DOI: 10.2478/s11686-010-0013-7

Acta Parasitologica, 2010, 55(1), 96–98; ISSN 1230-2821

VERSITA

CASE REPORT

Vivax malaria presenting with cerebral malaria and convulsions

Anupkumar R. Anvikar[1], Dinesh K. Singh[2], Ruchi Singh[1], Aditya P. Dash[1] and Neena Valecha[1]*

[1]National Institute of Malaria Research (ICMR), Sector 8, Dwarka, New Delhi, India; [2]Tirathram Shah Charitable Hospital, Delhi, India

Abstract

A patient was admitted with fever, vomiting, restlessness and convulsions. He was febrile and unconscious. Laboratory tests showed a low platelet count and ruled out enteric fever and dengue. His peripheral blood smear was positive for *Plasmodium vivax*. The presence of *P. vivax* monoinfection was confirmed by polymerase chain reaction and DNA sequencing. The report highlights the importance of considering the possibility of complications even in *P. vivax* malaria and formulation of strategies accordingly.

Keywords

Plasmodium vivax, cerebral malaria, India

A 20 year-old student having history of fever with chills and rigors for last four days and unconsciousness for last two hours was admitted to the intensive care unit of Tirathram Shah Charitable Hospital, Delhi, India in September 2008. He also had a history of convulsions (on two occasions), vomiting and restlessness during this period. There was no past history of convulsions.

On examination, he was febrile (102°F) and unconscious (Glasgow Coma Scale score: 8). His vital signs included pulse rate 92/min, respiratory rate 28/min and systolic blood pressure of 70 mm Hg. His spleen was palpable 2 cm below the costal margin. Neurological examination revealed normal reflexes and the fundus was normal. Laboratory investigations revealed the following: total serum bilirubin 2.56 mg/dl, serum ALT 162 IU/l, serum AST 75 IU/l, alkaline phosphatase 265 IU/l; total and differential leukocyte counts, renal function tests, blood glucose and serum electrolytes were within normal limits. CSF examination did not reveal any abnormality. Enteric fever and dengue were ruled out by blood culture, Widal Tube test and IgM ELISA, respectively. Platelet count was low (52000/µl). The electrocardiogram, electroencephalogram and computerized axial tomography were normal. The Giemsa stained blood smear was positive for *P. vivax* (parasite count: 48000 parasites/µl). Rapid diagnostic test (Falcivax®, Zephyr Biomedical Systems, India) was also positive for *P. vivax*.

The patient was treated with injectable artesunate, 60 mg at 0, 12, 24, 36, 48, 60 and 72 hours; followed by intramuscular chloroquine phosphate, 5 ml twice a day for three days. In addition, supportive therapy was given in the form of airway care, tepid sponging, hydration, antipyretics and third generation cephalosporin. He gained consciousness after three hours of admission. The blood pressure became normal on the second day of admission. Parasitaemia decreased to 2000 parasites/µl after 48 hours and was undetectable after 72 hours. Fever also subsided after three days. There were no neurological sequelae.

DNA extracted from blood using DNA extraction kit (Qiagen) was used for detection of malaria parasite as well as to rule out mixed infection by nested PCR assay as described by Rubio *et al*. (2002). The results confirmed *P. vivax* monoinfection (Fig. 1). For determination of sequence of small subunit ribosomal RNA (SSUrRNA) the part of SSUrRNA was amplified using *Plasmodium* specific primers rPLU1 and rPLU2 (Ng *et al*. 2008). PCR was done in 20 µl reaction volume containing 200 µmol/l of each dNTPs, 20 pmoles of each primer, 4.0 mM $MgCl_2$, 10 × Taq buffer and 1.0 U Taq polymerase (Bangalore Genei, Bengaluru, India) and 3 µl of genomic DNA as template following conditions as described earlier (Ng *et al*. 2008). Sequence of gel purified PCR product was determined using services of Macrogen (S. Korea); primers

*Corresponding author: neenavalecha@gmail.com

used for sequence determination are: rPLU1-5'-TCA AAG AAT AAG CCA TGC AAG TGA-3'; rPLU2-5'-TAC CCT GTT GTT GCC TTA AAC TCC-3'; rVIV1-5'CGC TTC TAG CTT AAT CCA CAT AAC TGA TAC-3'; rVIV2-5'-ACT TCC AAG CCG AAG CAA AGA AAG TCC TTA-3'. The sequence has been submitted to GenBank via accession no. GQ477744.

