Case Report

Autoimmune Hemolytic Anemia in 62 Year Old Lady with Mixed Connective Tissue Disorder with Subclinical Hypothyroidism: A Rare Presentation

Vipin Porwal, Pulkit Jain, Ashish Sharma*

Mixed connective tissue disease (MCTD) is an overlap syndrome characterized by the presence of U1RNP antibody with features of polymyositis, scleroderma, and systemic lupus erythematosus. A female 62-year-old patient presented with generalized body weakness since 4 months and shortness of breath for 3 months. The patient had a history of repeated blood transfusions, in view of a clinical history of recurrent blood transfusion with hypothyroidism (anti-TPO positive) with direct coomb test positive with ANA positive. She is a case of autoimmune hemolytic anemia. ANA immunoblot shows U1RNP positive, suggestive of mixed connective tissue disorder. She responded well with prednisolone (1-mg/kg) with a tapering dose.

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Keywords: Anaemia, Autoimmune hemolytic anemia, Mixed connective tissue disease, Subclinical hypothyroidism

Introduction

Autoimmune hemolytic anemia is an acquired disorder characterized by hemolysis and anemia, causing a decreased lifespan of RBC due to autoantibodies against red cells.[1] It can be due to warm, cold, or mixed antibodies.[2] Autoimmune hemolytic anemia can occur as idiopathic (primary) or secondary to other malignancies (leukemia, lymphoma, infections, or even autoimmune diseases).[1,3] Out of 1 to 3 out of 100000 patients per year incidence, warm autoantibodies resulting in AIHA constitute about 70 to 80%.[3] 50% of the above conditions are due to secondary causes.[3] Patients presenting with relevant history, symptoms of anemia and history of recurrent blood transfusion AIHA may be suspected. Patients need to undergo routine tests like CBC, reticulocyte count, and peripheral blood smear. LDH and haptoglobulin need to be tested to know the hemolytic anemia. Direct antiglobulin test may be performed in case of absence of other causes of hemolysis. AIHA is diagnosed by a positive direct antiglobulin test (direct Coombs test) in the absence of other possible causes of hemolysis. Sometimes, AIHA may follow years after severe SLE.[4] About two-thirds of patients of AIHA respond to steroids, which are used as first-line drugs. However, it is common that patients resent relapse and require close monitoring and slow, careful tapering.[5]

Case Report

A 62-year-old female patient presented with complaints of generalized body weakness for 4 months and shortness of breath for 3 months. History:- the patient had a history of hospitalization 5 months back with a complaint of loose stool. The patient had a history of recurrent blood transfusions. The patient had a history of subclinical hypothyroidism, diagnosed one month back and was on medication. No history of black stool, blood in vomitus, or fresh per rectal bleed. The patient had no history of chest pain, edema, palpitations, or cough. No history of anorexia, fever, weight loss, joint pain, rashes headache. The patient had no past history of coronary heart disease, hypertension and diabetes mellitus. The patient had no history of autoimmune disease. The patient had a bladder, bowel, and normal sleep pattern unaltered.

The patient's vital signs on presentation were blood pressure of 100/70 mmHg, temperature of 37.2°C, heart rate of 106 beats/min, regularly regular, normovolumic

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Table 1: Routine investigations

Laboratory parameters		*At the time of admission*
CBC	HB	3.1 g/dl
	WBC	2.56 X 10^3/μL
	RBC	1.83 X 10^6 /μL
	Platelet	313 X 10^3 /μL
	ESR	64
Renal function test	Urea	20.5 mg/dl
	Creatinine	0.6 mg/dl
Urine analysis	Pus cells	1–2/hpf
	Urine sugar	-
Liver function test	Total protein	1.7 g/dl
	Albumin	3.6 g/dl
	Globulin	4.3 g/dl
	SGPT	83.1 U/L
	SGPT	30.5 U/L
	ALP	142.2 U/L
Serum Electrolytes	Sodium	139.5 mmol/l
	Potassium	4.1 mmol/l
TSH		10.85 mIU/L
LDH		783.0 U/L
Direct coomb test		Positive
Indirect coomb test		Negative
Vit B12.		>1000 PG/ML
Ferritin		534 NG/ML
Iron		99.5 microgram/DL
Sickling test		Early negative, late negative
Folate		>20 NG/ML
ANA immunoblot		U1 RNP antigen positive
Complement C3		163.56 MG/DL (Normal Range 90-180 MG/DL)
Anti TPO		Positive

pulse, no radio radial, no radio femoral delay, respiratory rate of 18 breaths/min, and oxygen saturation of 99% on room air.

