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TRIPLE TROUBLE- IN A TERTIARY CARE SET UP

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ABSTRACT

Malignant tertian malaria, Dengue and Chikungunya are all mosquito-borne diseases. Dengue haemorrhagic fever and Malignant tertian malaria can be very lethal if treated late or not managed aggressively. Chikungunya can have prolonged morbidity. In case of triple infection with all these in a single patient the situation can be very challenging and lethal. Here we discuss a case of a sixteen-year-old male who was treated at our hospital with a triple infection of Malignant tertian malaria, Chikungunya and Dengue fever. The patient came in a state of altered sensorium due to neurological involvement, was ventilated and then followed up by haemodialysis for renal shut down. Ultimately the patient could be salvaged due to aggressive management in the critical care unit by a team of interdisciplinary experts.

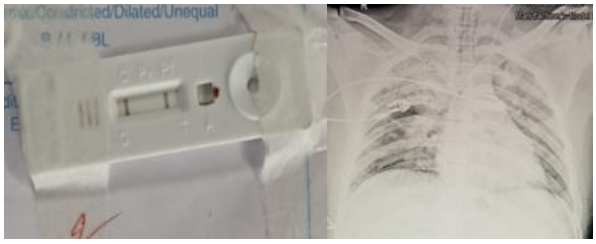
INTRODUCTION

Malignant tertian malaria is a deadly parasitic disease caused by Plasmodium Falciparum. Due to its aggressive nature, and usual occurrence in remote forest areas, patients usually present late to tertiary hospitals and by then they usually land up with multiorgan involvement. Other viral diseases like Chikungunya is equally very distressing when it presents in isolation. Very rarely, if both coexist, it becomes very dangerous and life threatening for the patients. Here we discuss a case of a 16-year-old male who presented to us with both these conditions. To add to his woes, he was also found to have tested positive for Dengue fever, which again could be extremely hazardous. After a long ordeal, the patient could be salvaged following a dexterous management strategy by a team of multiple disciplines.

All these are mosquito borne infections with a significantly high morbidity and mortality rate. Jharkhand is an endemic zone for all these conditions. This case is basically being highlighted so that the clinicians keep in mind – that in all patients presenting with fever with chills and rigors along with altered sensorium, timely intervention and aggressive management can save lives. Review of literature shows 7 similar cases reported from India (1), though 6 of them had Benign tertian malaria caused by P.Vivax.

Case summary

A sixteen-year-old male was admitted with a history of fever with chills and rigors of 5 days duration. There was no history of burning micturition, cough, or difficulty in breathing. He did not have any addictions and any known allergies. There was no known past illness or any history of hospitalization. On examination the patient was confused, irritable and not responding to verbal commands and had pallor and icterus, no cyanosis or dehydration. He was febrile, with a pulse rate of 128/minute, blood pressure of 120/70 mmHg, respiratory rate of 20/minute with no accessories. The Para check test was positive for P Falciparum (Picture 1), the saturation was 95% with 15 litres oxygen by mask, there was no neck rigidity and the Plantar were flexor. Examination of the cardiovascular, respiratory, and gastrointestinal system was unremarkable. During examination in the emergency room (ER) he had one episode of generalized tonic clonic seizures duly controlled by iv Midazolam followed up by iv Levetiracetam as maintenance therapy. Due to deterioration in his neurological status, he was intubated in the ER and shifted to critical care for further management. The Chest x-ray post ventilation showed severe ARDS (Picture 2) which is a natural fall out in MT Malaria.



Picture 1 - Para check test positive for P Falciparum
Picture 2 - Chest x-ray post ventilation suggestive of ARDS

Blood investigations were as in table 1. Urine and stool routine examination were normal. Blood culture did not reveal any microbial growth. Lab Tests for Malaria, Dengue and Chikungunya were positive., which was absolutely surprising. Every clinician in these parts of the world would've come across two tropical diseases in one single patient, but to have three meant triple trouble. We were actually worried about his survival now. Chest radiograph bilateral fluffy opacities. His electrocardiography (ECG) revealed sinus tachycardia. Arterial blood gas (ABG) showed pH of 7.331, PCo2 – 38 mmHg, PO2 – 50 mmHg, sodium (Na+) – 120 mmol/L, chloride (Cl –) - 89 mmol/L, potassium (K+) – 4.4mmol/L, bicarbonate (HCO3-) – 19.6 mmol/L, lactate – 4.0 mmol/L (suggestive of metabolic acidosis), Bilirubin (Bil) 8.1 mg/dl. G6PD level was normal, Sickling and Coombs test were both negative. Bedside ultrasound abdomen revealed gall bladder sludge-- no other significant abnormality was found.

