant proportion of classical adult PUO diagnoses when a systematic diagnostic protocol was applied [11]. Connors described Hodgkin and aggressive lymphomas as among medicine's great diagnostic imitators, particularly in settings where endemic infections share the same constitutional symptom profile [12]. These reports confirm that the masquerade pattern seen in this case reflects a broader underrecognised challenge in clinical practice in endemic regions.This case report presents a patient in whom genuine culture-confirmed typhoid fever and genuine bilateral nephrolithiasis coexisted with, and effectively masked, a Stage IIIB DLBCL for 14 months. To our knowledge, the specific combination of lymphoma-driven extrinsic ureteric obstruction mimicking stone disease — combined simultaneously with lymphoma-facilitated recurrent Salmonella typhi infections through immunosuppression — has not been previously described as a dual masquerade in a single patient in published literature. The objectives of this report are to describe the diagnostic pathway and its mechanisms of failure, to document the complete treatment protocol and cycle-by-cycle response including a unique vascular access complication, and to derive clinical learning points relevant to physicians practising in endemic settings.

Patient Profile

Parameter	Details
Age and Sex	38 years, Male
Occupation	Senior Software Engineer — sedentary role, high occupational stress
Marital Status	Married, two children aged 9 and 6
Smoking	Non-smoker (lifelong)
Alcohol	Non-alcoholic (lifelong abstainer)
Diet	Predominantly vegetarian
Family History	No haematological malignancy; father — hypertension; mother — type 2 diabetes

Immunisation History	Single-dose typhoid vaccine at age 22; booster not received
Weight at First Presentation	72 kg (BMI 25.3 kg/m²; height 169 cm)
Weight at Diagnosis (Month 14)	54 kg (BMI 18.9 kg/m²) — 18 kg total loss (25% of body weight)
Weight at Chemotherapy Month 4	61 kg — partial recovery on nutritional rehabilitation
Comorbidities at Diagnosis	None documented prior to this illness

Presenting Symptoms and Clinical History:-

The patient first sought medical attention 14 months before the confirmed diagnosis. His initial complaints were non-specific and individually consistent with conditions endemic to the region. The table below traces the clinical journey chronologically, including the differential diagnoses that were not considered at each juncture.

Period	Symptoms and Events	Working Diagnosis	Differential Diagnoses Not Considered
Months 1–2	Low-grade fever 99–100.6°F, fatigue, appetite loss, right flank discomfort	Viral fever; early UTI	Lymphoma; renal mass; TB
Month 3	Fever 103°F; Widal O:1:160; ciprofloxacin 14 days	Typhoid Fever — Episode 1	Lymphoma; infectious mononucleosis; occult malignancy
Months 4–5	Temporary relief; persistent fatigue; 5 kg weight loss; intermittent night sweats	Post-typhoid asthenia; nutritional deficiency	Lymphoma; tuberculosis; occult malignancy
Month 6	Fever recurrence; Widal O:1:320; blood culture Salmonella typhi; right flank pain worsens; USG: bilateral calculi R 9 mm L 5 mm; right hydronephrosis	Recurrent Typhoid and Nephrolithiasis — Episode 2	Lymphoma with immunosuppression; retroperitoneal mass causing ureteric obstruction
Months 7–8	IV ceftriaxone; tamsulosin; fever never fully clears; 9 kg total weight loss; E. coli UTI; haematuria	Complicated UTI and nephrolithiasis with recurrent typhoid	Lymphoma-driven obstruction; haematological malignancy
Months 9–10	Third febrile episode; Widal positive; urology referral; 9 mm stone — lithotripsy scheduled	Obstructive nephropathy from stone disease; lithotripsy planned	Extrinsic ureteric compression by lymph node; lymphoma
Months 11–12	Bilateral neck swellings self-detected; drenching night sweats; 15 kg total weight loss; right pleural effusion on CXR; lithotripsy deferred	Lymphoma first queried; urgent haematology referral	—
Month 13	LDH 1,040; CRP 138; CT: para-aortic mass 6.8 cm; mediastinal widening	Aggressive lymphoma strongly suspected	—

Month 14	MRI confirms retroperitoneal and mediastinal lymphadenopathy; PET-CT SUVmax 19.4; biopsy confirms DLBCL Non-GCB; treatment initiated	Confirmed: Stage IIIB DLBCL	—

Physical Examination at Oncology Referral:-
The following findings were recorded at the time of haematology and oncology referral in Month 13.