On examination, the patient had severe pallor present, icterus absent, cyanosis absent, and edema in lower limbs absent. On physical examination, she had pallor nails and pale skin. On CNS examination patient had consciousness, oriented to time, place and person. CVS examination: - normal precordium, S1S2 present tachycardia present. Respiratory examination: - Bilateral chest symmetrical, bilateral chest air entry present. Per abdomen:- soft non tender, no organomegaly present, bowel sound present.

The patient's blood sample was preserved, and an urgent 2 RCC transfusion was done.

O positive blood group was found on type and screen and cross match process. For close monitoring of hemodynamic and transfusion reactions, the patient was admitted to the intensive care unit. Routine investigations are shown in Table 1.

Peripheral smear examination shows macrocytic anemia, thrombocytosis, and neutrophilic leucocytosis with left shift up to myelocytes. Toxic granules were seen in a few neutrophils. Stool occult blood was negative. G6PD 30 minutes. Vit B12 > 1000 pg/mL. Ferritin 534 ng/mL. ECHO reveals normal LV systolic function at 60%. No RWMA at rest. Concentric LVH with grade I LV diastolic dysfunction. MAC present (PML) with mild MR. Mildly sclerosed aortic valve with PG- 09 mmHg. Mild TR , RVSP 18 mmHg + RAP. No clot/pericardial effusion (Annexure 1).

Reticulocyte count 9% (Annexure 2) positive direct and negative indirect Coombs with warm antibodies in addition to several other antibodies (Annexure 3).

HIV, hepatitis B surface antigen, and Hep C antibody are non-reactive. ANA ELSIA 34.04 AU/mL (Annexure 4) rheumatoid factor positive 40 IV/mL (Annexure 5); CCP IgG 11.78 AU/mL. ANA immunoblot shows U1RNP positive (Annexure 10).

In view of a clinical history of recurrent blood transfusion with hypothyroidism (anti-TPO positive) with direct coomb test positive with ANA positive. She is a case of Autoimmune hemolytic anemia.

She responded well with prednisolone (1-mg/kg) with a tapering dose. She now has hemoglobin 10 g.

Discussion

Infection and stressful event can be a precipitating factor for autoimmune disorders.

Mixed connective disorders is a rare autoimmune disease that has features overlapping one of the connective disease like rheumatoid arthritis, systemic sclerosis, dermatomyosistis, and polymyositis. Due to variable presentation, diagnosis is difficult. Initial presentation of MCTD as hematological manifectation is still rare.

Patient had severe anaemia, which found to be a case of autoimmune hemolytic anemia on investigation. Autoimmune hemolytic anaemia is rare disorder with incidence of 1 to 3 per 100000 per year. AIHA is classified according to the temperature at which autoantibodies optimally bind to red blood cells. AIHA warm antibody it accounts for about 80 to 90% of cases in adults and 10% of cases have cold agglutinin disease.[6]

Autoimmune hemolytic anemia can occur due to various reasons, including genetics, malignancies, infections or other autoimmune disorders. The patient undergoes an investigation to find out the cause of AIHA. On ANA screening, find to be positive patient underwent immunoblot ANA and was found to be Serum u1RNP positive.

AIHA is known to occur in 5 to 10% of patients with connective tissue disease. But initial presentation of MCTD as Autoimmune hemolytic anemia is very rare. Our patient had no other symptoms of MCTD, such as myositis or, polyarthritis or Raynaud's phenomenon. Rajashree S. Khot *et al*. show the presence of an old lady with MCTD with warm Autoimmune hemolytic anemia with tuberculosis.[7]

A patient has the involvement of wrist joint and elbow, with RA factor low positive with low positive anti-CCP with high ESR, with a duration of symptoms of > 6 weeks, which follows the criteria of rheumatoid arthritis.

Espinosa-Orantes A *et al*., show the presence of rheumatoid arthritis with warm immune hemolytic anemia. RA and SLE disease unusual overlap is found in Rhupus syndrome. This syndrome shows less SLE-associated damage and more RA-associated manifestations.

Here is a case of overlap syndrome with an initial presentation due to the presence of AIHA, elevated levels of anti-CCP and no erosive arthritis.[8]

Karki P Prasai P. shows the presence of Hashimoto thyroidis with autoimmune hemolytic anemia.[9]

The patient was started on steroid prednisone (1-mg/kg per day) as medical treatment and was tapered after 2 weeks. And the patient improved.

