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Original Research Article

Observations on Green Color of Serum from a Patient with Suspected Pulmonary and Extra-Pulmonary Tuberculosis: A Case Report

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Abstract:

Introduction: When Clinical laboratory receive samples with unusual characteristics, laboratory needs to evaluate possible interference and causes.

Case Description: Patient with suspected pulmonary and extra-pulmonary tuberculosis has green color of serum. On laboratory examination, anemia, leukocytosis, lymphocytopenia, mixed hyperbilirubinemia, hypoalbuminemia, hyponatremia, elevated creatinine, hypocalcemia, high ferritin with normal iron and low transferrin was found.

Conclusion: There is no history of infusion of dye, rheumatoid arthritis. However, possibility of elevated biliverdin and elevated ceruloplasmin as cause for green color of serum could not be ruled out. Looking for causes for abnormal characteristics of serum in clinical laboratory may be useful by providing important clue to underling disorders. However, in limited resource settings, final search for cause for such abnormal characteristics may not always be feasible.

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Introduction

Normally majority of serum samples in clinical biochemistry are colorless to pale yellow. In addition to usual icteric, hemolysed and turbid samples, occasionally clinical biochemistry laboratories also receive samples with different characteristics like brown coloration, green coloration, dark orange coloration and blue coloration and highly viscus samples.

These characteristics may be significant in two ways. On one hand it might affect patient's result by causing interference during analysis resulting in either false high or false low results. On the other hand, laboratory and clinicians may want to know chemical entity responsible for abnormal color /property; which may provide clue to some underlying cause of patient's disease. So, during processing of blood samples for separation of plasma/serum, observation of color and unusual properties is essential.

Case Description:

The laboratory received plain sample of a 42 years old unattended male with history of fever for 10 days, chest pain, breathlessness for 8 days and dry cough for 4 days, with history of chronic alcoholism for 5 years. On centrifugation, serum was found to be green in color.

Patient was conscious with pulse rate 130 beats/min, respiratory rate 20/mins with normal temperature. Blood pressure was 90/60 mmHg with SPo_2 95% on room air. Patient was advised chest x-ray (PA), USG (A+P+T), ECG, CBC, LFT, RFT, total protein, albumin, ascitic fluid total protein , albumin, MPR, ADA, ascitic fluid Gram stain.

Chest x-ray was suggestive of bilateral pulmonary infiltrate.

USG abdominal findings suggestive of mild ascites for which ascitic tap was done and 200ml of peritoneal fluid was tapped. Liver shows grade 1 fatty changes and hepatomegaly with 17.5 cms size. Gall bladder is distended & shows sludge in it. Gall bladder wall is edematous and pericholeystic collection is present.

Laboratory findings are shown in following Tables.

Table 1: CBC report of the patient.

Parameter	Result	Reference Range
Hemoglobin	6.50 gm/dL	13-17 gm/dL
RBC	2.12*10^6/ cmm	4.5-5.5*10^6/ cmm
WBC	17600/ cmm	4000-10000/ cmm
Neutrophils	90.00%	40-70%
lymphocytes	6.00%	20-40%
Eosinophils	2.00%	1-6%
Monocytes	2.00%	2-10%
Platelet	Adequate	

Table 2: Routine urine examination of the patient.

Parameter	Result	Reference Range
Quantity	20ml	
Color	Yellow	
Appearance	Clear	
Albumin	Absent	Nil
Sugar	Absent	Nil
Pus Cells	1-2/ hpf	0-5/ hpf
Red Blood Cells	Nil/ hpf	0-2/ hpf
Squamous Epithelial Cells	Nil/ hpf	0-15/ hpf
Crystals	Not seen	Nil
Casts	Not seen	Nil

Ascitic fluid Gram stain : In Gram Stain of the ascitic fluid polymorphonuclear cell or organisms not seen.

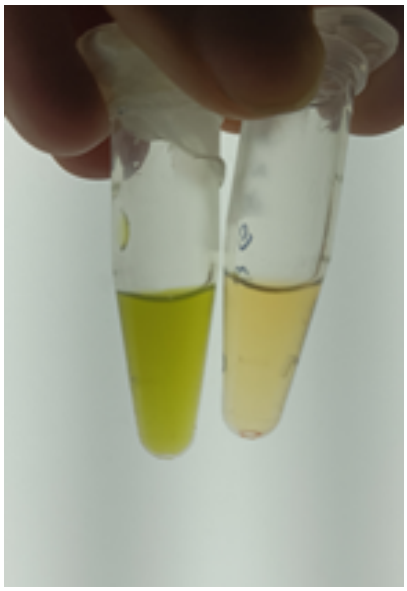

Figure 1: Green color of patient serum (left) compared with normal serum (right)

Table 3: Routine Biochemistry examination of the patient

Parameter	Result(day1)	Result(day2)	Reference Range
Total Bilirubin	6.6	3.7	mg/dL <1.3
Direct Bilirubin	5.4	2.6	mg/dL <0.4
Indirect Bilirubin	1.2	1.1	mg/dL <1.3
Alanine Transaminase	28	25	U/L
Creatinine	1.27	1.86	mg/dL 0.9-1.3
Sodium	126.09	114.70	mmol/L 136-145
Potassium	3.64	4.13	mmol/L 3.5-5.1
Albumin	-	1.8	g/dL 3.5-5.2
Urea	-	34	mg/dL 13-43
Uric Acid	-	4.9	mg/dL 2.6-7.2
Calcium	-	6.0	mg/dL 8.6-10.2
Phosphorus	-	3.4	mg/dL 2.5-4.5

Amylase	-	19	U/L 28-100
Lipase	-	4	U/L 0-5
Iron	-	86	microgram/dL 41-141
TIBC	-	140	microgram/dL 251-406
UIBC	-	48	microgram/dL120-470
Ferritin	-	1197	microgram/dL 20-250

Case discussion: Literature search was performed online to find possible causes for green discoloration of serum. Effort was made to find if any of patients' clinical features and laboratory results can correlate with green color of patient's serum.

