Readers' Forum

Can *Plasmodium Vivax* Cause Cerebral Malaria?

Q. *Currently, I am seeing several patients with complaints of fever, headache and altered sensorium in whom the peripheral blood smear is positive for Plasmodium vivax. Can this parasite cause cerebral malaria?*

Y.S. Chavan,
Trimurthy Maternity and Child Care Centre, Somesh Colony, Nanded 431 601 (M.S.).

A. Cerebral malaria is believed to be caused exclusively by the *Plasmodium falciparum* species. However, occasionally one may encounter subjects with fever and neurological manifestations in whom the only positive contributory investigation is the presence of *Plasmodium vivax* in the peripheral blood smear examination. In this situation, first, it is important to remember that mild alteration in sensorium can occur due to high fever resulting from virtually any pathology. Second, it is imperative to exclude the probability of a coincidental presence of *Plasmodium vivax* (especially in an endemic zone) in a subject suffering from another serious underlying infective neurological condition. In this category, recognition of a mixed plasmodial infection, in which the *Plasmodium falciparum* parasite may have been missed on a *routine* peripheral blood smear examination, is of paramount importance.

A diagnosis of vivax cerebral malaria should only be entertained after exclusion of these two aforementioned commoner possibilities. Several clinical and autopsy reports have reaffirmed the occasional ability of *Plasmodium vivax* species to cause classical cerebral malaria (1-5). Reports of a mini epidemic of virulent vivax infection have also appeared in the Russian literature(4).

The clinical picture of vivax cerebral malaria is indistinguishable from the classical falciparum cerebral malaria. The mechanism of cerebral manifestations in this condition is debatable. Cerebral edema, cerebral capillary plugging with parasitized erythrocytes, perivascular edema with hemorrhage and malarial granuloma have been described. These pathological changes too, are identical to falciparum cerebral malaria(5). However, in contrast to comatose form of subtertian malaria, only single parsites partially plugging cerebral capillaries have also been seen(3,4). In addition to the recognized mechanical disturbances of cerebral capillaries, biochemical (hypoalbuminemia), toxic and perhaps allergic and immunological reactions may also play a role in causing cerebral manifestations. The cerebral oxygen supply may be further compromised by shock and cerebral edema(l).

The management protocol recommended for classical cerebral malaria should be followed; however, chloroquin can be safely utilized since resistance of *Plasmodium vivax* to this antimalarial is virtually unknown. To ensure adequate treatment, it becomes imperative that one's thinking be flexible as regards the causative organism in cerebral malaria.

H.P.S. Sachdev,
Professor,
Department of Pediatrics,
Maulana Azad Medical College,
New Delhi 110 002.

REFERENCES

1. Sachdev HPS, Man Mohan. Vivax cere bral malaria.] Trop Pediatr 1985, 31: 213-215.
2. Verma KC, Magotra ML. Vivax cerebral malaria in Jammu. Indian Pediatr 1976, 13: 229-231.
3. Hill GJ, Knight V, Coatney RG, Lawless DK. Vivax malaria complicated by aphasia and hemiparesis. Arch Int Med 1967, 112: 863-868.
4. Tarjev EM, Gontayava AA, Rotenburg SS. Fulminant type of tertian malaria. Trop Dis Bull 1944,41: 257-258.
5. Dhayagude RG, Purandare NM. Autopsy study of cerebral malaria with special ref erence to malarial granuloma. Arch Pathol 1943, 36: 550-558.

Chemotherapy for Malaria

Q. *It is mentioned that primaquine should be avoided in subjects below 3 years of age. In view of the recent upsurge of cases of malaria in infants and neonates, I seek the following clarifications, (i) What is the standard regimen to be followed for the treatment of vivax malaria and its prevention (with special reference to neonates, if indicated); (ii) Standard regimen to be followed for treatment of resistant falciparum malaria in children under 3 years of age; and (iii) Recommended chemotherapy for cerebral malaria.*

S.B. Deopujari,
Shree Intensive Care Unit,
15/3, Dr. B.N. Ylxare Road,
Dhantoli, Nagpur.

A. Standard Regimen for Treatment of *Plasntodium Vivax* Malaria

The aim of therapy in malaria caused by *Plasmodium vivax* is to rapidly kill the asexual parasites, *i.e.,* schizonts (clinical cure) and to eliminate exoerythrocytic forms of parasite persisting in the liver (radical cure). Chloroquine phosphate (or hydroxychloroquine sulfate) is a potent schizonticated malaria since the strains are mostly sensitive to this drug. It should preferably be given orally in a dose of 25 mg/kg body weight over 3 days (10 mg base/kg initial dose followed by 5 mg/kg 6 hours later and 5 mg/kg daily for 2 days)(l). The dosage schedule of chloroquine is the same for children under 3 years including neonates. In certain situations like persistent vomiting or if the child can not be induced to swallow the tablet or syrup of chloroquine it may be administered in a dose of 5 mg/kg/dose by intra muscular route or intravenous infusion (with 10 ml/kg of isotonic saline or 5% dextrose given over 2-4 hours), repeated after 12 hours and switch over to oral route as soon as possible. Intramuscular chloroquine is not recommended in young children as it has been reported to precipitate convulsions and shock. It should not be given by subcutaneous route as its absorption is slow(2).