Conclusion

Mixed connective disorder is an autoimmune chronic inflammatory disease with unclear etiology.

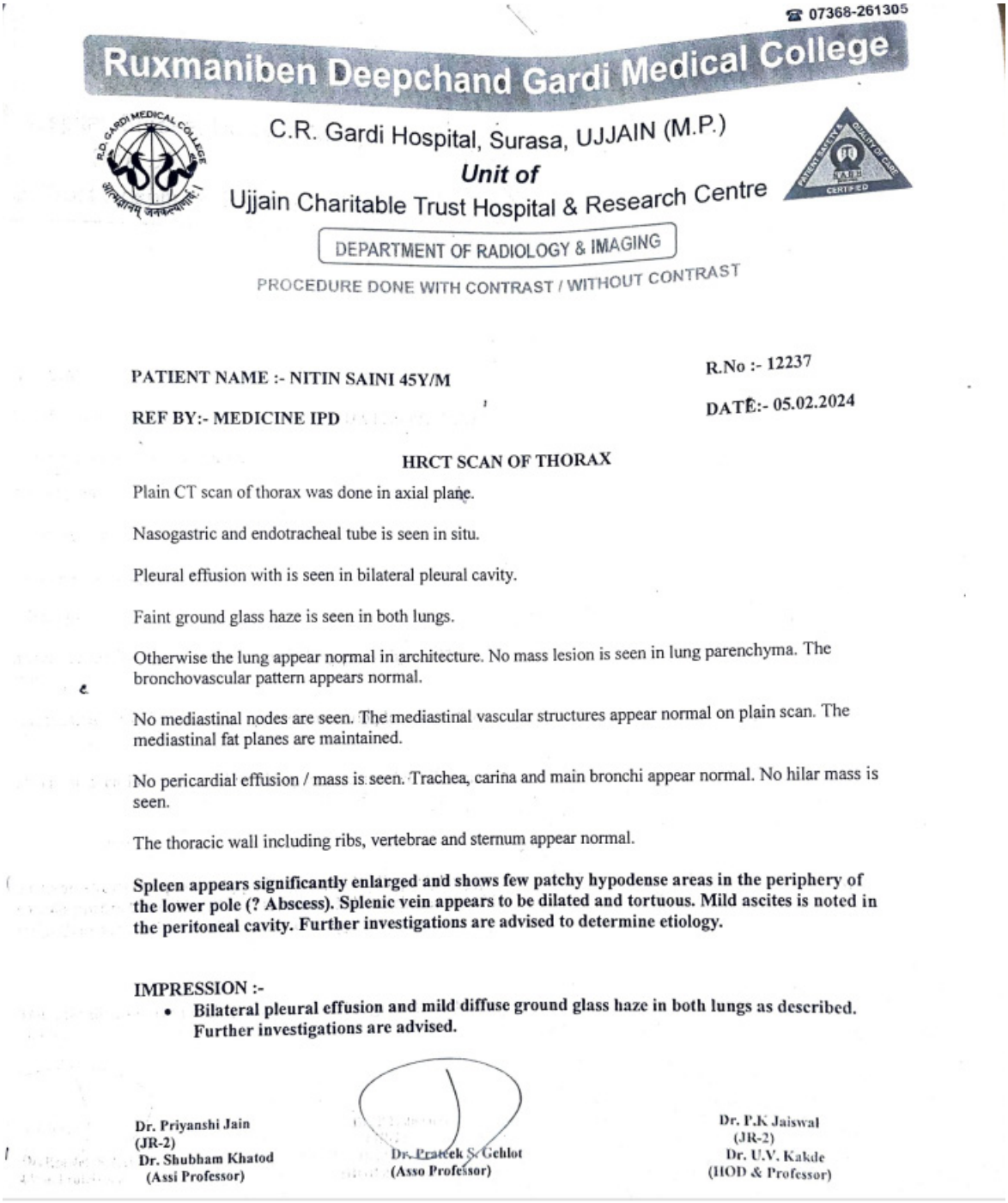
Other disease processes can present as autoimmune hemolytic anemia, highlighting the importance of work-up to be done thoroughly for timely diagnosis and management of underlying conditions.

Autoimmune hemolytic anemia can present as various spectrums and physicians need to be aware of it.

