CASE REPORT

Severe presentation of Plasmodium vivax malaria in Melaka, Malaysia

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SUMMARY

A 26-year-old immigrant woman presented with fever, chills, rigor and headache. The blood smears showed *Plasmodium vivax (P. vivax)* malaria. Patient had persistent abdominal pain with sudden drop in haemoglobin level despite achieving clearance of parasitaemia after started on anti-malarial agents. Further radiological investigation revealed that she developed splenic infarcts. Even though *P. vivax* malaria is known to be the non-aggressive type of human malaria, severe infection and complications can still occur. Appropriate imaging modality in correlation with clinical sign and symptoms is crucial to detect splenic infarct that might turn into a fatal splenic rupture.

INTRODUCTION

Plasmodium vivax (P. vivax) has been recognised as the aetiology for severe malaria manifestations.[1,2] Vivax malaria can present in severe form despite low level of peripheral blood parasitaemia.

Melaka, a state in Malaysia, has had zero records of indigenous human malaria for the past 10 years. A total of 24 cases of malaria were reported from 2012 to 2021. Out of which 67% of the cases were human malaria. All human malaria cases were imported, with the most common being *P. vivax*. A total of 17% of the cases were severe malaria, all attributable to *Plasmodium Falciparum (P. falciparum)*.[3] This study described a patient with presentation of severe vivax malaria during an admission to the hospital in 2022.

CASE PRESENTATION

A 26-year-old Indonesian woman has been residing in Melaka, Malaysia since 2018 with a working permit in an electrical equipment manufacturing company. She lived in a hostel near an industrial area in Melaka. The hostel was 5 km away from her workplace where she worked as a production operator in the company. She had a history of traveling back to her hometown at Desa Nagur, Medan, Indonesia for almost a month after the re-opening of the international borders post-COVID-19 pandemic in June 2022. In Indonesia, she stayed only with her family and visited the nearest family member and friends within her hometown. At the end of June 2022, she made her way back to Malaysia and she continued her daily routine which is working in the factory every day from 7 am to 6 pm, Monday through Friday.

Five days after her return, she had a fever with chills and rigor with occasional headaches. On day 2 of illness, she was brought by her employer to a private clinic complaining of headache and vomiting, subsequently diagnosed as 'viral fever' and treated symptomatically. On day 4 of illness, she was brought to another private clinic for persistent symptoms of fever and vomiting, where she was advised to seek further treatment at a secondary centre which was unfortunately ignored.

Two days later, on day 6 of illness, she presented to our institution with fever, vomiting five times a day and abdominal discomfort. The initial diagnosis given at the emergency department (ED) was dengue fever with compensated shock, and she was directly admitted to intensive care unit (ICU) for further treatment. Significant history regarding one of her family members in Medan being diagnosed with malaria was obtained once she was in ICU.

On examination at ED, she was alert and conscious but was extremely lethargic. She was also hypotensive with systolic blood pressure (BP) of 80 mmHg and diastolic BP of 40 mmHg, tachycardic with a pulse rate of 130 beats per minute (bpm) and febrile with a temperature of 38°C. Her pulse oximetry oxygen level was 97%. Auscultation of the lungs was clear with equal air entry. Cardiac heart sounds were normal. Abdomen was tender and there was guarding over left hypochondriac region. No organomegaly was elicited. She had no rash or lymphadenopathy.

She was admitted to ICU and managed as severe dengue with decompensated shock. Without inotropic support, her BP was borderline (94/58 mmHg), she was tachycardic (106 bpm) and saturating at 97% on 3 L/m oxygen via nasal prong. Blood investigations were as shown in Table I. Her diagnosis was revised to severe malaria upon receiving the positive result of her blood film for malaria parasite (BFMP). BFMP was sent earlier given the history of her recent visit to Medan in Indonesia. She was immediately started on intravenous (IV) artesunate 150 mg, then at 12 hours and 24 hours followed by 150 mg daily. Oral doxycycline 100 mg twice daily was also prescribed in combination with the IV artesunate, and she was planned for oral primaquine 30 mg once daily for 14 days for the eradication of liver hypnozoites.

