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Case Report

Reversible pancytopenia: A diagnostic dilemma

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Abstract

Hydroxychloroquine (HCQS) is a medication initially developed for treatment of malaria. It is used for various rheumatological and skin disorders with various side effects and drug reactions. A 61 years old female presented with fever and pancytopenia with polymorphic skin lesions and sore throat. After exclusion of the common causes, a diagnosis of HCQS induced pancytopenia was made which is a rare side effect of HCQS. The pancytopenia improved following stopping HCQS and the case was diagnosed after detailed history and examination and considering the differentials.

The importance of the case lies in the fact that clinicians should consider drug induced pancytopenia, as it is a reversible cause and can be diagnosed with ease after stopping the offending drug.

Keywords: HCQS, Pancytopenia

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1. Introduction

Pancytopenia is a serious complication of several disorders with high morbidity and mortality. It is important to diagnose the reversible causes of pancytopenia as the condition reverses after stopping the causative medications. Vitamin B12 and folic acid deficiency must also be ruled out with importance of dietary history as the dietary deficiencies are reversible. Dengue and other infectious diseases may also cause pancytopenia which may reverse following successful therapy.

HCQS was USFDA approved in 1955 for the treatment of malaria[1] HCQS and chloroquine (CQ) belong to 4 aminoquinolone group.[2] HCQS has less toxicity compared to CQ.[3] HCQS can lead to various haematological complications like anaemia, leukopenia, thrombocytopenia, agranulocytosis. There are very few documentation of HCQS thrombocytopenia with a diagnosis of HCQS induced thrombocytopenia in 12 COVID 19 cases in 2021.[4] Pancytopenia is decrease of all three cell lines of blood. It is a common pathway due to infections, autoimmune diseases, genetic causes etc. Haemoglobin is less than 13 gm/dl in males, and less than 12 gm/dl in females, total leukocyte counts less than 4000/mm3 and platelet count less than 1,50,000/mm3 or absolute leukocyte count less than 1800 per microlitre.[5,6] Aetiology may vary. It may be due to decreased production, increased destruction or marrow infiltration,

A study from India in 2013 showed commonest causes are hypersplenism, infections and bone marrow suppression due to cancer, chemotherapy, drugs and radiotherapy and megaloblastic anaemia.[7] Another study from India showed megaloblastic anaemia to be the commonest cause followed by aplastic anaemia.[8] Various antimicrobials, diuretics and anti-rheumatoid arthritis agents cause pancytopenia, but HCQS is a very uncommon cause.

Here, an interesting case of reversible pancytopenia due to HCQS was presented which improved following stopping the offending drug.

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2. Case Report

A 61 years old non diabetic, non-hypertensive, non-addict, female, housewife by occupation on mixed diet presented in Emergency with sore throat for the last 7 days with history of fever, cough and sputum production for similar duration. The patient was admitted in General Medicine Ward of a Tertiary Care Hospital in South 24 Parganas district in West Bengal. Fever was intermittent with chills and rigor, relieved with sweating without any headache, body ache, joint symptoms or bleeding from any site. Patient had history of chronic eczema on both lower limbs with extensive polymorphic light eruptions over back since last 1 year which responded to therapy and recovered at the time of presentation. Skin biopsy showed lichenoid reaction from back and lower limb biopsy showed Id reaction. Sore throat was not associated with loss of taste or smell and intermittent non-productive cough was present.

There was no history suggestive of bladder bowel involvement, nor was there any history of rash, neck swelling. There was no history of haemoptysis or past history suggestive of pulmonary tuberculosis or contact.

There was no history of exposure to toxins or chemotherapy and patient did not give any history of similar presentation previously.

On examination, the patient was alert, conscious and cooperative with fever. Neck was supple and general survey revealed mild pallor with skin lesions in both lower limbs and back, blackish macular areas with patchy hypopigmentation which was much better than previous presentation to the dermatologist as patient was receiving treatment with some medications. Patient was hemodynamically stable with petechial spots in the palate and skin. There was no icterus or pedal swelling.

On examination of the haematological system, there was anaemia with petechial spots without any lymphadenopathy, organomegaly or sternal tenderness. Examination of the respiratory system revealed fine crepitations in left lower lung fields without any adventitious sounds or wheezing. Cardiovascular system and other system examinations were unremarkable. On examination of the oral cavity, there was pharyngeal inflammations without any ulcers or leucoplakia.

A provisional diagnosis of dengue fever was made with differentials of viral pneumonia, enteric fever.

