



# Exflagellation in *Plasmodium vivax* Malaria: Diagnostic Dilemmas and Solutions

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## Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Report

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## ABSTRACT

Trophozoites gametocytes and Schizonts are the most common developmental stages of *Plasmodium vivax* found in human blood. Exflagellation of microgametes occurs in mosquitoes but not in humans during the life cycle malaria parasite. Exflagellation can occur in collected human blood and may cause diagnostic confusion with organisms such as spirochetes and trypanosomes. We present an unusual case of exflagellation in a six-year-old male patient with exflagellated microgametes, an unusual form of *Plasmodium vivax* in a human peripheral blood smear that may create diagnostic confusion with organisms such as spirochetes and trypanosomes.

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## 1. INTRODUCTION

Malaria, caused by parasites of the genus *Plasmodium* and transmitted to humans by the anopheles mosquito, is still the leading cause of death worldwide, and early diagnosis and rapid treatment are required to prevent adverse outcomes [1]. In 2021, the WHO estimated 247 million malaria infections and 619,000 deaths worldwide [2]. The sexual phase of *Plasmodium* happens in mosquitoes and the asexual phase happens in man the intermediate host. All asexual stages of *Plasmodium vivax*, including ring forms, late trophozoites, schizonts, and gametocytes, are commonly seen in human blood. Sexual stages of *Plasmodium vivax* including exflagellation of microgametocytes happen in mosquitoes.

## 2. EXFLAGELLATION OF MICROGAMETOCYTES IN MOSQUITO

Exflagellation is the process by which activated male microgametocytes develop motile flagellar microgametes that detach from the residual body by binding to erythrocytes in mosquitoes [3]. Successful exflagellation was considered a reasonable proxy for the viability of mature male gametocytes [4]. *Plasmodium* gametocytes can recognize the intestinal environment after being swallowed during blood feeding in order to commence sexual reproduction and infect the midgut of the mosquito. Temperature changes, pH changes, and the presence of the insect-specific chemical xanthurenic acid have all been proven to be key stimuli detected by gametocytes in order for them to activate and begin sexual reproduction [5,6]. One male gametocyte forms approximately around 6-8 microgametes [3]. Ex flagellated forms of microgametocytes and microgametes are reported rarely in humans.

In this case report, we discuss an unusual case of a patient-reported with an exflagellation of microgametes in peripheral blood. Under the microscope, exflagellated microgametes form resembles both *Trypanosoma* species and spirochetes, creating a diagnostic quandary.

## 3. CASE REPORT

The case was reported at SRL Diagnostics; Dubai Health Care City.

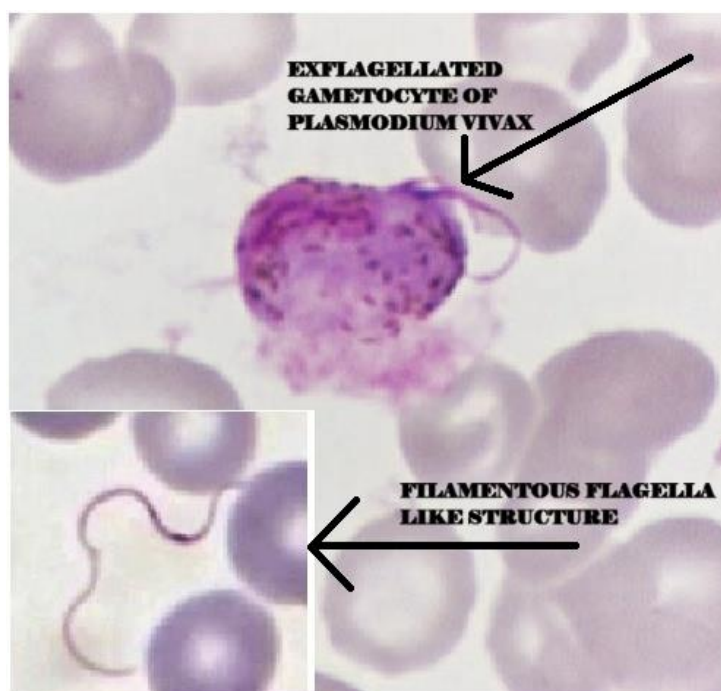
A 6-year-old male patient presented with a fever who had a recent traveling history to India from the United Arab Emirates. An EDTA sample collected from an outside clinic was transported at ambient temperature to our reference laboratory for examination. Blood smear was prepared from the EDTA blood and stained with Leishman stain. A blood smear was examined under a microscope identified ring forms, trophozoite, and schizont forms of *Plasmodium vivax*. In addition to intraerythrocytic parasites, multiple extraerythrocytic, thin, long, filamentous extra erythrocytic flagella-like structures were observed, leading to the initial assumption that this was a case of malaria with a coinfection by *Trypanosoma* species or spirochetes such as *Borrelia*. However, after a detailed examination of the extraerythrocytic structures, they were identified as exflagellated microgametocytes of *Plasmodium vivax*.

## 4. DISCUSSION

Exflagellation of microgametes in human peripheral blood are reported rarely. Ford J et al (2003) reported a similar case of exflagellation of *Plasmodium vivax*. Mukund N. Sable et al. (2019) in their study well described the exflagellation of microgametes in human peripheral blood and its diagnostic dilemma due to the resemblance with *Trypanosoma* species and *Borrelia*, a spirochete.

The reason behind the rare phenomenon explained is when blood containing plasmodium microgametocytes collected in an anticoagulant test tube when subjected to environmental factors, including change in pH and temperature;(drop in temperature with increase in PH results) in increased CO<sub>2</sub> which results in exflagellation [7]. When blood collected in anticoagulant tubes comes into contact with the air environment, resulting in a drop in CO<sub>2</sub>, the pH rises, mimicking the change that gametocytes are subjected to when they reach the mosquito gut and triggering exflagellation [5].

A careful morphological examination with improved knowledge is required in differentiating the exflagellated form of *Plasmodium*, which appears as a thin filamentous structure of around 10-15 in length with an oval-shaped dark blue nucleus. *Borrelia*, on the other hand, is 5-20 in length with a spiral structure and no nuclei, and *Trypanosoma* has an undulating membrane, kinetoplast, and a nucleus [8].



**Fig. 1. Patient blood smear showing Ex flagellation of *Plasmodium vivax***

## 5. CONCLUSION

Exflagellation can occur in human blood and may cause diagnostic confusion with organisms such as spirochetes and trypanosomes. With rising globalisation and frequent travel requirements in today's world, it is important for clinical laboratories and physicians globally to be aware of all common and unusual morphological forms of malarial parasites found in human blood to avoid errors in diagnosis.

## CONSENT

As per international standards or university standards, parental(s) written consent has been collected and preserved by the author(s).

## ETHICAL APPROVAL

As per international standards or university standards, written ethical approval has been collected and preserved by the author(s).

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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