System	Findings
General	Cachectic; chronically ill appearance; BMI 19.1; pallor; mild icterus
Vitals	Temperature 99.6°F; HR 108 bpm; BP 106/68 mmHg; SpO2 96% on room air; RR 18/min
Lymph Nodes	Bilateral cervical chains: multiple firm, discrete, non-tender nodes — largest 3.1 cm on left; bilateral axillary and inguinal lymphadenopathy
Abdomen	Splenomegaly — spleen 4 cm below costal margin; no hepatomegaly; right lumbar tenderness on deep palpation; no ascites
Chest	Decreased breath sounds and dullness at right base — small pleural effusion
Cardiovascular	Tachycardia; no murmurs; no raised JVP
Musculoskeletal	Generalised muscle wasting; no bone tenderness
Skin	No purpura, petechiae, or rash; no oral candidiasis

Investigations:-
Tests Before Lymphoma Was Suspected:-
All investigations during the first 12 months were directed toward the established diagnoses of typhoid, nephrolithiasis, and UTI. Each result, while genuine, reinforced the existing misdiagnosis and precluded consideration of lymphoma.

Investigation	Result	Interpretation at the Time	Missed Implication
Widal Test — three occasions	O antigen 1:160 rising to 1:320	Typhoid confirmed; rising titre attributed to re-infection	Rising titre in a treated patient may indicate lymphoma-driven immunosuppression rather than re-exposure
Blood Culture (Month 6)	Salmonella typhi bacteraemia	Confirmed typhoid — treated accordingly	Third Salmonella infection in 9 months — underlying immune defect not evaluated
Urine Culture (Month 9)	E. coli >100,000 CFU/mL	UTI attributed to urinary stasis from stone	Persistent urinary stasis may reflect extrinsic obstruction by lymphadenopathy
Ultrasound Abdomen (Month	Bilateral renal calculi; right hydronephrosis	Stone disease confirmed; hydronephrosis attributed	Retroperitoneal nodes not visualised — ultrasound has

6)		to calculus	well-recognised limitations in this region
CBC (Month 9)	Hb 10.4 g/dL; WBC 7,100; Plt 340,000; mild eosinophilia	Anaemia of chronic disease	Unexplained eosinophilia can occur in NHL; anaemia with weight loss should prompt malignancy review
ESR (Month 9)	82 mm/hr	Attributed to ongoing infection	Persistently elevated ESR despite treated infection should prompt malignancy workup
Kidney Function (Month 8)	Creatinine 1.4 mg/dL	Dehydration and stone obstruction	Progressive renal impairment despite hydration warrants cross-sectional imaging
Chest X-Ray (Month 10)	Small right pleural effusion	Reactive effusion secondary to infection	Mediastinal widening not flagged; unexplained effusion should raise lymphoma suspicion

Tests After Lymphoma Was Suspected:-

Investigation	Result	Clinical Significance
LDH	1,040 IU/L — markedly elevated	High cell turnover; key prognostic marker in DLBCL
Beta-2 Microglobulin	5.2 mg/L — elevated	Adverse prognostic marker; correlates with tumour burden in DLBCL
Uric Acid	9.2 mg/dL	Elevated tumour cell turnover; pre-treatment tumour lysis syndrome risk identified
CRP and ESR	CRP 138 mg/L; ESR 94 mm/hr	Persistent systemic inflammation not attributable to treated infection
CECT Abdomen and Pelvis	Para-aortic mass 6.8 cm compressing right ureter; bilateral hydronephrosis; mesenteric nodes	Critical finding — obstruction identified as lymphoma-driven, not primarily from renal calculus
Contrast-Enhanced MRI	Bulky retroperitoneal and pelvic lymphadenopathy; splenic involvement; right ureteric displacement by nodal mass confirmed	Definitive anatomical mapping; shaped biopsy and treatment planning
PET-CT Whole Body	FDG-avid nodes: cervical, mediastinal, para-aortic, pelvic; SUVmax 19.4; no marrow uptake	Stage IIIB confirmed; Deauville 5-point scale used for response assessment as per Lugano Classification [2]
Excisional Biopsy — Left Cervical Node	DLBCL Non-GCB subtype; Ki-67 88%	Definitive histological diagnosis; rapid proliferative activity

Immunohistochemistry	CD20+, CD79a+, BCL2+, BCL6+, MUM1+, CD10−, MYC+ at 35%	Non-GCB (Activated B-Cell) subtype confirmed — associated with inferior outcomes on R-CHOP [6]
FISH	BCL2 rearrangement positive; MYC rearrangement negative	Single-hit lymphoma; double-hit biology excluded
Bone Marrow Biopsy	No lymphoma infiltration	Stage III rather than Stage IV confirmed
Echocardiogram	LVEF 64%; structurally normal	Baseline cardiac documentation required before doxorubicin

Unique Complication:-
Lymphoma-Driven Ureteric Obstruction Misattributed to Stone Disease From Month 6 onwards, progressive right hydronephrosis and rising creatinine were attributed to a 9 mm obstructing right renal calculus. This attribution was supported by ultrasound findings, urology review, and the patient's colicky flank pain. Extracorporeal shock wave lithotripsy (ESWL) was formally scheduled.The CECT at Month 13 overturned this assumption entirely. A 6.8 cm para-aortic lymph node mass was encasing and displacing the right ureter at the L3 to L4 level. The renal calculus was genuine but incidental. Had ESWL proceeded without retroperitoneal imaging, the obstruction would have been unrelieved, renal function would have continued deteriorating, and the lymphoma would have remained undetected.
This case highlights a critical principle: hydronephrosis that is disproportionate to the identified stone burden, or that fails to resolve with standard conservative management, requires contrast-enhanced cross-sectional imaging of the retroperitoneum before any urological intervention is undertaken.

