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Case Report

Imported malaria with chikungunya co-infection: A case report

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ABSTRACT

Malaria is a parasitic disease caused by *Plasmodium falciparum* and is associated with acute febrile episodes. The disease burden is highest in Southeast Asia. Various measures are being taken to curb the disease in different countries. Even after the introduction of various programmes there has been reports of imported malaria which has been transported from highly endemic countries to less endemic or countries not having cases of Malaria. Not only this, various other viral disease come in as coinfection with malaria which makes the situation even worse. Here we describe one such case of malaria imported from traveller from Nigeria to India who also developed coinfection with Chikungunya.

1. Introduction

India accounts for the highest disease burden for malaria in all of Southeast Asia with 0.84 million confirmed malaria cases and 194 related deaths in 2017.[1] Even though there has been consistent decline in cases and deaths over past decade, malaria problem in our country is disturbing. With the aim to eliminate malaria by 2030, India has launched National framework for Malaria elimination in 2016. Malaria is caused by the apicomplexan parasite, *Plasmodium (P. falciparum, P. vivax, P. malariae, P. ovale, P. knowlesi)* transmitted by female anopheles mosquitoes. *P. falciparum* contributed to about 60% of malaria cases in 2016.[1] *P. falciparum* causes severe malaria which gives rise to fatal complications including cerebral malaria, acute kidney injury, severe anemia, jaundice, acidosis, acute respiratory distress syndrome.[2] Resistance of the parasite to antimalarials and insecticides are factors for continued high morbidity. Furthermore, missed diagnosis of malaria due to low parasite density and asymptomatic patients are reservoirs for gametocyte production and contribute to continued transmission.[3] Along with the above, cross border malaria and imported malaria also is a big hindrance in effective disease control.[4,5] Imported malaria is defined as any malaria infection whose origin can be traced to a malarious area outside the country in which the infection as identified.[6] As a country that is on path of malaria elimination, these factors must not be neglected. There have been few reports regarding imported malaria in India. Here we present a case of fatal imported malaria.

2. Case Report

A 25 year old male laborer working in a stone crusher factory in Nigeria for 2 years, returned to his home in Azamgarh, Uttar Pradesh, India after one year on 8^{th} of May 2019. Since his return he complained of high-grade fever associated with chills and diarrhea along with general malaise, headache, and few episodes of vomiting. He visited the nearest hospital the three days after his arrival where laboratory tests were done which showed hemoglobin as 8.9 g/dL; white blood cell counts 6400 cumm

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(lymphocytes 13%, neutrophils 78%, eosinophils 3% and monocytes 1%); platelet count 1,60,000/ mL and Serum Creatinine 2.9 mg/dL. The rapid diagnostic test (RDT) based on immunochromatography for malarial parasite turned out to be positive with peripheral blood smear (PBS) findings consistent with *P. falciparum* malaria. Although he got relieved of diarrhea by conservative management but developed new onset altered sensorium accounting to poor Glasgow coma scale (GCS) and low urinary output.

He was then started with the antimalarial drug treatment including Injection Falcigo (Artesunate) 3VAC IV (total 60 x 3 150 mg) once daily for 10 days and Tablet Primaquine 15 mg twice daily for 15 days along with 3 sittings of hemodialysis which went uneventful. The patient did not respond well and was still unconscious and therefore was referred to our hospital after 10 days of treatment.

After being admitted in our hospital, the serological investigations were positive for Anti chikungunya virus IgM antibody (NIV CHIK MAC ELISA kit version 3.4, Pune). The RDT was still positive for *P. falciparum*, but the PBS was negative for malaria. The Computed tomography (CT) head showed multiple hyperdense foci in multiple draining areas suggestive of a picture of post falciparum malaria. The patient was still unconscious and on ventilatory support. The laboratory tests showed serum creatinine 6.73 mg/dL despite of another two hemodialysis sittings in our hospital. The antimalarial treatment was continued with Tablet Primaquine 15 mg twice daily for another 5 days and Injection Falcigo was stopped after completion of 10 days of treatment. Despite all the efforts, the patient could not be saved.

