Falciparum Malaria Infection in a Case of Sickle Cell Trait; Unbalancing the Balanced Polymorphism

Amar Amale · Sourya Acharya · Samarth Shukla · Sameeksha Dubey

Received: 13 January 2012 / Accepted: 14 April 2012 / Published online: 3 May 2012
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Abstract Suffers of Sickle cell trait are protected against plasmodium falciparum malaria because of the law of balanced polymorphism. We present a case of sickle cell trait infected with severe falciparum malaria unbalancing of balanced polymorphism.

Keywords Sickle cell trait · Balanced polymorphism · Malaria

Introduction

Red blood cells coursing through veins deliver critical oxygen to tissues and organs throughout the body. Sickle cell anemia disrupts this important process by distorting normally flexible, disc-shaped red blood cells into stiff crescents that get stuck inside of blood vessels. The resulting blockages lead to pain and organ damage [1]. Carriers of the sickle cell trait are to a large extent resistant to malaria however they are not completely protected from the disease and they still need to take precautions against malaria.

Case

A 24 year old female presented with fever with chills and rigors since 3 days, pain and swelling in large as well as

small joints with chest pain since 2 days. Her past history was insignificant. Drug history suggested intake of iron supplementation and multivitamins over a period of 5–6 years. General examination revealed significant pallor and icterus. Systemic examination was normal. Investigations: hemoglobin 3.5 gm/dl, MCV 84/ μ l, WBC 17,000/ mm^3 DLC: P = 80 % L = 16 % M = 1 % E = 1 % B = 2 %, platelet count 60,000/cumm. Kidney function test was normal. Liver profile showed elevated total bilirubin of 4.5 mg/dl with un-conjugated of 3.2 mg/dl and conjugated of 1.3 mg/dl. LDH was raised (550 IU). Peripheral smear showed sickle shaped cell and gametocytes of plasmodium falciparum. Hemoglobin electrophoresis revealed AS pattern. X-ray chest was normal. Paracheck using “advantage mal card” which uses monoclonal anti-Pf pLDH antibody and monoclonal anti-Pan specific pLDH was done which came out to be positive. Next morning she developed breathlessness. Systemic examination revealed bilateral coarse crepitations and bronchial breathing. ABG showed respiratory acidosis with Po_2 of 36, PCo_2 of 52 with Po_2/Fio_2 of 182 and pH of 7.21. Chest X-ray was suggestive of ARDS (Fig. 1). She was intubated and put on mechanical ventilated. Injectable Artesunate, Tab. Doxycycline, Tab. Folic acid was given through Ryel’s tube. Empirical antibiotics were also given. Sufficient hydration and 4 unit blood transfusion was given following which her condition improved. She was extubated and later discharged after 7 days.

Discussion

Balancing selection refers to a number of selective processes by which multiple allels are actively maintained in the gene pool of population at frequencies above that of

A. Amale (✉) · S. Acharya (✉) · S. Shukla · S. Dubey
JNMC, DMIMS University, Sawangi (Meghe), Wardha,
Maharashtra 442004, India
e-mail: mr_amaralways@yahoo.co.in

S. Acharya
e-mail: souryaacharya@yahoo.co.in

Fig. 1 X ray showing heterogenous opacity in left middle and lower zone with mild peribronchial at perihilar region suggestive of ARDS

genetic mutation. These usually happens when the heterozygote for the alleles have a higher adaptive value than the homozygous. In this way genetic polymorphism is conserved (Table 1).

Such a balance is seen more simply in sickle-cell anaemia, which is found mostly in tropical populations in Africa and India. An individual homozygous for the recessive sickle haemoglobin (HgbS) has a short expectancy of life,

whereas the life expectancy of the standard haemoglobin (HgbA) homozygote and also the heterozygote is normal (though heterozygote individuals will suffer periodic problems). The sickle-cell variant survives in the population because the heterozygote is resistant to malaria and the malarial parasite kills a huge number of people each year. This is balancing selection or genetic polymorphism, balanced between fierce selection against homozygous sickle-cell sufferers, and selection against the standard HgbA homozygotes by malaria. The heterozygote has a permanent advantage (a higher fitness) so long as malaria exists; and it has existed as a human parasite for a long time. Because the heterozygote survives, so does the HgbS allele survive at a rate much higher than the mutation rate [2, 3].

Red cells from people with sickle trait do not sickle to any significant degree at normal venous oxygen tension. Very low oxygen tension will cause the cells to sickle [4]. The sickle cell gene is found more commonly among persons of African descent where malaria is endemic and the sickle cell trait confers a selective advantage: resistance to severe malaria. The mechanism of this protection however, remains incompletely understood. Proposed mechanisms include decreased parasite growth in the red cells and enhanced removal of parasitized cells.

This interesting case signifies that the balancing selection/law of selective polymorphism sometimes is unbalanced by unknown factors. Probably this case landed up in hyperhemolytic crises solely due to falciparum infection.

Table 1 Schematic diagram representing consequences of failed balanced polymorphism

ARDS was predominantly due to complicated falciparum malaria. Infected RBC's might have precipitated sickling resulting in vaso-occlusive crises. In a recent large cohort study in Kenya, sickle cell trait was found to be ~50 % protective against mild clinical malaria, 75 % protective against hospitalization for malaria, and 90 % protective against severe or complicated malaria [5]. These association is frequent in Africa where both conditions coexist. In the US, sickle cell disease is common and affects ~1 in 350 black newborns each year [6], but because malaria is not endemic, the association of the two diseases is rare and seldom discussed. Still, the protection is not complete, as is evident with our patient who had complicated malaria. Although patients with sickle cell trait are relatively protected, malaria is a major cause of morbidity and mortality with sickle cell disease. Malaria precipitates hyperhemo-lytic crises with markedly decreased hemoglobin concentration and infarctive crises [7, 8]. Prompt recognition is essential as early institutional therapy in such patients may prevent further deterioration.

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