References

1. Liebman HA, Weitz IC. Autoimmune hemolytic anemia. Medical Clinics. 2017 Mar 1;101(2):351-9.
2. Mohanty B, Ansari MZ, Kumari P, Sunder A. Cold agglutinin-induced hemolytic anemia as the primary presentation in SLE-A case report. Journal of Family Medicine and Primary Care. 2019 May 1;8(5):1807-8.
3. Kalfa TA. Warm antibody autoimmune hemolytic anemia. Hematology 2014, the American Society of Hematology Education Program Book. 2016 Dec 2;2016(1):690-7.
4. Firestein GS, Budd RC, Gabriel SE, McInnes IB, O'Dell JR. Kelley and Firestein's textbook of rheumatology. Elsevier Health Sciences; 2016 Jun 21..
5. Bass GF, Tuscano ET, Tuscano JM. Diagnosis and classification of autoimmune hemolytic anemia. Autoimmunity reviews. 2014 Apr 1;13(4-5):560-4.
6. Srikanth M, Lokesh S, Dutta A, Danasekaran V. Auto Immune Mixed Haemolytic anaemia: A rare presentation of SLE.
7. Khot RS, Patil A, Rathod BD, Patidar M, Joshi PP. Uncovering the unusual: a case of mixed connective tissue disease with rare presentation, atypical complications, and therapeutic dilemmas. Cureus. 2023 Mar;15(3).
8. Espinosa-Orantes A, Hernandez-Vera MA, Juarez-Villa JD, Anahí Guadalupe GE, Flores G. Rheumatoid arthritis and autoimmune hemolytic anemia as first manifestation of rhupus. Case reports in rheumatology. 2020;2020(1):8870643.
9. Karki P, Prasai P, Chetri VA, Gautam A, Maskey R. Autoimmune Hemolytic Anemia with Autoimmune Hypothyroidism: A Case Report. JNMA: Journal of the Nepal Medical Association. 2023 Jul;61(263):614.

ANNEXURES



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Unit of

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DEPARTMENT OF RADIOLOGY & IMAGING

PROCEDURE DONE WITH CONTRAST / WITHOUT CONTRAST

PATIENT NAME :- NITIN SAINI 45Y/M **R.No :- 12237**

REF BY:- MEDICINE IPD **DATE:- 05.02.2024**

HRCT SCAN OF THORAX

Plain CT scan of thorax was done in axial plane.

Nasogastric and endotracheal tube is seen in situ.

Pleural effusion with is seen in bilateral pleural cavity.

Faint ground glass haze is seen in both lungs.

Otherwise the lung appear normal in architecture. No mass lesion is seen in lung parenchyma. The bronchovascular pattern appears normal.

No mediastinal nodes are seen. The mediastinal vascular structures appear normal on plain scan. The mediastinal fat planes are maintained.

No pericardial effusion / mass is seen. Trachea, carina and main bronchi appear normal. No hilar mass is seen.

The thoracic wall including ribs, vertebrae and sternum appear normal.

Spleen appears significantly enlarged and shows few patchy hypodense areas in the periphery of the lower pole (? Abscess). Splenic vein appears to be dilated and tortuous. Mild ascites is noted in the peritoneal cavity. Further investigations are advised to determine etiology.

IMPRESSION :-

- **Bilateral pleural effusion and mild diffuse ground glass haze in both lungs as described. Further investigations are advised.**

Dr. Priyanshi Jain
(JR-2)
Dr. Shubham Khatod
(Assi Professor)

Dr. Prateek S. Gehlot
(Asso Professor)

Dr. P.K Jaiswal
(JR-2)
Dr. U.V. Kakde
(HOD & Professor)

DEPARTMENT OF IMAGING
SECTION OF MRI / C T SCAN

Patient Name	: Mr. SAINI NITIN BABULAL	IP/OP No	: 2324291	Age	: 45
Refered By	: Dr. Ravi Rathi	Bed No	: 458	Sex	: M
Date	: 16/01/2024	Ref No	: 77042918		
Ward	: 04th Floor				
User ID	: 0620 17/01/2024 3:51:08 PM	Page No	: 1		

HRCT CHEST

Technique: HRCT chest has been performed from thoracic inlet to the level of adrenals and is evaluated with appropriate window settings.

Clinical details: Follow up case of disseminated histoplasmosis with pulmonary edema. Previous CT scan dated 02.01.2024 is available for comparison.