Lymphoma-Facilitated Recurrent Typhoid Fever:-
DLBCL produces progressive impairment of T-cell and B-cell mediated immunity. Salmonella typhi is an obligate intracellular pathogen whose clearance depends on intact cell-mediated immunity. In this patient, the three confirmed Salmonella typhi infections were not independent re-exposures; they represent a pattern of pathogen recurrence enabled by lymphoma-driven immunosuppression. Each infection provided a convincing, treatable clinical explanation for the fever and systemic decline that were, in reality, manifestations of the underlying malignancy. This dual masquerade — mimicking stone disease through ureteric compression while simultaneously enabling recurrent typhoid through immunosuppression — constitutes, to our knowledge, a novel combined presentation not previously described in a single case report.

Final Diagnosis :-

Parameter	Details
Primary Diagnosis	Diffuse Large B-Cell Lymphoma — Activated B-Cell or Non-GCB Subtype
Stage (Ann Arbor)	Stage IIIB — lymphoma on both sides of the diaphragm; all three B symptoms confirmed
B Symptoms	Persistent fever >38°C for more than 1 month; drenching night sweats; weight loss of 18 kg (25% of body weight)
IPI Score	3 of 5 — High-Intermediate Risk
Ki-67	88% — highly proliferative
Concurrent Findings	Bilateral nephrolithiasis (incidental); resolved E. coli UTI; right ureteric obstruction (lymphoma-driven); right pleural effusion (lymphomatous)
Duration from First Symptom to Diagnosis	14 months

Figure 1 — Significant Points in the Diagnostic Pathway
The following table summarises the five critical clinical junctures at which cross-sectional imaging or haematological evaluation was indicated but not performed, illustrating the mechanism of the 14-month diagnostic delay.

Clinical Juncture	Signal Present	Action Taken	Action Required	Consequence of Omission
Month 5 — After treated typhoid	Persistent fatigue, 5 kg weight loss, night sweats beginning	Attributed to post-typhoid asthenia	B symptom triad evaluation; haematology review	Third typhoid episode; further months of undiagnosed lymphoma
Month 6 — Rising Widal in treated patient	O antigen 1:320 after completed antibiotics	Repeated typhoid treatment	Evaluate for immunosuppression underlying recurrence	Lymphoma not considered despite third Salmonella episode
Month 6 — Hydronephrosis on USG	9 mm stone; hydronephrosis; creatinine rising	Stone management; lithotripsy considered	CT or MRI to exclude extrinsic compression when hydronephrosis exceeds stone burden	6.8 cm para-aortic mass missed for 7 further months
Month 9 — Third febrile episode	Three Salmonella infections; 12 kg weight loss	Third antibiotic course; urology referral	Haematology referral; serum LDH; CT staging	Diagnosis delayed further; lithotripsy nearly performed on wrong lesion
Month 11 — Patient self-detects neck lumps	Bilateral lymphadenopathy with all three B symptoms; pleural effusion on CXR	Lymphoma queried; haematology referral made	Urgent CT staging; excisional biopsy	Referral correctly made here — diagnosis followed 3 months later

Pre-Chemotherapy Interventions:-
Before initiating systemic chemotherapy, the multidisciplinary team undertook the following preparatory measures:-

- Right ureteric DJ stenting was performed to relieve lymphoma-mediated obstructive uropathy and protect residual renal function before nephrotoxic agents were introduced.
- Allopurinol 300 mg daily and aggressive intravenous hydration commenced for tumour lysis syndrome prophylaxis, given the high Ki-67 index of 88% and bulky disease.
- Nutritional rehabilitation initiated under dietitian supervision with high-calorie oral supplementation three times daily.
- Pre-chemotherapy vaccinations administered: Pneumococcal (PCV13), Influenza, and Meningococcal.
- Baseline echocardiogram confirmed LVEF 64%, required before doxorubicin administration.
- Sperm banking arranged given the patient's age and the gonadotoxic risk of cyclophosphamide.
- Dental clearance obtained to minimise the risk of odontogenic sepsis during neutropenic phases.
- Patient and family counselling by the psycho-oncology team covering diagnosis, treatment duration, expected adverse effects, occupational leave, and financial planning.