Table 1

Investigations	Value Day1	Value Day3	Value Day10	Normal Range
Haemoglobin (Hb)	7 gm/dl	6.3 gm/dl	8.1 gm/dl	11.5- 16.5 gm/dl
Total leucocyte & platelet count	13830 percumm	11160 percumm	9630 percumm	4000-11000 percumm
Differential count neutrophils	86%	83%	76%	60-70%
Fibrinogen	491 mg/dl			200-400 mg/dl
Platelet count	1.21 lacs percumm	1.94 lacs percumm	2.82 lacs percumm	1.5 lacs-4.5 lacs percumm
C-reactive protein (CRP)	25.13 mg/dl		5.47 mg/dl	0.08-0.79 mg/dl
D Dimer	10.88 mcg/ ml			mcg/ml
Total serum proteins	4.7 gm/dl	5.0 gm/dl	5.5 gm/dl	6.6- 8.3 gm/dl
Serum albumin	2.22 gm/dl	2.03 gm/dl	2.70 gm/dl	3.5- 5.2 gm/dl
Serum globulin	2.48 ml	2.97 ml	2.80 ml	2.5- 3.5 ml
Serum creatinine	5.39 mg/dl	6.04 mg/dl	3.49 mg /dl	0.5-1.5 mg/dl
Total bilirubin	9.45 mg/dl	3.11 mg/dl	1.97 mg/dl	0.2-1 mg/dl
Direct	5.04 mg/dl	1,42 mg/dl	0.59 mg/dl	0.1-0.5 mg/dl
Alanine transaminase (ALT)	62.90 U/L	55.0 U/L	48.0 U/L	0-45 U/L
Aspartate transaminase (AST)	302 U/L	122 U/L	93 U/L	0-35 U/L
Alkaline Phosphatase (ALP)	140 U/L	101 U/L	88 U/L	53-141 U/L
PT(INR)	1.23	1.31	1.28	0.8-1.2
Serum Sodium	128 mEq/l	135 mEq/l	146 mEq/l	136-146 mEq/l
Serum potassium	4.9 mEq/l	4.6mEq/l	3.7 mEq/l	3.5- 5.5 mEq/l
Blood urea	181 mg/dl	151 mg/dl	89 mg/dl	18-45 mg/dl

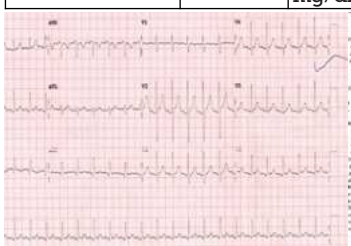


Figure 1
ECG

Figure 2
ABG

In the critical care unit, he was put on a mechanical ventilator, and treated with Injection Artesunate @ 2.4 mg /kg administered intravenously at 0 hours, 12 hours, 24 hours and then administered once daily for next 7 days along with injection Cefepime 1 gm intravenously twice, capsule Doxycycline 100 mg twice orally along with intravenous fluids, regular Blood glucose level and urine output monitoring. This was followed up by tab Primaquine 45 mg stat on the second day since the G6PD was normal. It must kept in mind that Doxycycline also prevents the viral replication in Dengue and thus served a dual purpose here. Also, the second day onwards he had hypotension with decreased urine output that could not be corrected with intravenous fluids and plasma expanders. Vasopressors were started and titrated as per mean arterial pressure (MAP). The Nephrologists opinion was taken for hyponatremia, hyperkalaemia, high creatinine, and decreased urine output. Sustained low efficiency dialysis (SLED) was advised. Over the next 7 days times SLED was done five times along with packed cell transfusions. A total of 5 units were transfused during his stay. The fall in haemoglobin was evident due to haemolysis which is a known complication of plasmodium falciparum and Dengue. Intravenous fluids were given as per regular assessment of inferior vena cava (IVC) diameter. The first 5 days saw no improvement in the sensorium of the patient as well as urine output, though the blood pressure was maintained with vasopressors. After 7 days, with alternate days SLED, urine output started improving, and his sensorium as well. He was now conscious, afebrile and responding to commands. After the 8th day, his vasopressors were gradually tapered. Weaning from ventilator was attempted and a Y piece trial was given, which he could withstand. The next day he was extubated and put on non-invasive ventilation (NIV). He was shifted to the general ward and after observing him for another 2 days he was discharged in a stable condition.

DISCUSSION

Malaria is a very common parasitic disease in countries like India and Jharkhand is an endemic zone for the same. Since clinical manifestations of Malaria may appear similar to other infectious diseases like urinary tract infection, pneumonia, Filaria, Ascending cholangitis etc, anyone coming with high grade fever along with chills and rigors should be tested for clinical malaria. In our hospital all similar patients are tested by the malaria card test which picks up the histidine rich protein. Though the sensitivity and specificity of malaria card test is 29% and 89% respectively, but low sensitivity may be accountable for the low parasitaemia level. (2) Thick smear for malarial parasite is again sent for microscopic examination. Early diagnosis and complete treatment of malaria aims for complete cure, prevention of complications and eventually preventing deaths and minimizing drug resistance.