Imaging Findings:

Tracheostomy, Ryle's tube and central line are seen in situ.

As compared with the previous scan, present study reveals -

Marked increase in pulmonary edema with multiple patchy - confluent perihilar ground glass opacities / consolidations seen in present scan.

Marked increase in bilateral pleural effusions with atelectasis of underlying lung segments also noted.

Bony cage and adjacent soft tissue appear unremarkable.

Tracheo-bronchial tree and esophagus appear normal.

No significant mediastinal/axillary lymphadenopathy noted.

Dr. Kiran Chouhan, MD
Consultant Radiologist

Dr. Neeti Mittal, MD
Consultant Radiologist

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SECTION OF MRI / C T SCAN

Patient Name	: Mr. SAINI NITIN BABULAL	IP/OP No	: 2324291	Age	: 45
Refered By	: Dr. Ravi Rathi	Bed No	: 1112	Sex	: M
Date	: 02/01/2024	Ref No	: 77042764		
Ward	: 11th Floor				
User ID	: 0620 03/01/2024 1:31:59 PM	Page No	: 1		

CECT ABDOMEN + CHEST

Technique: A plain and post contrast (oral + IV) CT study of the abdomen and chest has been performed.

Clinical details: Patient presented with decreased appetite / weight loss for 1 month. Fever for 15 days. Left upper quadrant abdominal pain with altered sensorium for 5 days. Patient had pancytopenia with AKI with dyselectrolytemia. Bone biopsy suggestive of histoplasmosis.

Imaging Findings:

CECT abdomen -

Liver is moderately enlarged, measures approximately 17 cm in maximum craniocaudal extent and shows heterogeneous appearance / enhancement. Intrahepatic biliary radicles appear undilated.

Few enlarged lymph nodes are noted along the celiac axis / hepatic artery, the largest one measuring 2.0 x 1.5 cm.

Gall bladder is well distended and does not reveal any radio-opaque calculus or wall thickening.

Spleen is markedly enlarged, measures approx 19.4 in maximum craniocaudal extent and reveals a moderate sized wedge shaped hypoenhancing lesion in its lower body region, measures approximately 5.6 x 2.2 x 1.5 cm - likely splenic infarct.

Adrenals, pancreas and both kidneys appear normal in size and do not reveal any focal lesion.
Urinary bladder is well distended and appears normal.
Small and large bowel loops appear unremarkable.
Abdominal vasculature appears unremarkable.

There is mild ascites with generalised mesenteric fat stranding and subcutaneous oedema.

Visualized bones appear unremarkable.

Patient Name	: Mr. SAINI NITIN BABULAL	IP/OP No	: 2324291	Age	: 45
Refered By	: Dr. Ravi Rathi	Bed No	: 1112	Sex	: M
Date	: 02/01/2024	Ref No	: 77042764		
Ward	: 11th Floor				
User ID	: 0620 03/01/2024 1:31:59 PM	Page No	: 2		

CECT chest -

Diffuse ground-glass haziness with mild septal thickening seen involving both lungs, predominantly in perihilar region with relative sparing of the subpleural region.

Mild centrilobular emphysematous changes are noted involving bilateral upper lobes.

There is mild right pleural effusion with underlying basal atelectasis.

Few centimeter subcentimeter sized mediastinal lymph nodes are noted.

Trachea and main stem bronchi appear normal,
Mediastinal vascular structures are unremarkable.
Trachea and main stem bronchi appear normal.
Visualized bones appear unremarkable.

Impression:

In a k/c/o histoplasmosis, present CT reveals moderate hepatomegaly and marked splenomegaly with likely a splenic infarct along with changes of volume overload and pulmonary edema as described.