Treatment Protocol:-

Phase 1 — Induction: R-CHOP-15 Every 15 Days for 6 Months:-

Standard first-line treatment for DLBCL is R-CHOP-21. In this patient, R-CHOP-15 was adopted based on three concurrent adverse features: Non-GCB subtype with known inferior outcomes on standard R-CHOP-21, associated with 5-year PFS of 48% versus 73% for GCB subtype [6]; Ki-67 of 88% indicating rapid inter-cycle tumour regrowth; and IPI score of 3 (high-intermediate risk). The RICOVER-60 trial demonstrated the benefit of dose-dense R-CHOP-14 in aggressive DLBCL [7]. G-CSF support on Day 3 of each cycle is mandatory with R-CHOP-15.

Drug	Class	Dose and Route	Schedule	Mechanism
Rituximab	Anti-CD20 Monoclonal Antibody	375 mg/m² IV	Day 1 each cycle	Targets CD20 on malignant B-cells; induces apoptosis and ADCC
Cyclophosphamide	Alkylating Agent	750 mg/m² IV	Day 1	Cross-links DNA; prevents tumour cell replication
Doxorubicin (Hydroxydaunorubicin)	Anthracycline	50 mg/m² IV push	Day 1	DNA intercalation; topoisomerase II inhibition; vesicant
Vincristine (Oncovin)	Vinca Alkaloid	1.4 mg/m² IV (max 2 mg)	Day 1	Disrupts microtubule polymerisation; arrests mitosis
Prednisolone	Corticosteroid	100 mg orally	Days 1 to 5	Synergistic anti-tumour and anti-inflammatory effect

Supportive and Prophylactic Medications:-

Medication	Indication and Rationale
G-CSF (Filgrastim or Pegfilgrastim)	Day 3 each cycle; mandatory with R-CHOP-15 to prevent febrile neutropenia
Ondansetron and Dexamethasone pre-chemotherapy	Anti-emetic prophylaxis
Pantoprazole 40 mg once daily	Gastroprotection during prednisolone Days 1 to 5
Co-trimoxazole three times weekly	Pneumocystis jirovecii pneumonia prophylaxis throughout treatment
Acyclovir 400 mg twice daily	Herpes zoster reactivation prophylaxis
Intrathecal Methotrexate at Cycles 1, 4, and 8	CNS prophylaxis — high CNS-IPI risk group; estimated 2-year CNS relapse risk >10% [8]
Blood glucose monitoring	Prednisolone Days 1–5 causes transient hyperglycaemia requiring monitoring

Phase 2 — Maintenance: Rituximab Monthly for 4 Months:-

Following confirmed complete metabolic remission after induction, the patient received Rituximab 375 mg/m² IV once monthly for 4 cycles to consolidate the deep remission achieved, given Non-GCB biology, Ki-67 of 88%, and the 14-month period during which the disease advanced without treatment.

Vascular Access Complication During Chemotherapy — Peripheral Thrombophlebitis and PICC Line Insertion:-

A clinically significant and underreported complication arose during the delivery of the first three chemotherapy cycles. This complication — peripheral thrombophlebitis followed by the need for PICC line insertion — is documented here as an additional real-world challenge encountered during the treatment of this case.

Peripheral IV Cannula Complications — Cycles 1 to 3:-

The first three cycles of R-CHOP-15 were administered through peripheral intravenous cannulae inserted in the forearm and antecubital veins, as is standard initial practice. After Cycle 1, the patient reported mild burning and discomfort at the cannula site during infusion. The infusion rate was reduced and the arm elevated.After Cycle 2, the patient developed progressive erythema, swelling, and an intense burning sensation along the course of the cannulated vein in the forearm. The skin overlying the vein appeared visibly red and indurated, with a cord-like, palpable, tender vein on examination extending proximally from the cannula site. The patient described the appearance and sensation as resembling a superficial skin burn injury — intensely uncomfortable and visually distressing.By Cycle 3, multiple cannulation attempts were required and the peripheral venous access had significantly deteriorated. Superficial thrombophlebitis had extended further proximally with worsening erythema, warmth, induration, and firm venous cord formation along the forearm. The patient was in significant pain and the clinical team was concerned about the risk of chemical injury or extravasation on subsequent cycles.

Doppler Ultrasound Evaluation:-

Given the clinical findings of progressive venous induration, palpable cord, and skin changes, the patient underwent venous Doppler ultrasound of the affected arm. The study confirmed superficial thrombophlebitis of the peripheral forearm veins at and proximal to the cannulation sites. No deep vein thrombosis (DVT) was identified. The findings were consistent with chemotherapy-induced superficial venous thrombosis — a recognised complication of cytotoxic drug delivery through peripheral veins, particularly with the vesicant and irritant agents in the R-CHOP regimen.

Decision for PICC Line Insertion:-

Following the Doppler findings and multidisciplinary review, a PICC (Peripherally Inserted Central Catheter) line was inserted before Cycle 4 under ultrasound guidance, with the catheter tip positioned in the distal superior vena cava at the cavoatrial junction. Correct positioning was confirmed on post-insertion chest X-ray. The procedure was completed without complication.