Investigations revealed pancytopenia with haemoglobin of 7.9 mg/dl, total leukocyte count of 620 cells/mm3 and platelet counts of 30,000/mm3 with normal levels of Random blood sugar, urea, creatinine and electrolytes. LFT revealed mild transaminitis and mildly reduced albumin with normal globulin levels. MCV was normal with increased RDW and ESR was raised at 32mm in 1st hour. PBS revealed microcytosis with hypochromia. Reports of MP slide, Dual antigen, Dengue profile, Typhi Dot M, Scrub Typhus, IgM Leptospira antibody, SARS COV 2 RT PCR, blood culture, urine culture, sputum cs were sent with Rheumatoid Factor, Anti CCP ab and ANA HEP 2.Chest X ray revealed increased broncho vascular markings on both lung fields with normal ECG, echocardiography.

Patient was started on paracetamol tablets with Syrup sucralfate and injection cefoperazone sulbactam was started with fluconazole as absolute neutrophil count was less than 500/mm3. Patient was treated with supportive management and drugs that may aggravate pancytopenia was avoided with avoidance of intramuscular injections. Skin specialist advised steroid ointment for skin lesions.

All reports of fever profile were negative and patient was put on warm saline gargle for sore throat. Fever decreased and patient started to recover and was put on oral liquid diet from day 2 of admission.

Detailed medication history revealed intake of hydroxychloroquine tablets 200 mg twice daily for last 6 months for the skin lesions.

Results of rheumatological profile, Vitamin B12, RBC and serum folate were unremarkable and CT Brain done to rule out thrombocytopenia induced ICH was also normal. HCQS was stopped and patient started improving, Bone marrow was adviced, but patient refused. Haemoglobin rose to 10 mg/dl, total leucocyte count recovered to 5100/mm3 and platelets rose to 1.7 lakhs/mm3 within 7 days of admission. Sputum AFB was negative on 2 days and thyroid profile was also normal. Iron profile was unremarkable.

A diagnosis of HCQS induced pancytopenia was made and patient was discharged on day 11 of admission with advice of follow up in Haematology and skin OPD.

3. Discussion

Pancytopenia is a condition in haematology where all three peripheral cell lines of blood are decreased with haemoglobin less than 12 gm/dl in females, WBC less than 4000/mm3 and platelet count less than 1,50,000/mm3[9] or absolute neutrophil count less than 1800/microlitre.

Pancytopenia is associated with various conditions, unlike a disease.[10] It may be associated with malignant and benign lesions and may be due to increased damage or decrease in production of cells.

NSAIDS, Chemotherapeutic agents and toxic chemicals like lindane, DDT may cause pancytopenia. Complications are anaemia, bleeding and risk of infections.

HCQS has multiple side effects like rashes in the skin, corneal accumulation and retinopathy which mandates regular eye checkup.[11] Haematological complications are rare and includes agranulocytosis, aplastic anaemia and mild decrease in total leucocyte count with around 4.8% incidence.[12] Most cases are reversible and only develop after

several months of therapy.[13] HCQS, a 4 aminoquinoline with a gradual kidney clearance and a large volume of distribution may lead to increased concentrations causing haematological manifestations.[11,13]

HCQS has many uses such as treatment of malaria, SLE, skin lesions like polymorphic light eruptions, skin lesions due to granuloma and panniculitis. CBC should be monitored once a month for the initial three months and then after every 4-6 months to detect and treat haematological complications.[14]

Modification of quinine by hydroxylation was done in 1945 to reduce the toxicity.[15] HCQS 200 mg contains 155 mg base and orally used.

Mechanisms of action are

1. Lysosome alkalisation
2. T cell response blockage
3. Blocking toll like receptor 7 and 9
4. Inhibition of immune signals
5. Phospholipase A2 inhibition
6. Nitric oxide production stimulation
7. Immunomodulator
8. Anti-viral effect
9. Anti-thrombotic effect

As the medication has wide spread uses caution should be taken to explain the risks and side effects of therapy and regular clinical and biochemical monitoring which was lacking in the case discussed here.

So the importance of the case report is not only to identify HCQS as the offending agent of drug induced pancytopenia, but also to instruct the patient for regular clinical and bio chemical monitoring to avoid complications.

4. Conclusion

Pancytopenia causes high risk of morbidity and mortality with many causes, both benign and malignant. It is important to diagnose the reversible causes of pancytopenia like drugs, chemicals, infections, dietary deficiencies for prompt identification of the case and subsequent timely management to avoid complications. HCQS, a reversible cause of pancytopenia has to be used with caution with strict instructions for clinical and bio chemical monitoring to avoid complications.

5. Conflicts of Interest

None.

6. Source of Funding

None.

7. Patient Consent

Patient did not allow to take pictures of the skin lesion.

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