Revivissance précoce du plasmodium vivax : à propos d'un cas
Recurent plasmodium vivax malaria : about one case

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RÉSUMÉ

Le paludisme est l'une des infections parasitaires les plus menaçantes de l'être humain. Quelques espèces sont connues par leurs forme récurrentes ou biens les épisodes de revivissance due aux hypnozoïtes dormants. Ceci était surtout rapporté avec le plasmodium vivax et malariae. Ces hypnozoïtes sont résistants aux traitements de première ligne et surtout la Chlorquine. Nous rapportons l'observation d'un enfant âgé de 12 ans, hospitalisé pour fièvre prolongée, immigrant de Syrie et aux antécédents de paludisme traité au Sudan. Les explorations de première intention étaient sans anomalies. Un examen au microscope d'une goute épaisse et un frottis sanguin a permis de poser le diagnostic. Un recours à RT-PCR a permis d'identifier l'espèce plasmodium vivax. L'évolution était favorable sou Chloroquine. La Primaquine à la RT-PCR était prescrite en deuxième intention pour éradiquer les hypnozoites.

ABSTRACT

Malaria is a one of the most important threateningparasitic infection affecting human beings. Some species are known for a recurrent infection due to dormant hypnozoites such as plasmodium vivax and plasmodium malariae. Theses hypnozoites do not response to Chloroqine. We report a case recurrent malaria in a 12 years old boy, immigrating from Syria and having a history of malaria treated in Sudan that goes to one year ago. He presented a prolonged fever with asthenia. All examinations were clear. A thick and thin film blood smears helped to make the diagnosis. The species were identified on microscope examination then RT-PCR. It showed plasmodium vivax. The outcome was favorable on Chloroquine then the patient received Primaquine to eradicate the hypnozoites.

Mots-clés : paludisme, plasmodium vivax, revivissance du plasmodium, enfant.

Key words : malaria, plasmodium vivax, recurrent malaria, child.

INTRODUCTION

Malaria is a one of the most important threatening parasitic infection affecting human beings. Out of Plasmodium genus causinginfection in humans, *Plasmodium falciparum* and *Plasmodium vivaxare* the two most important agents responsible for causing the majority of the malaria infections [1]. Across the world, 4% of the malaria infections are caused by *P.vivax. Plasmodium Vivaxis* is known to cause less severe symptoms than *P. falciparum*. It is also known to have a recurrent infection due to dormant hypnozoites [2]. We are reporting a case of a 12 years old child with an early relapse of Vivax malaria.

CASE REPORT

A 12 year old boy was admitted for acute fever with severe asthenia and head ache that had evolved over the past 5 days. He has been staying in Tunisia for 04 months. He emigrated from Syria. No medical history was reported. The examination showed an asthenic boy, with a sweaty body. The cardio-vascular system, pulmonary, abdominal

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and ear-nose-throat examinations were normal. The blood count was normal. The C-reactive protein was barely positive (30g/l). Alanine aminotransferase was 39 IU/l, aminotransferase 45 IU/l. a lumbar ponction brought back a normal CSF. The patient presented a spontaneous apyrexia for 24 hours followed by a relapse of the same symptoms. An increase in C-reactive protein was detected in the examinations (30 to 83 g/l). procalcitonin assay was not available. A further digging in the medical history with the father revealed an old infection with malaria that was managed one year ago in Sudan. The patient received some injections. The treatment couldn't be identified. A relapse of malaria was suspected. A thick and thin film blood smears were practiced and showed some enlarged red blood cells with ameboid ring and some Schüffner's dots in Giemsa-stained slides (figure 1,2,3).

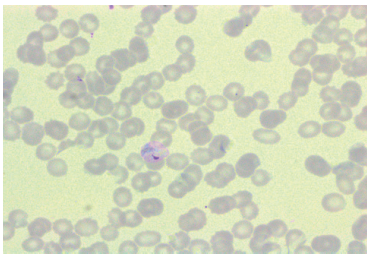

Figure 1 : Ameboid ring in an enlarged and distorted infected rbc.

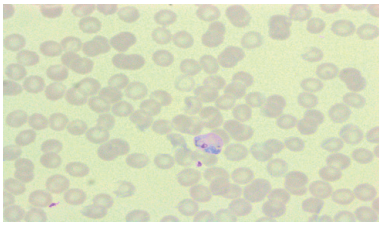

Figure 2 : enlargement in the infected red blood cell, The "halo" is suggestive of Schüffner's dots.

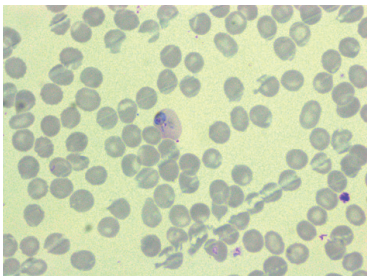

Figure 3 : Trophozoites in thick blood smears.

The parasite was present in 0.3% of the red blood cells on microscopic examination. The diagnosis of P. vivax malaria was made. We completed with a molecular test (RT.PCR) that confirmed the diagnosis. The patient has received chloroquin 600 mg for the first two days then 300 mg for the third day. Symptoms have improved then disappeared within 24 hours. A thin blood steam was practiced 5 days after the treatment that showed a decrease of the number of the parasite in red blood cells. The patient was called back to receive Primaquine to treat both liver hypnosoites and extra vascular merosoites in bone marrow to avoid another relapse.
He received 15 mg a day for 14 days.