PICC Line Maintenance Protocol:-

Following PICC line insertion, the patient was placed on a structured maintenance protocol for the remainder of the treatment course:

- Heparin flush (10 units/mL, 10 mL) administered once weekly on non-chemotherapy days to maintain catheter patency and prevent intraluminal thrombosis
- Normal saline flush (10 mL) performed before and after every chemotherapy infusion and every blood draw through the PICC
- PICC line dressing changed once weekly under sterile technique, or immediately if soiled or lifting
- Catheter insertion site assessed at every clinic visit for signs of infection, phlebitis, or displacement
- Patient and family educated on PICC line care at home — signs of infection, keeping the site dry, and when to seek emergency review
- All subsequent chemotherapy infusions, blood draws, and intravenous medications delivered through the PICC — no further peripheral cannulation required

From Cycle 4 onward, chemotherapy was delivered smoothly and safely through the PICC line with no further vascular access complications. The patient reported significant relief from the distress, pain, and skin changes associated with the earlier peripheral cannulation.

Vascular Access Summary:-

Cycle	Access Method	Complication	Action Taken
Cycle 1	Peripheral IV cannula	Mild burning at cannula site during infusion	Infusion rate reduced; arm elevated; warm compress post-infusion
Cycle 2	Peripheral IV cannula	Progressive erythema and induration; cord-like vein; skin red and burn-like in appearance	Topical heparin gel; NSAIDs for analgesia; arm elevation; escalated monitoring
Cycle 3	Peripheral IV cannula — multiple attempts	Significant thrombophlebitis; burning extending proximally; venous cord; multiple cannulation failures	Venous Doppler ultrasound confirmed thrombophlebitis; no DVT; PICC line insertion arranged before Cycle 4
Cycle 4 onward	PICC line — tip confirmed at distal SVC	No further vascular access complications	Weekly heparin flush 10 units/mL; normal saline flush pre and post infusion; weekly sterile dressing; patient education
Maintenance phase	PICC line continued	No complications throughout maintenance	Weekly heparin flush maintained; site inspected each visit; PICC removed at end of treatment

Results:-

Cycle-by-Cycle Response During Induction

Cycle	Clinical Response	Key Laboratory Values	Adverse Effects and Management
1 (Week 1–2)	Fever resolved within 5 days of Rituximab infusion; night sweats reduced; appetite improving	LDH 1,040 to 740 IU/L; ANC nadir 1,200 Day 8	Grade 2 nausea — ondansetron effective; alopecia begins; low-grade TLS managed with IV fluids and allopurinol
2 (Week 3–4)	B symptoms fully resolved; left cervical node reduced 3.1 to 1.8 cm; tolerating solid meals	LDH 540; CRP 42 mg/L; ANC nadir 900 — G-CSF given	Grade 3 neutropenia; febrile episode Day 10 — IV piperacillin-tazobactam; blood cultures negative; recovered Day 14
3 (Week 5–6)	Weight 58 kg from nadir 54 kg; appetite returning; part-time remote work resumed	LDH 310; Beta-2 microglobulin 2.8 mg/L; Creatinine 1.0	Grade 1 peripheral neuropathy in fingertips (vincristine); constipation; Grade 1 mucositis
4 (Week 7–8)	DJ stent removed — repeat USG confirms hydronephrosis resolved as para-aortic mass regresses	ANC nadir 800; Hb 11.2 g/dL; Platelets 290,000	Vincristine neuropathy worsening — dose reduced 25%; steroid hyperglycaemia — metformin 500 mg BD started
5 — Interim PET-CT	Interim PET-CT: Deauville Score 2 —	LDH 198 IU/L; CRP 11 mg/L	Complete alopecia; fatigue improving; neuropathy stable after

(Week 9–10)	near-complete metabolic response across all nodal stations		vincristine dose reduction
6 (Week 11–12)	No palpable lymphadenopathy; spleen not palpable; pleural effusion resolved on CXR; weight 61 kg	Hb 12.1 g/dL; LDH 180	Mild myalgia; mood low — psycho-oncology referral; sleep disturbance
7 to 12 (Weeks 13–24)	Progressive clinical improvement each cycle; full-time remote work from Cycle 9; weight 63 kg	LDH normalising; CBC recovering with G-CSF; Creatinine 0.90	Cumulative vincristine neuropathy managed with dose cap; fatigue main complaint; no new toxicities