Bilirubin's: Bilirubin is the breakdown product of hemoglobin. Under physiological conditions in human adults $1\text{-}2\times10^8$ erythrocytes are broken down per hour. Thus in a 70kg human being, per day 6g of hemoglobin is turned over[1]. When hemoglobin is broken down the protein globin breaks down into the constituent amino acids which are reused. The iron released enters into the liver and goes into the iron pool. Most of the hemoglobin is broken down in the reticuloendothelial cells of the liver, spleen and bone marrow. The breakdown is initiated by enzyme heme oxygenase which is a substrate inducible enzyme. Heme gets broken down into biliverdin which is a green colored pigment. In mammals an enzyme biliverdin reductase immediately acts on the biliverdin to produce bilirubin, which then combines with the plasma protein albumin and is carried into the liver. It is estimated that 1g of heme yields 35mg of bilirubin. [1]

Patient's bilirubin was elevated, as shown in Table-3. If biliverdin to bilirubin conversion is hampered by any acquired or genetic deficit in biliverdin reductase, biliverdin may be elevated [2] . In such cases, patient's serum may appear green colored in diseases causing hyperbilirubinemia.

Alternatively, bilirubin formed may be oxidized in to biliverdin pre-analytically due to contamination by oxidizing agent or in-vivo by oxidizing drug.

Imaging dyes: Imaging dyes like Patent blue can be used for diagnosis of many cancers that metastasize via the lymphatic system and are used to accurately determine the nodal involvement, which is critical for prognosis and treatment. The clinical method for determining the first draining lymph node or SLN, used for clinical staging of melanoma and breast cancers, involves injection of the patent blue dye proximal to the primary tumor before imaging or clinical examination. Patent blue V belongs to the group of triarylmethan dyes along with iso-sulfan blue, its isomer. In general, approximately 5% of the total dye diffused from the injection site is retained by the lymphatics, while the remaining enters the bloodstream. [3] It is known to have a low protein-binding affinity, binds weakly to serum albumin to form a complex that has a slow rate of renal excretion, which may account for the green-colored discoloration.

However, there was no history of use of such dyes in the patient.

Rheumatoid arthritis: Green colored serum is noted in some patients with rheumatoid arthritis, but the nature of green color remains unknown. A definite green colour was present in 12.5 percent of the rheumatoid population, being more common in women than men.[4] It was noted that green serum was not seen in patients with clinically or radiologically more severe cases, presence of subcutaneous nodules or to previous treatment with phenylbutazone, antimalarial drugs, corticosteroids, or gold. but was found more frequently in those with arthritis of longer duration of more than 10 years, who were anaemic and who had a higher rheumatoid factor titre in serum. [4]

However, this patient had no features of rheumatoid Arthritis.

Ceruloplasmin: The green color in serum is also found in patients with elevated ceruloplasmin, a blue, copper containing glycoprotein. Elevated levels (35–70 mg/100 mL) were found in such blood samples. The elevation of serum ceruloplasmin in pregnancy has been attributed to estrogens. The significance of rise in ceruloplasmin level is unknown. A few patients with Wilson's disease have intermediate amounts of ceruloplasmin, and these patients respond much more to the administration of estrogen. [5]

Ceruloplasmin is high in a neoplastic and inflammatory states as it behaves as an acute phase reactant, Increased level shown in carcinomas, leukemia's, Hodgkin disease, primary biliary cirrhosis, systemic lupus erythematosus and rheumatoid arthritis. High levels occur in pregnancy, with estrogens and with oral contraceptive use when the agent contains estrogen as well as progesterone. It is also increased in copper intoxication.

Ceruloplasmin was not measured in the patient. However, high ceruloplasmin is known to cause elevated ferrtin. Ceruloplasmin exhibits a copper-dependent oxidase activity. It is a ferroxidase that converts highly toxic ferrous iron to its non-toxic ferric form. [6]

Other causes

- Presence of Gram-negative cryophilic contaminants such as the Pseudomonas species
- Use of medications such as sulfonamides.
- Paraquat (herbicide) Poisoning- Patient comes with complain of severe hypoxia, hypotension, and lactic acidosis with blue-green vomit to Casualty. [7]

Conclusion

The patient under investigation had no history of infusion of dye, rheumatoid arthritis. However, possibility of elevated biliverdin and elevated ceruloplasmin could not be ruled out. Looking for causes for abnormal characteristics of serum in clinical laboratory may be useful by providing important clue to underling disorders. However, in limited resource settings, final search for cause for such abnormal characteristics may not always be feasible.

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