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Consultant Radiologist

Dr. Neeti Mittal, MD
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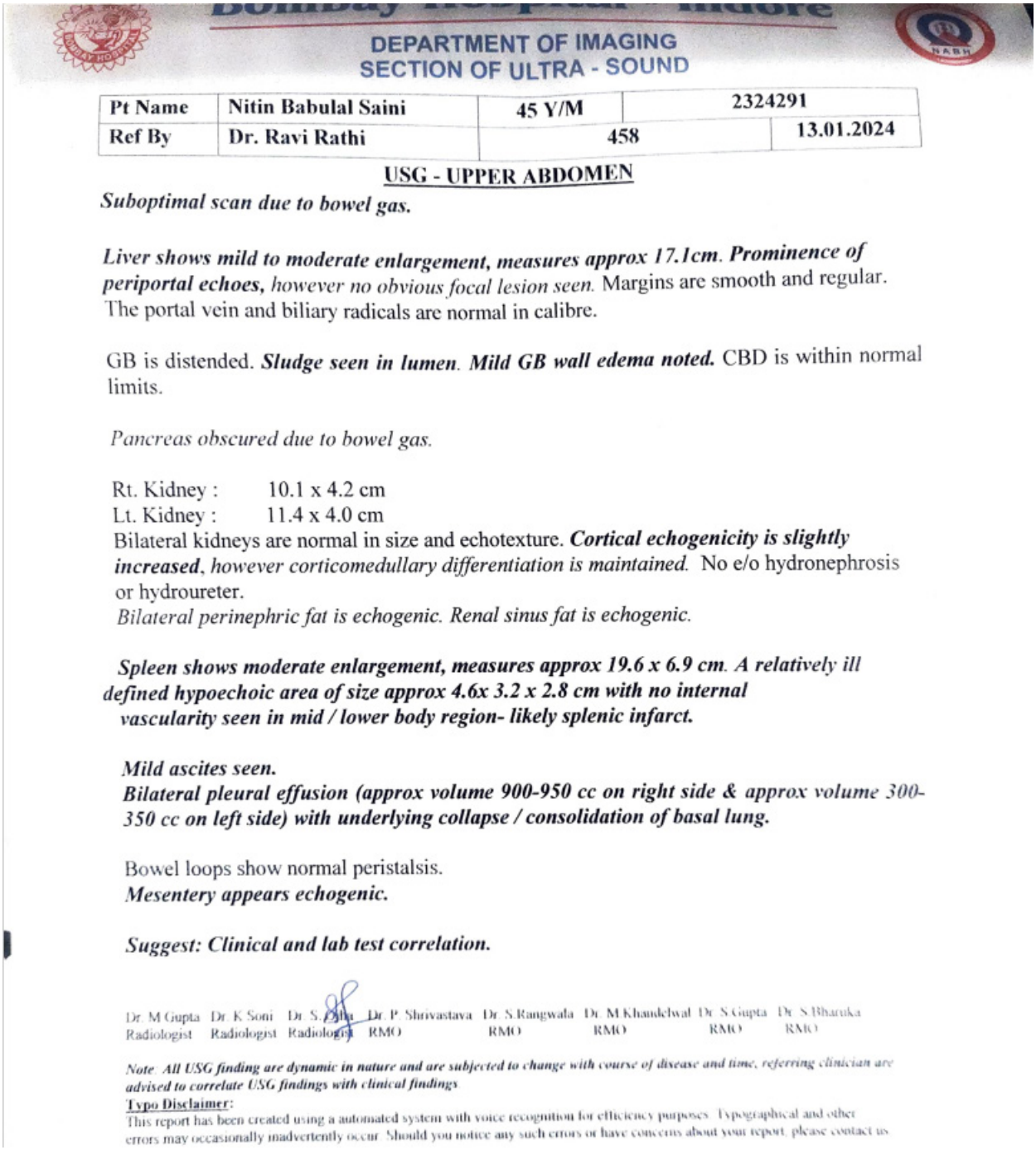

DEPARTMENT OF IMAGING
SECTION OF ULTRA - SOUND

Pt Name	Nitin Babulal Saini	45 Y/M	2324291
Ref By	Dr. Ravi Rathi	458	13.01.2024

USG - UPPER ABDOMEN

Suboptimal scan due to bowel gas.

Liver shows mild to moderate enlargement, measures approx 17.1cm. Prominence of periportal echoes, *however no obvious focal lesion seen.* Margins are smooth and regular. The portal vein and biliary radicals are normal in calibre.

GB is distended. ***Sludge seen in lumen. Mild GB wall edema noted.*** CBD is within normal limits.

Pancreas obscured due to bowel gas.

Rt. Kidney : 10.1 x 4.2 cm
Lt. Kidney : 11.4 x 4.0 cm
Bilateral kidneys are normal in size and echotexture. ***Cortical echogenicity is slightly increased,*** *however corticomedullary differentiation is maintained.* No e/o hydronephrosis or hydroureter.
Bilateral perinephric fat is echogenic. Renal sinus fat is echogenic.