End-of-Induction Assessment:-

Parameter	Finding	Interpretation
PET-CT (End of Induction)	Deauville Score 1 — no FDG-avid lesions in all previously involved nodal stations	Complete Metabolic Response
CT Abdomen and Pelvis	Para-aortic region clear; 6.8 cm mass fully resolved; right ureter unobstructed	Complete Radiological Response
LDH	172 IU/L — within normal range	Normalised
Beta-2 Microglobulin	1.9 mg/L — normal	Normalised
CBC	Hb 12.9 g/dL; WBC 5,600; ANC 3,200; Plt 310,000	Bone marrow recovery confirmed
Creatinine	0.88 mg/dL	Renal function fully restored
Body Weight	63 kg (BMI 22.0 kg/m²)	9 kg gained from nadir
LVEF Post-Induction	60% — minor reduction from baseline 64%	Within acceptable anthracycline monitoring threshold; cardiology follow-up planned
ECOG Performance Status	1; full-time remote work resumed	Significant functional recovery

Maintenance Phase Response:-

Month	Dose	Status	Notes
Month 1	375 mg/m² IV	No lymphadenopathy; LDH normal; weight 64.5 kg	Mild infusion chills — paracetamol pre-medication; resolved promptly
Month 2	375 mg/m² IV	CBC stable; neuropathy now Grade 0 to 1	Well tolerated; fatigue 2 out of 10; patient cycling regularly
Month 3	375 mg/m² IV	Surveillance CT: no new lymphadenopathy; all prior nodes resolved	Complete remission maintained; psychological status significantly improved

Month 4	375 mg/m² IV	End-of-treatment PET-CT: Deauville Score 1; complete metabolic remission confirmed	Treatment completed; patient enters surveillance in full remission

Adverse Effects Summary:-

Adverse Effect	Grade	Agent	Management and Outcome
Febrile Neutropenia (Cycle 2)	3	Cyclophosphamide and Doxorubicin	IV piperacillin-tazobactam; G-CSF accelerated; blood cultures negative; resolved Day 14
Peripheral Neuropathy	1 to 2	Vincristine — cumulative	Dose reduced 25% and capped at 2 mg from Cycle 4; stabilised Grade 1; resolving at end of maintenance
Nausea and Vomiting	1 to 2	Multi-agent	Ondansetron and dexamethasone pre-chemo; adequately controlled all cycles
Alopecia	3 — complete	Cyclophosphamide and Doxorubicin	Counselled pre-treatment; wig support arranged; regrowth 6 weeks post-final cycle
Mucositis	1	Cyclophosphamide and IT MTX	Chlorhexidine mouthwash; sodium bicarbonate rinses; self-resolving each cycle
Steroid-Induced Hyperglycaemia	Moderate	Prednisolone Days 1–5	Metformin 500 mg BD from Cycle 4; glucose monitoring each cycle; normalised between cycles
Fatigue	2 to 3 induction; 1 maintenance	Multi-agent and disease burden	Physiotherapy; structured rest; nutritional optimisation; Grade 1 by end of treatment
Cardiac — LVEF reduction	1 — subclinical	Doxorubicin cumulative 360 mg/m²	LVEF 60% at end of induction; Echo at 6 and 12 months post-treatment scheduled
Psychological Distress	Significant	Diagnosis; prolonged misdiagnosis; treatment burden	Psycho-oncology from Cycle 6; family therapy; peer support group; no pharmacotherapy required
Rituximab Infusion Reactions	1	Rituximab	Paracetamol and chlorphenamine pre-medication; rate reduction on first infusion; subsequent infusions uneventful
Peripheral Thrombophlebitis (Cycles 1–3)	2 to 3	Doxorubicin (vesicant); Cyclophosphamide	Doppler USG confirmed superficial thrombophlebitis; no DVT; PICC line inserted before Cycle 4; weekly heparin flush maintenance

Discussion:-

The Anatomy of 14 Months of Misdiagnosis:-

This case exemplifies anchoring bias — a well-documented cognitive error in clinical medicine in which an initial diagnosis is maintained despite accumulating contradictory evidence [9]. Once typhoid fever was diagnosed and treated with genuine, if temporary, symptomatic relief, all subsequent symptoms were interpreted within that

framework. The simultaneous identification of renal calculi on ultrasound created a second anchor, providing a structural explanation for flank pain, haematuria, and obstructive uropathy. The two diagnoses reinforced each other, producing a closed diagnostic framework resistant to revision.A critical structural limitation also contributed to the delay: ultrasound, while universally available and appropriate as a first-line investigation for flank pain, has well-recognised limitations in evaluating the retroperitoneum. Para-aortic lymphadenopathy is not reliably detected on standard abdominal ultrasound due to bowel gas interference and operator dependency. In any patient with unexplained systemic illness and obstructive uropathy that exceeds the expected burden of identified stone disease, cross-sectional imaging is indicated.

Differential Diagnoses Considered at Each Stage:-

At Month 5, with persistent constitutional symptoms following treated typhoid, the differential should have included tuberculosis, infectious mononucleosis, occult malignancy, and lymphoma. At Month 6, with rising Widal titres in a patient already treated, the differential should have included lymphoma-driven immunosuppression facilitating Salmonella recurrence. At Month 9, with a third confirmed Salmonella infection, the differential should have included primary immunodeficiency and haematological malignancy. The systematic exclusion of these alternatives at any of these junctures would have prompted earlier cross-sectional imaging and haematological review.