DISCUSSION

Malaria is one of the plagues of the globe. Despite the commendable progress in reduction of the mortality in the last decade, this disease continues to threaten about 216 million people worldwide causing 4,45,000 deaths in 2016 [2]. *Plasmodium Falciparum* is the most virulent species which often leads to serious neurological and hematological sequelae in infected patients. *Plasmodium Vivax*, is the most geographically widespread parasite involved in malaria. It contributes to an important share of the disease burden affecting an estimated 8.55 million on 2016 worldwide. In recent years, *P. Vivax* has been reported to cause severe infections associated with mortality. Despite its low parasite biomass, severe complications might include the symptoms ranging from altered sensorium, seizures, cerebral malaria, jaundice, acute respiratory distress syndrome (ARDS), shock, acute kidney injury and severe hemolytic anemia [4,5]. Nowadays, thanks to progress in molecular biology, it has become possible to demonstrate *P. Vivax* as a unique cause of the underlying multi-organ dysfunctions and the life threatening conditions similar to those caused by *P. falciparum*. *Plasmodium vivax* parasites have the unique feature of forming dormant liver stages (hypnozoites) that can reactivate weeks or months after a parasite-infected sand fly bite, leading to new symptomatic blood stage infections [8]. The relapse of the *Plasmodium vivax* was most likely described after 3 to 5 years of the primary infection. On average, as shown from experience, the elimination of P. vivax can be achieved after 3 years at least, compared with the elimination of *P. falciparum*, which can be achieved in only 1 year [9]. Despite the low pyrogenic threshold (the level of parasitemia associated with fever), it is known to be responsible of a greater inflammatory syndrome (table I).

Table 1 : pathological process of p.vivax and potential mechanisms of severe disease.

Pathobiological process in *P. vivax*	**Potential contribution to severe malaria**
Destruction of non-infected RBCs	Severe anemia despite small parasite biomass
invasion and destruction of reticulocytes	Very short RBC lifespan and failure to replace destroyed RBCs: contribution to severe anemia
Increased fragility of infected and non-infected RBCs	severe anemia
Probable faster parasite growth rates in chloroquine-resistant *P. vivax*	severe anemia
Possible pooling of RBCs in the spleen	Potential contribution to anemia
Increased deformability of infected RBCs	Unlikely to contribute to microvascular obstruction or severity
Relapse	Recurrent hemolysis and severe anemia
Recrudescence of chloroquine-resistant *P. vivax*	Recurrent hemolysis and severe anemia

Greater cytokine production relative to *P. falciparum*	Organ-specific inflammation, including increased alveolar-capillary membrane permeability and acute lung injury. Hypothesized contribution to impaired utero-placental cirulation and low birth weight. Dyserythropoiesis and anemia. Endothelial activation. Greater hemodynamic compromise in setting of acute or chronic comorbidity.
Rosetting	Potential contribution to hypothesized but as-yet uncharacterized microvascular obstruction and end-organ pathology
Leukocyte aggregation by paroxysm plasma	Possible organ-specific inflammation, including acute lung injury. Possible contribution to hypothesized but as-yet uncharacterized microvascular obstruction and end-organ pathology.
Maternal anemia	Low birth weight
Splenic hematoma (±trauma) and thrombocytopenia	Splenic rupture
Less well characterized processes	
Putative cytoadherence of *P. vivax*-infected RBCs	Possible targeting of inflammatory responses to the lung: acute
Endothelial activation, dysfunction and/or injury	Lung injury. Speculative contribution to hypothesized, but as-yet uncharacterized, microvascular obstruction and end-organ pathology. Increased alveolar-capillary permeability and acute lung injury. Impaired utero-placental circulation and low birth weight. Possible contribution to hypothesized, but as-yet uncharacterized, microvascular obstruction and end-organ pathology.
Altered thrombostasis, thrombocytopenia and microvascular thrombosis	Possible contribution to hypothesized but as-yet uncharacterized microvascular obstruction and end-organ pathology
Comorbidities	Potential for a non-fatal comorbidity to become fatal with the fever and anemia of acute vivax malaria exacerbating hypoxia and/or hemodynamic compromise

Although the inflammatory correlates ofthe lower pyrogenic threshold were described. However, some studies linked the continuous inflammatory syndrome and the severe symptoms to high level of Gamma Delta (γδ) T cells. The high level of (γδ). T cells were described even during the asymptomatic period when the patient has the dormant hypnozoites, which is responsible for cytokine secretion [11]. Two principal molecules are used for *P.vivax* treatment. Chloroquine is the main (Gold standard) treatment and Primaquine is prescribed in chloroquine resistant forms or for the patients that present a relapse due to the dormant forms of the parasite [6,7]. The prescribed doses are 15 mg a day for 14 days period.

CONCLUSION

Long considered mild infection by P.vivaxis is now known for its severe and fatal complications and to its severe inflammatory disease. The relapsing forms might cause presentations that are even more serious. One of the major problems facing malaria elimination programs at its final stage is the difficulty in detection of cases under conditions of drastic reduction of intensity of malaria transmission. Therefore an eradication of the dormant forms might be indicated in first place.

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Conflict of interests : none.