Vivax malaria has been considered to be benign for decades. However, various unusual presentations have been reported including respiratory, neurological complications and even death. Neurological syndrome has also been shown to be linked with *vivax* malaria (Kochar *et al*. 2007a). Seizures have been repeatedly observed in severe *vivax* malaria, and the cause has been attributed to the possible cerebral malaria, hypoglycemia, hyponatremia and lactic acidosis (Kochar *et al*. 2007b). Cerebral malaria in *P. vivax* infection has been linked to metabolic changes instead of sequestration (Rogerson and Carter 2008). However, there is another view which states the association of *vivax* malaria with blockade of the blood flow and production of TNF (Clark and Alleva 2009).

Thapa *et al*. (2007) reported two cases of *vivax* malaria from eastern India presenting with convulsions. Both the patients were unconscious at the time of admission. The patient had a low thrombocyte count. The association of platelet depletion and *vivax* malaria has been observed by various workers (Aggarwal *et al*. 2005, Rodríguez-Morales *et al*. 2006). A study from Mumbai has reported six cases of *vivax* malaria with thrombocytopenia, where the level of platelets ranged from 14000 to 92000/µl (Katira and Shah 2006). A recent study from India has reported cerebral malaria as a complication of *vivax* malaria in five out of 40 cases (Kochar *et al*. 2009).

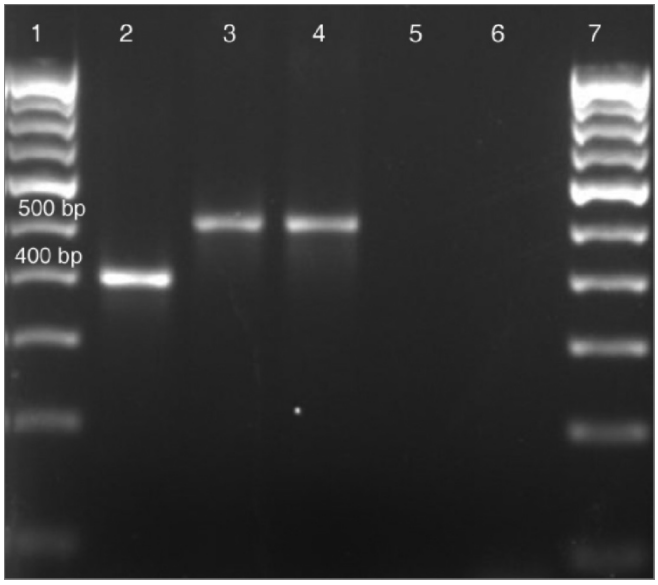

Fig. 1. PCR diagnosis of the patient sample. **1.** Marker = 100 bp ladder. **2.** Positive *P. falciparum* control. **3.** Positive *P. vivax* control. **4.** Patient sample (amplified using *P. vivax* primers). **5.** Patient sample (amplified using *P. falciparum* primers). **6.** Negative control. **7.** Marker = 100 bp ladder

Present report highlights the importance of suspecting complications even in *P. vivax* malaria. This is particularly important since there is a tendency to suspect *P. falciparum* infection whenever such situation arises, on the basis of rapid test using HRP II antigen.

P. vivax strains from India are in general sensitive to chloroquine but resistance has been recorded in some reports (Dua *et al*. 1996, Singh 2000). A therapeutic efficacy study from western India has also shown chloroquine resistance in *vivax* malaria (Srivastava *et al*. 2008). Whether chloroquine resistance is a contributing factor for complications needs to be studied.