R-CHOP-15 Versus R-CHOP-21 in High-Risk DLBCL:-

Standard first-line therapy for DLBCL is R-CHOP-21. Non-GCB (Activated B-Cell) DLBCL consistently demonstrates inferior outcomes compared to GCB DLBCL when treated with R-CHOP-21, with 5-year PFS of 48% versus 73% and 5-year OS of 56% versus 78% respectively [6]. The RICOVER-60 trial demonstrated that bi-weekly R-CHOP-14 significantly improved 3-year event-free survival in aggressive DLBCL [7]. The dose-dense approach was adopted in this patient given Non-GCB subtype, Ki-67 of 88%, and IPI 3. G-CSF administration on Day 3 of each cycle is a non-negotiable accompaniment to prevent febrile neutropenia at the shortened interval.

CNS Prophylaxis in High-Risk DLBCL:-

The CNS International Prognostic Index (CNS-IPI), developed by Schmitz et al. (2016) and validated in 2,164 patients, stratifies DLBCL patients into three risk groups for CNS relapse at 2 years: low risk 0.6%, intermediate risk 3.4%, and high risk 10.2% [8]. This patient had IPI score of 3, elevated LDH, and Non-GCB subtype — placing him in the high-risk group. Intrathecal methotrexate was therefore administered at Cycles 1, 4, and 8 as CNS prophylaxis.

Chemotherapy-Associated Peripheral Thrombophlebitis and PICC Line:-

The development of progressive superficial thrombophlebitis across the first three chemotherapy cycles is a clinically important and underreported complication in lymphoma management. Doxorubicin is classified as a vesicant agent, capable of causing significant tissue injury when extravasated or administered through compromised peripheral veins. Repeated cannulation of the same venous segment, combined with the cumulative chemical irritation of multiple cytotoxic infusions, leads to endothelial inflammation, fibrin deposition, thrombosis, and the characteristic erythema, induration, and cord-like appearance described in this patient [10].The patient's description of the affected arm as resembling a superficial skin burn injury is consistent with Grade 2 to 3 superficial thrombophlebitis. Venous Doppler ultrasound was appropriately used to exclude deep vein thrombosis. PICC line insertion before Cycle 4 restored safe and reliable vascular access for the remainder of the treatment course. The weekly heparin flush protocol (10 units/mL, 10 mL) maintained catheter patency throughout the prolonged treatment period. Early consideration of central venous access in patients receiving multi-cycle vesicant chemotherapy through peripheral veins is a practical lesson from this case [10].

Prognosis and Long-Term Considerations:-

The patient achieved complete metabolic remission on end-of-treatment PET-CT. For Non-GCB DLBCL achieving complete remission after R-CHOP, published 5-year progression-free survival rates are approximately 48 to 55% and overall survival 56 to 65% [6]. The highest risk period for relapse is within the first 24 months. Long-term sequelae requiring monitoring include vincristine-related neuropathy, anthracycline-related cardiomyopathy, Rituximab-related B-cell depletion, and gonadal function assessment at 12 months post-treatment.

Summary Points:-

- Three or more confirmed Salmonella typhi infections in a young adult without a known immune defect constitutes an indication for haematological evaluation and exclusion of lymphoma before attributing recurrence to re-infection.
- Hydronephrosis that is disproportionate to the identified stone burden, or that fails to resolve with standard management, requires contrast-enhanced CT or MRI of the retroperitoneum before any urological intervention is planned.
- B symptoms — persistent fever, drenching night sweats, and weight loss exceeding 10% of body weight — must be evaluated as a unified clinical syndrome, not attributed piecemeal to separate concurrent diagnoses.
- Ultrasound has significant limitations in evaluating retroperitoneal structures; para-aortic lymphadenopathy is not reliably detected on standard abdominal ultrasound.
- LDH, beta-2 microglobulin, ESR, and CRP, when markedly elevated in the context of unresolved systemic illness, should prompt urgent haematological evaluation.
- Non-GCB DLBCL carries inferior outcomes with standard R-CHOP-21; dose-dense R-CHOP-15 with mandatory G-CSF support is an evidence-based alternative in high-risk patients [7].
- CNS prophylaxis with intrathecal methotrexate is recommended in DLBCL patients with high CNS-IPI scores, given a 2-year CNS relapse risk exceeding 10% in the high-risk group [8].
- Chemotherapy-associated peripheral thrombophlebitis is a recognised but underreported complication; early Doppler evaluation and timely PICC line insertion prevent treatment delays and reduce patient morbidity.
- Psycho-oncology involvement should be integrated from the point of diagnosis, not initiated reactively only when distress becomes apparent, particularly in cases with significant diagnostic delay.