3. Discussion

Light microscopy of Giemsa/Leishman-stained blood smears is gold standard for diagnosis with detection limit of about 4 to 20 parasite/μl but cannot reliably detect <5-10 parasites/ul.[7] RDTs have major role in resource poor countries and are accurate. They use *P. falciparum* histidine rich protein 2 (*Pf*HRP2) and pan-Lactate dehydrogenase (pLDH) for diagnosis of *P. falciparum* and pLDH and aldolase for other species. RDTs can remain positive for several days following the clearance of parasitemia, as antigen clears later from the bloodstream. *Pf*HRP2 protein is released upon schizont rupture and is thus found in the supernatants of cultured parasites and in the blood of parasite-infected individuals. This enables the detection of *Pf*HRP2 when sequestered parasites cannot be detected by microscopy. As *P. falciparum* parasites develop in the infected red blood cells from ring stage to trophozoites, they disappear from the peripheral circulation and cytoadhere to various organs in the host The *Pf*HRP2 RDT is not useful for the prediction of parasite responses to therapy because of the persistence of the antigen in the peripheral blood circulation after parasite clearance. Molecular tests are being increasingly used and are mainly important for research and epidemiology purposes. They have limit of detection of 0.02 to 1 parasites/μl.[7] These can be used for diagnosing malaria even when parasite are present in low densities and in asymptomatic cases to help national health programmes.

3.1. Imported malaria

Due to increasing urbanization and global economic growth, there is lot of migration and human transfer between countries. As a result drug resistant and virulent strains have spread.[8] Large scale human exchange and travelling occurs between India and Africa. In 2017, the WHO African region contributed to 92% of malaria cases and 93% of malaria deaths. Nigeria confers to about 50% of malaria cases in West Africa.[1] This high endemicity and excessive severe infections create a difficult scenario for the travelling individual. Only few case reports have been published on imported malaria in India.[9] This calls attention to the fact that that malaria importation to eliminating countries is also important and a major barrier to achieving malaria elimination.[5,8] The incubation period of *P falciparum* malaria is 9 to 14 days and since this patient developed clinical features within 2 days of arrival to India, this is a case of imported malaria.

3.2. Co-infection malaria and chikungunya

Malaria is a parasitic disease transmitted by Anopheles mosquito, and chikungunya is a viral disease transmitted by Aedes mosquito. Both the vectors coexist in South Asia, Africa, South America and can simultaneously cause diseases in a single individual.[10] The overlapping clinical signs and symptoms of febrile illnesses like scrub typhus infection, Zika virus disease, leptospirosis, chikungunya with Malaria raises the concern to distinguish between the two. Some systematic review have pointed out that most commonly identified coinfection happens with malaria and dengue co-infection followed by the dengue/chikungunya, malaria/chikungunya, and malaria/dengue/chikungunya co-infections.[11] There is evidence of cross reactivity in serology between dengue and chikungunya therefore to differentiate the two, duplex PCR is useful. Plasmodium, Dengue virus and Chikungunya virus all infect different cell types in humans and might influence immune effector mechanism by down regulating proinflammatory cytokines like IL-12 and IFN-γ.[10,12] Hence, for people returning from endemic areas showing fever, along with malaria, dengue & chikungunya should be tested. As dengue and chikungunya are both arthropod borne viruses which share a common vector, geographical areas and common clinical features, concurrent infection with both viruses transmitted from 2 different mosquitoes or single mosquito harboring both infections is possible.

4. Conclusion

Importance of reporting imported cases of malaria in India from other endemic countries is so that when eventually India comes on verge of malaria elimination, we are not blindsided by imported malaria and that we can increase continuing surveillance and monitoring of these cases as well to achieve sustained elimination.

5. Source of Funding

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6. Conflicts of Interest

There is no conflict of interest.

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