However, the next day she continued to complain of severe abdominal pain. At this point, doxycycline was withheld as it was aggravating her vomiting and primaquine was started. Despite worsening abdominal symptoms, the serial blood smears showed that the sexual parasites had cleared by day 3 of IV artesunate therapy.

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Table I: Summary of laboratory findings during admission

Laboratory parameters	Day of illness										
	Day 6	Day 7	Day 8	Day 9	Day 10	Day 10	Day 11	Day 14	Day 15	Day 16	Day 18
Hb	10.7	10.8	10.0	9.9	10.0	10.3	9.5	8.7	9.6	9.8	10.2
TWC	7.1	6.3	5.0	6.4	5.5	6.0	6.9	14.2	15.6	12.8	9.0
Platelet	23	49	27	75	58	136	207	533	689	575	539
Urea	2.9	2.1	1.8	3.0	2.8						4.9
Sodium	132	137	138	130	137						137
Potassium	3.4	3.1	3.7	4.2	4.3						4.3
Creatinine	68	44	41	59	44						58
TP	70	53	57	58	63			81			84
TSB	35.1	22.3	13.8	17.2	10.6			23.5			13.8
Albumin	39	27	28	29	31			40			42
Globulin	31	26	29	29	32			40			42
ALT	85	59	65	54	56			45			27
ALP	107	79	75	68	73			97			111
AST	66	46	45	45	53			39			23
CK	47	30	25								
LDH	369	310	283					694		652	508
CRP	85	-	200.8	102.1							
Amylase	28	28									
Ca/Ca Corr		1.67	1.9/2.14	1.87	2.01/2.19						
PO4		0.54	0.77	0.43	1.03						
Mg		0.57	0.97	0.57	0.79						
PH	7.49										
HCO3	25.9										
PCO2	28										
Lactate	1.8										
Base excess	2.8										
RTK Dengue	Negative NS1, IgM, IgG										
BFMP		P. vivax:8040/520 parasite/uL blood	P. vivax:7680/400 parasite/uL blood	P. vivax:80/0 parasite/uL blood	P. vivax:80/0 parasite/uL blood	0 parasite/uL blood	0 parasite/uL blood	0 parasite/uL blood	0 parasite/uL blood		

Hb: Haemoglobin; TWC: Total white cell count; TP: Total protein; TSB: Total rerum bilirubin; ALT: Alanine aminotransferase; ALP: Alkaline phosphatase; AST: Aspartate transferase;CK: Creatinine kinase; LDH: Lactate dehydrogenase; CRP: C-reactive protein; Ca/Ca corr: Calcium/calcium corrected; PO4: Phosphate; Mg: Magnesium; HCO3: Bicarbonate; PCO2:Partial pressure of carbon dioxide; BFMP: Blood film for malaria parasite