The report highlights that *P. vivax* infection can present with altered mental state and convulsions apart from the usual symptoms. Areas with higher *P. falciparum* proportion are classified as high risk and priority is given for introduction of new, rapid and better diagnostic tools and effective drugs. The observation of these clinical presentations are warning signals for better vigilance in *P. vivax* areas which are at present classified as low risk.

References

Aggarwal A., Rath S., Shashiraj. 2005. *Plasmodium vivax* malaria presenting with severe thrombocytopenia. *Journal of Tropical Pediatrics*, 51, 120–121. DOI: 10.1093/tropej/fmh107.

Clark I.A., Alleva L.M. 2009. Is human malarial coma caused, or merely deepened by sequestration? *Trends in Parasitology*, 25, 314–318. DOI: 10.1016/j.pt.2009.04.003.

Dua V.K., Kar P.K., Sharma V.P. 1996. Chloroquine resistant *Plasmodium vivax* malaria in India. *Tropical Medicine and International Health*, 1, 816–819.

Katira B., Shah I. 2006. Thrombocytopenia in *Plasmodium vivax* malaria in children. *Journal of Vector Borne Diseases*, 43, 147–149.

Kochar D.K, Das A., Kochar S.K., Saxena V., Sirohi P., Garg S., Kochar A., Khatri M.P., Gupta V. 2009. Severe *Plasmodium vivax* malaria: a report on serial cases from Bikaner in northwestern India. *American Journal Tropical Medicine and Hygiene*, 80, 194–198.

Kochar D.K., Sirohi P., Kochar S.K., Bindal D., Kochar A., Jhajharia A., Goswami J. 2007a. Post malaria neurological syndrome – a case of bilateral facial palsy after *Plasmodium vivax* malaria. *Journal of Vector Borne Diseases*, 44, 227–229.

Kochar D.K., Pakalapati D., Kochar S.K., Sirohi P., Khatri M.P., Kochar A., Das A. 2007b. An unexpected cause of fever and seizures. *Lancet*, 370, 908. DOI: 10.1016/S0140-6736(07)61417-2.

Ng O.T., Ooi E.E., Lee C.C., Lee P.J., Ng L.C., Pei S.W., Tu T.M., Loh J.P., Leo Y.S. 2008. Naturally acquired human *Plasmodium knowlesi* infection, Singapore. *Emerging Infectious Diseases*, 14, 814–816. DOI: 10.3201/eid1405.070863.

Rodríguez-Morales A.J., Sánchez E., Vargas M., Piccolo C., Colina R., Arria M. 2006. Anemia and thrombocytopenia in children with *Plasmodium vivax* malaria. *Journal of Tropical Pediatrics*, 52, 49–51. DOI: 10.1093/tropej/fmi069.

Rogerson S.J., Carter R. 2008. Severe *vivax* malaria: Newly recognised or rediscovered? *PLoS Medicine*, 5, 875–877. DOI: 10.1371/journal.pmed.0050136.

Rubio J.M., Post R.J., van Leeuwen W.M., Henry M.C., Lindergard G., Hommel M. 2002. Alternative polymerase chain reaction method to identify *Plasmodium* species in human blood samples: the semi-nested multiplex malaria PCR (SnM-PCR). *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 96, Suppl. 1, S199–S204. DOI: 10.1016/S0035-9203(02)90077-5.

Singh R.K. 2000. Emergence of chloroquine resistant *vivax* malaria in south Bihar (India). *Transactions of the Royal Society of Tropical Medicine and Hygiene*, 94, 327.

Srivastava H.C., Yadav R.S., Joshi H., Valecha N., Mallick P.K., Prajapati S.K., Dash A.P. 2008. Therapeutic responses of *Plasmodium vivax* and *P. falciparum* to chloroquine, in an area of western India where *P. vivax* predominates. *Annals of Tropical Medicine and Parasitology*, 102, 1–10. DOI: 10.1179/136485908X311759.

Thapa R., Patra V., Kundu R. 2007. *Plasmodium vivax* cerebral malaria. *Indian Pediatrics*, 44, 433-434.

(Accepted November 20, 2009)