Similarly, another mosquito borne disease like Dengue has varying clinical manifestation. It can range from Dengue classical fever to Dengue haemorrhagic fever and multiorgan dysfunction syndrome, capillary leak syndrome, haemorrhage etc. Jharkhand being an endemic zone, Dengue card test, Dengue ELISA is again done routinely for all patients coming in with fever. Since both the conditions can potentially be life threatening, early diagnosis and prompt management is a must. Concurrent infection of Dengue with Plasmodium falciparum has been reported from France (3). Simultaneous infection with Plasmodium vivax, Plasmodium falciparum and Dengue has also been reported earlier (4)

Another mosquito borne disease is Chikungunya caused by Chikungunya virus (CHIKV). Symptoms include high grade fever, excruciating joint pains, rash and body ache. Symptoms may mimic the manifestations of Dengue fever. Joint pain is reported in 87- 98% of cases, usually involving more than one joint (5)

Patients of Chikungunya may develop neurological disorders like Myelitis, Guillain Barre Syndrome, Myositis etc. In our hospital this is diagnosed with the ELISA technique and detects the IgM levels. It can also be diagnosed with the RT PCR kits. One of the studies depicts clinical profile of Dengue fever and coinfection with Chikungunya (6)

Many studies have reported coinfection of Dengue and Chikungunya in recent years (7)(8). Both these diseases share a common mode of transmission but different species of mosquitoes, Aedes aegypti as the principal vector and Aedes albopictus as secondary. have been the implicating vectors. Based on the clinical presentation Dengue fever is classified as Dengue fever, Dengue haemorrhagic fever, Dengue shock

syndrome and the Expanded dengue syndrome (9). Chikungunya is usually not very fatal, so usually in most hospitals this is not tested. Thus, it is advisable for all clinicians to order tests for both Dengue and Chikungunya for patients with high fever coming from endemic areas.

Joint pain may be a common clinical feature in both conditions, but in Dengue the joint pains may subside with improvement in the clinical state but in Chikungunya it may prolong up to a few months, with post chikungunya residual arthritis (6)

Leukopenia was observed in 52% and leukopenia in 33% of dengue cases. (6) Thrombocytopenia was evident in dengue and the coinfection group (6). No specific antiviral agent is indicated for Chikungunya and Dengue, Paracetamol is advised for fever and body ache while steroids and non-steroidal anti-inflammatory drugs are avoided. Platelet transfusion should be done judiciously, and single donor apheresis transfusion should be preferred over random donor platelets to decrease transfusion related risks. (6) Hepatic dysfunction with deranged liver enzymes is another finding in Dengue with coinfection- this ultimately settles as the patient recovers.

National centre for vector borne disease control under the ministry of family welfare, Government of India has laid down guidelines for the management of Malaria including plasmodium falciparum (10). Plasmodium falciparum may lead to complications in 0.5 to 2 % and the mortality may be as high as 30% if treatment is not started timely (10).

Some diseases which may mimic severe malaria are Septicaemia, Encephalitis, Meningitis, Leptospirosis and Viral infections. Therefore, it becomes necessary to diagnose by immunological tests or microscopy. The transmission pattern varies but intense transmission is seen in Jharkhand, Chhattisgarh, Orissa and Madya Pradesh (10).

Hyperpyrexia is to be treated with tepid sponging and Paracetamol. Dehydration is to be managed with intravenous saline; urine output is to be monitored - maintain negative fluid balance and avoid pulmonary congestion. Serum creatinine and urine output monitoring is necessary and rising creatinine and decreased output will require serial haemodialysis as was done in our case. Similarly, serum potassium should be monitored, and one should look for hyperkalaemia or hypokalaemia. which should be immediately treated. In case of pulmonary oedema or ARDS ventilation may be required. Platelet transfusion is required for low platelet count < 20000 cubic mm or with bleeding tendencies. Packed cell transfusion is required for a Haemoglobin less than 9 gm/dl. (12)

Review of literature shows 7 cases of triple infection with Malaria, Dengue and Chikungunya from India (11), 6 of them were actually plasmodium Vivax, and NOT Falciparum

Thus, there is a great need to increase the awareness about the mixed infections amongst physicians for a correct diagnosis and management. Strong clinical judgement on the part of the physician is imperative to select the right series of tests and understand the diagnostic implication of each disease. Delay or failure to recognize the concurrent infections can delay the initiation of proper therapy resulting in an increased morbidity and mortality.

Conflict of interest: nil

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