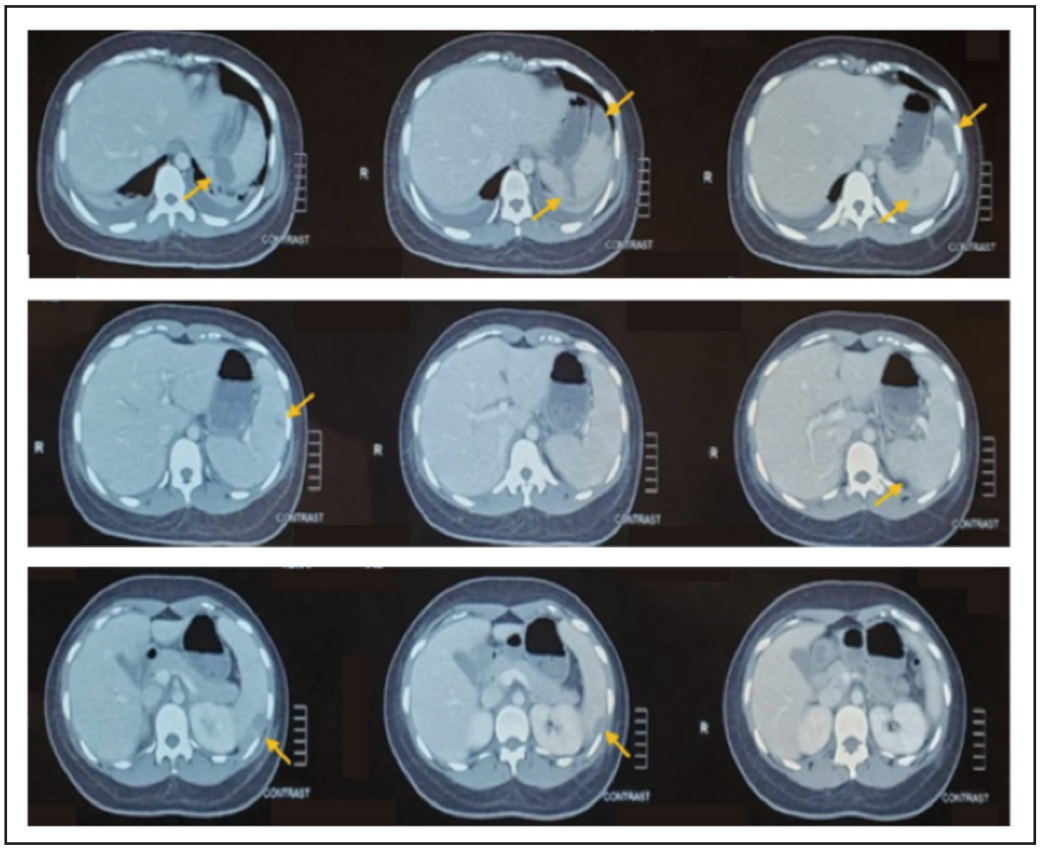

Fig. 1: CT Abdomen and pelvis showing multiple wedge-shaped non-enhancing hypodense lesions in the spleen with the largest lesion in the upper pole measuring 2.2 cm × 4.0 cm × 2.9 cm, representing splenic infarct (yellow arrows pointing to the infarcts within the spleen).

In view of increasing abdominal pain, an urgent ultrasound (USG) abdomen was carried out which showed free fluid in the pelvis. On the next day, the pain intensified. It was localised at the left hypochondriac region with radiation to the tips of the scapula and aggravated by breathing. Thus, an urgent CT of the abdomen was done revealing multiple splenic infarcts with the largest lesion in the upper pole measuring 2.2 cm × 4.0 cm × 2.9 cm (Figure 1).

She was managed with analgesic and close monitoring. She required one-pint packed cell transfusion due to symptomatic anaemia when her haemoglobin (Hb) dropped from 10.3 g/dl to 8.7 g/dl. Her haemoglobin level was stable subsequently. Over the next few days, she responded well to the treatment, and her symptoms resolved. IV artesunate was switched to tablet Riamet. On day 18 of illness, after three consecutive negative smears, she was then discharged with oral primaquine to complete the 14 days eradication therapy course as outpatient.

The patient has completed her treatment with artesunate and primaquine. She was scheduled for monthly BFMP for one year. Repeated BFMP done during follow-up and was negative for 6 months consecutively. She complied with the follow-up schedule and did not complain of any adverse event or reoccurrence of symptoms.

DISCUSSION

This case is classified as an imported human malaria case. *P. vivax* and *P. falciparum* represent the two most frequent forms of human malaria. In terms of severity, *P. falciparum* has received more attention than *P. vivax*. It is a well-known phenomenon that *P. falciparum* causes cytoadherence to endothelial receptors mediated by the surface proteins, thus facilitating the sequestration of parasitised red blood cells in the microvasculature.[4] However, it is increasingly appreciated that *P. vivax* is also capable to cause severe manifestations of malaria as well as mortality.