Spleen shows moderate enlargement, measures approx 19.6 x 6.9 cm. A relatively ill defined hypoechoic area of size approx 4.6x 3.2 x 2.8 cm with no internal vascularity seen in mid / lower body region- likely splenic infarct.

Mild ascites seen.
Bilateral pleural effusion (approx volume 900-950 cc on right side & approx volume 300-350 cc on left side) with underlying collapse / consolidation of basal lung.

Bowel loops show normal peristalsis.
Mesentery appears echogenic.

Suggest: Clinical and lab test correlation.

Dr. M Gupta	Dr. K Soni	Dr. S. Gupta	Dr. P. Shrivastava	Dr. S.Rangwala	Dr. M.Khandelwal	Dr. S.Gupta	Dr. S.Bharuka
Radiologist	Radiologist	Radiologist	RMO	RMO	RMO	RMO	RMO

Note: All USG finding are dynamic in nature and are subjected to change with course of disease and time, referring clinician are advised to correlate USG findings with clinical findings.

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Neuberg Supratech

REFERENCE LABORATORIES

(A unit of Neuberg Diagnostics Private Limited)

LABORATORY REPORT

Name	:Mr. NITIN SAINI	Sex/Age	: Male/ 45 Years	H.ID : 236H03628	Case ID : 31201607178
Ref By	:Dr. Self	Dis.Loc.	:		Pt ID :
Bill. Loc.	:INDORE DIAGNOSTIC SOLUTIONS PVT LTD QUALITY DIAGNOSTICS INDORE				Pt. Loc. :
Registration Date & Time	: 30-Dec-2023 21:33	Sample Type	: Biopsy		Ph # :
Sample Date & Time	: 30-Dec-2023 21:33	Sample Coll. By	:		Ref Id :
Report Date & Time	: 03-Jan-2024 08:47	Acc. Remarks	:		Ref Id2 :

Histopathology Report

Specimen :

Bone marrow trephine biopsy for histopathological examination.

Macroscopic Examination :

Received single elongated pieces of bony tissue measuring 0.5cm in length. Whole processed.

1[HE]

Microscopic Examination :

Sections reveal marrow tissue with normal cellularity. The myeloid precursors show normal distribution & maturation. The erythroid series reveal normoblastic maturation.The megakaryocytes & plasma cells are normal in number and morphology. There is increased histiocytes with intracellular capsulated organism morphologically consistent with histoplasma capsulatum.

Impression :

Histoplasmosis, BM trephine biopsy.

There is no evidence of granulomatous pathology, metastatic deposits or plasma cell proliferative disorder in the examined material.

---------- End Of Report ----------

Grossing By : Dr. Chetana Bora

For test performed on specimens received or collected from non-NSRL locations, it is presumed that the specimen belongs to the patient named or identified as labeled on the container/test request and such verification has been carried out at the point generation of the said specimen by the sender. NSRL will be responsible Only for the analytical part of test carried out. All other responsibility will be of referring Laboratory.

Soma

Dr. Soma Yadav

M.D. (Pathology)

Printed On : 03-Jan-2024 08:57

Quality & Diagnostics Imaging

Dr. Ankita Kothari
MBBS, MD, DNB (Pathology)
Ex. SR, TMH, Mumbai
Reg.No. MP-14455

Patient Name	: Mr. Nitin Saini	Registered On	: 30-Dec-2023 06:01 PM
Patient ID	: 301223104	Sample Collected On	: 30-Dec-2023 06:01 PM
Age/Gender	: 45 Years / Male	Sample Reported On	: 01-Jan-2024 02:59 PM
Ref. By	: Universal	Sample Type	: BLOOD
Mob No	: 9827505058	Sample ID	

Bone Marrow Aspiration

Test Name	Observed Values
EASE OF ASPIRATION :	Easy
CELLULARITY :	Normocellular
M:E RATIO :	4:1
ERYTHROPOIESIS :	Normoblastic
GRANULOPOIESIS :	Sequential
MEGAKARYOPOIESIS :	Normal
LYMPHOCYTES :	Within Normal Limits.
PLASMA CELLS :	Increased
ABNORMAL CELLS :	Increased macrophage number seen.
PARASITE :	Smear show oval budding yeast like parasite in many macrophages resembling histoplasma.
IMPRESSION :	Bone marrow infiltration by parasite, most likely histoplasma. Kindly correlate with trephine biopsy.

END OF REPORT

Page 1 of 1

Dr. Vinay Bohara
MD,DM Haematology
FBMT Haematologist