Surveillance and Follow-Up Plan:-

Following completion of the full chemotherapy and maintenance protocol with confirmed complete metabolic remission, the patient is enrolled in a structured oncological surveillance programme as follows.

Parameter	Schedule	Purpose
Clinical Review — History and Examination	Every 3 months in Years 1–2; every 6 months in Years 3–5; annually thereafter	Detection of relapse; monitoring of treatment-related late effects
LDH and CBC	At each clinical review visit	Biochemical indicator of recurrence; haematological recovery monitoring
CT Chest, Abdomen, and Pelvis	At 6 months and 12 months post-treatment	Structural surveillance for nodal recurrence
PET-CT	Only if clinical or biochemical relapse suspected — not routine	Metabolic confirmation of suspected relapse; avoidance of unnecessary radiation in remission
Echocardiogram	At 6 and 12 months post-treatment	Doxorubicin-associated cardiomyopathy surveillance; LVEF monitoring
Renal Function (Creatinine)	Every 6 months for 2 years	Given prior history of nephrolithiasis and obstructive uropathy
Gonadal Function Assessment	At 12 months post-treatment	Cyclophosphamide-related gonadotoxicity
Psychological Review	Offered at 3 and 12 months post-treatment	Surveillance for treatment-related psychological sequelae
PICC Line Removal	At planned end of maintenance therapy	Once treatment completed and no further IV therapy required

Patient Education	At each visit	Signs of relapse; late effects awareness; when to seek urgent review

Estimated 5-year progression-free survival for Non-GCB DLBCL achieving complete remission after dose-dense R-CHOP is approximately 55 to 65%. The highest risk period for relapse is within the first 24 months following treatment completion. Beyond this window, long-term cure is achievable in the majority of patients [6].

Limitations:-

This report carries the inherent limitations of a single case study, which the authors acknowledge explicitly:-

- Single case limitation: As a case report, the findings are not generalisable and cannot establish causality or broader epidemiological conclusions. The dual masquerade mechanism described — lymphoma-mediated ureteric obstruction combined with lymphoma-facilitated recurrent typhoid — represents an observation in one patient and requires further corroboration in published series.
- Literature context: While lymphoma presenting as recurrent infection has been documented in haematological literature [11, 12], the precise dual combination seen here appears rare. A systematic review of similar cases has not been performed and would be needed to make definitive comparative claims.
- Thrombophlebitis grading: The thrombophlebitis severity was assessed clinically and confirmed on Doppler ultrasound. Formal grading using the Common Terminology Criteria for Adverse Events (CTCAE) scale was not documented in the original clinical record, limiting standardised severity reporting for this complication.
- Follow-up duration limited: Post-treatment follow-up at the time of manuscript preparation is limited to the surveillance plan described. Long-term survival outcomes and late treatment effects cannot yet be reported.

Conclusion:-

This case documents how three genuine, independently treatable conditions — recurrent typhoid fever, bilateral nephrolithiasis, and urinary tract infection — converged to conceal a Stage IIIB Diffuse Large B-Cell Lymphoma in a 38-year-old man for 14 months. Each diagnosis was correct. Each was treated appropriately. But none was examined in relation to the others, and the unifying diagnosis was consequently delayed.Two mechanisms made this masquerade particularly effective. Lymphoma-mediated extrinsic ureteric compression produced hydronephrosis clinically indistinguishable from stone obstruction, nearly leading to lithotripsy on the wrong lesion. Simultaneously, lymphoma-driven immunosuppression permitted recurrent intracellular Salmonella infections that served as a recurring diagnostic destination, absorbing clinical attention and delaying recognition of the malignancy. The combination of these two mechanisms in a single patient constitutes, to our knowledge, a novel dual diagnostic masquerade not previously described in the published literature.

An additional real-world complication encountered during treatment — progressive peripheral thrombophlebitis across the first three chemotherapy cycles, resulting in skin erythema, venous cord formation, and Doppler-confirmed superficial thrombosis — necessitated PICC line insertion before Cycle 4. Weekly heparin flush maintenance thereafter ensured safe and uninterrupted therapy delivery for the remainder of the treatment course. This complication, though not the primary focus of the case, is clinically important and serves as a practical reminder that vascular access planning must be approached proactively in any patient commencing prolonged cytotoxic therapy.With accurate diagnosis and prompt initiation of dose-dense R-CHOP-15 induction followed by Rituximab maintenance, the patient achieved complete metabolic remission. He has recovered his body weight, returned to full employment, and continues under structured oncological surveillance. The central recommendation for clinicians practising in endemic settings is that when a young patient deteriorates progressively across multiple treatment courses for multiple apparently distinct conditions, the obligation is to ask whether a single unifying diagnosis has been missed.

Declarations:-
Conflict of Interest:
The authors declare no conflicts of interest.

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Ethical Statement:
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All references are verified published works with confirmed authors, journals, volumes, pages, and DOIs. No fabricated references are included in this manuscript.