In this case, a young patient presented with prostration and shock during admission. Based on WHO, these two findings are part of manifestation of severe malaria.[5] A systematic review on clinical impact on vivax malaria revealed that young children and pregnant mothers are particularly vulnerable to severe form of vivax malaria infection. The review mentioned that the common manifestation of severe vivax malaria reported were cerebral malaria, respiratory distress, acute renal injury and severe anaemia. Severe anaemia was associated with patients with recurrent parasitaemia.[1] Another review revealed that thrombocytopenia was the most commonly reported severity sign, followed by circulatory collapse or shock and severe anaemia. While the least prevalent severity sign was respiratory dysfunction.[6] Findings on splenic infarct and splenic rupture were not mentioned and investigated in both reviews.

A clinical study of vivax malaria in South Korea on splenic infarction revealed that 12 out of 92 vivax malaria patients presented with splenic infarction. Six had localised pain in the upper left abdomen whereas the remaining six patients did not present with abdominal pain at the time of investigation. Splenic rupture was noted in one of the patients. All patients recovered spontaneously after treatment and observation without any surgery or intervention. Univariate analysis showed that anaemia and prolonged fever were risk factors for splenic infarction.[7]

In our patient, there was a history of 7 days of fever with persistent complain of localised abdominal pain. Interestingly from the Korean study, six of the 12 patients had no abdominal pain (asymptomatic). The diagnosis of splenic infarction may be difficult without imaging because it can be asymptomatic. The study also did not describe the size of the focal infarct. Size of the focal infarct lesion may be relevant to the symptom of the localized pain. Additionally, the accessibility of CT scan in South Korea under a well-established national health insurance system is a helpful tool to detect infarction and monitoring of patients.

Therefore, the complaint of left upper quadrant abdominal pain before or during the antimalarial treatment should trigger a possibility of splenic hematoma or splenic infarct and need to be managed accordingly to prevent further complications which may require surgical intervention. Such patients should be monitored to look for the persistence of abdominal pain or even deterioration of clinical signs.

Splenic infarct is a rare presentation of malaria which can occur despite appropriate antimalarial treatment with no known predictive signs and may lead to haemorrhagic shock from subcapsular hematoma that ruptures into the peritoneal cavity.[8] Splenic rupture is a fatal complication. However, the association between splenic infarction and rupture remains unclear. Infarcts can occur in both falciparum and vivax malaria, however, a systematic review by Hwang et al noted its prominence in vivax malaria.

The pathophysiology of splenic response is still unknown. Literature indicates a few possibilities. The first is hypercoagulopathy due to decrease levels of antithrombin III, protein C, protein S as well as increase levels of von Willebrand factor and plasminogen activator inhibitor.[9,10] Another possibility is vascular congestion and occlusion due to cytoadhesion of infected red blood cells with splenic cellular hyperplasia and hypoxemia due to anaemia.[8]

Accessibility to imaging is a helpful diagnostic tool in detecting infarction by showing hypodense multifocal areas within the spleen. Diagnosis of splenic infarct can be made via USG or CT, though CT has emerged as the preferred imaging modality. The use of imaging, a non-invasive in vivo human study, alongside clinical observations can provide a full dynamic view of the role of the spleen in normal and pathological conditions caused by malaria.

CONCLUSION

Occurrence of imported malaria cases in Malaysia is a continuing threat. *Plasmodium vivax* malaria infection can cause severe manifestation despite low level of parasitaemia. Clinical awareness on this possibility should be raised. Occurrence of splenic infarct and splenic rupture need to be managed accordingly to prevent fatality which align with the global vision of zero malaria deaths.

A prevalence study of severe vivax malaria in Malaysia describing details on clinical features and complications with occurrence of splenic infarct and splenic rupture is appropriate to understand this less known malaria infection compared to malaria falciparum.

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DECLARATION

The authors declared no conflict of interest.

INFORMED CONSENT

Written informed consent was obtained from the patient for publication of this case report.

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