For radical cure, primaquine is recommended by the WHO in a dose of 0.3 mg/kg/day to be given orally for 14 days(3). However, in the Indian programme, due to logistic considerations and because of its potential toxicity, the radical treatment is recommended only for 5 days. Primaquine

is not recommended for presumptive treatment of malaria. Childrne receiving primaquine should be watched for its toxic manifestations such as methemoglobinemia, hemolytic anemia, hemoglobinuria (in G-6-PD deficient children), neutropenia arid renal dysfunction.

Primaquine in young children: Primaquine should not be given to children less than 3 years of age because of its potential adverse reactions. These children should be only treated with chloroquine for acute attack and followed by chemoprophylaxis for several months.

Primaquine in G-6-PD deficient children: Relapse of *P. vivax* malaria in G-6-PD deficient young children can be prevented by avoiding use of primaquine and continuing chemoprophylaxis for several months after treating an acute attack(2).

Standard Regimen for Treatment of Resistant Falciparum Malaria

Quinine is recommended for the treatment of falciparum malaria in the areas with known drug resistance to chloroquine or if the malarial attack does not respond to first line antimalarial within 48-72 hours. Quinine sulfate is given orally in a dose of 25 mg/kg/ 24 hours to be given in three 8 hourly doses for 7-10 days(l,3). Quinine can be given parenterally whenever oral administration is not possible. Quinine dihydrochloride is administered intravenously in a loading dose of 20 mg salt/kg with initial dose of 10 mg salt/kg in 5% dextrose over 4 hours followed by 10 mg salt/kg over 2-4 hours (maximum 1800 mg/24 hours) until oral therapy can be started. Intramuscular administration is equally efficacious(2). It is desirable to monitor blood glucose levels as quinine may exacerbate hypoglycemia. If the response is not satisfactory the course of quinine can be repeated with a single dose of pyrimethamine sulphadoxine (1.25 mg/kg of pyrimethamine on the last day) or clindamycin (20-40 mg/kg/24 hours in 3 doses for 3 days).

Mefloquine (single dose of 25 mg/kg) and halofantrine (8 mg/kg in 3 doses at 6 hourly intervals, to be repeated after 1 week) are also effective antimalarial drugs but not recommended in children weighing < 15 kg. Recent trials with pyronaridine (32 mg/kg orally given over 3 days like chloroquine) and artesunate (4 mg/kg/day orally for 3 days along -with mefloquine 25 mg/kg on second day) have also shown promising results in drug resistant falciparum malaria.

Treatment of Cerebral Malaria

Parenteral quinine is the recommended treatment for cerebral malaria in areas where chloroquine resistant falciparum malaria is common. Quinine dihydrochloride is administered in a loading dose of 20 mg salt/kg in isotonic fluid by constant-rate intravenous infusion over 4 hours. Follow it with 10 mg salt/kg by the same means over 4 hours, 8 hourly until patient can swallow tablets. Oral quinine is given as 10 mg salt/kg 8 hourly to complete 7 days' treatment(l). Loading dose should not be usaed if the patient has received quinine or mefloquine within previous 24 hours. Intravenous quinine for 3 days followed by a single dose of pyrimenthamine-sulphalene (metakelfin) has also been tried with good results(4). Quinine is contraindicated in the presence of hemoglobinuria.

If quinine is not available, quinidine gluconate should be administered intravenously in a loading dose of 10 mg/kg (maximum 600 mg) in normal saline slowly over 1-2 hours followed by a slow infusion of 0.02 mg/kg/minute until oral therapy can commence. Oral quinidine gluconate is

given 7.5 mg base/kg, 8 hourly to complete 7 days treatment. It is desirable to monitor blood pressure and ECG while the patient is on quinidine.

If neither quinine nor quinidine is available, chloroquine hydrochloride may be administered by slow intravenous drip in a dose of 5 mg base/kg in 10 ml/kg of isotonic saline infused over a 3-4 hour period. This dose is repeated 6 hours later. The volume of saline can be adjusted between 5-20 ml/kg depending upon the state of hydration.

Primaquin in a single dose is required to eradicate falciparum gametocytes (there is no exo-erythroytic phase in *Plasmodium falciparum* malaria and the gametocidal effect is beneficial in making the subject non infective to others). Apart from antimalarial drugs, particular attention should be given to hyperpyrexia, fluid and electrolyte imbalance, cerebral edema, convulsions and shock which may be life threatening in cerebral malaria.

A.K. Patwari,
Professor, Department of Pediatrics, Lady Hardinge Medical College and Associated Kalawati Saran Children's Hospital, New Delhi 110 001.

REFERENCES

1. World Health Organization. Practical Chemotherapy of Malaria. Report of a WHO Scientific Group. Geneva, WHO, 1990, 75.
2. Clyde DF. Malaria. *In:* Nelson Text Book of Pediatrics, 15th edn. Eds. Behrman RE, Kliegman RM, Arvin AM. Bangalore, Prism Books, 1996, page 974-978.
3. World Health Organization. The Clinical Management of Acute Malaria. WHO Regional Publications, South-East Asia Series No. 9, New Delhi, WHO, 1990, p 66.
4. Thapa BR, Marwaha RK, Kumar L, Mehta S. Cerebral malaria in children - Therapeutic considerations. Indian Pediatr 1988, 25: 61-65.