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A Diagnostic Red Herring: Dengue And Scrub Typhus Co-Infection

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Abstract:
Background*: Dengue is a commonplace pediatric infection in the tropics especially during the monsoon season. Though it has a characteristic presentation of febrile illness with maculopapular rash, one must also remember other diseases with a similar presentation which may require a completely different route of management. Dengue and scrub typhus are close differentials of each other, with the matter frequently complicated by cross-reactivity on diagnostic tests and co-infection.*
Case Summary*: We present a case of a 4-year-old female child who presented to us with high grade fever since 5 days, a maculopapular rash all over the body, and pedal edema. There was no organomegaly or cardiac murmur. Initial investigations showed low platelets with positive Dengue NS1 and IgM on rapid kits and ELISA both. She was treated with intravenous fluids and antipyretics, and vitals were monitored strictly as per protocol. Though the child's activity and oral intake improved and platelet count increased, she continued to have high grade fever spikes even on the tenth day of illness. The diagnosis was revised when a thorough examination revealed an eschar on the scalp. Scrub Typhus IgM was sent which was positive and the child was started on Doxycycline to which she responded well.*
Conclusion: *This case highlights the importance of early recognition of close mimics of febrile illnesses, especially those with rash. Prompt investigations and treatment are instrumental in preventing complications. In this case positive serology for dengue fever (whether due to cross reactivity or co-infection) ended up being a red herring which delayed the diagnosis and treatment of this child.*
Key Word: *Dengue; Scrub Typhus; Cross- reactivity; Eschar; Thrombocytopenia*

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I. Introduction

Dengue Fever is an important cause of fever with rash in the pediatric population with significant morbidity and mortality in the tropical countries. It is caused by an arthropod borne virus transmitted by the mosquito *Aedes aegypti.* The clinical picture of dengue fever is characterized by fever, myalgia, retroorbital pain, and a maculopapular rash which appears typically on the fifth or sixth day of infection. Severe forms may often have peripheral edema, serositis, and hepatosplenomegaly. Scrub typhus is a life-threatening mite-borne infection caused by the organism *Orientia tsutsugamushi.* The clinical picture is very similar to dengue fever often leading to diagnostic and therapeutic delays. This is further complicated by the serology for both these infections which have been known to show some cross-reactivity. Moreover, other tests like complete hemogram also show similar features of thrombocytopenia with hemoconcentration. A useful clinical clue is the characteristic eschar of scrub typhus which usually develops at the site of the mite bite. In case of prolonged illness or clinical non-improvement, a diagnosis of dengue fever should definitely be revised in view of significant overlap with its mite-borne counterpart, scrub typhus. We hereby present a case of a 4-year-old girl illustrating this very diagnostic dilemma.

II. Case Summary

A 4-year-old female child presented to us with complaints of high-grade fever and loose stools for 5 days associated with a generalized maculopapular rash and bilateral pedal oedema. On enquiry the mother also felt the abdomen was slightly distended. There was no history of vomiting, bleeding form any site, reduced urine output, or altered sensorium. There was no recent history of travel either.

On examination, the child was febrile (39◦C) and irritable but consolable. She had well felt peripheral pulses with warm extremities and a blood pressure of 90/60 mmHg. Her pulse rate was 120 beats per minute and respiratory rate was 32 cycles per minute. The Oxygen saturation was 97% on room air. There were no hepatosplenomegaly or signs of dehydration.

Initial investigations revealed thrombocytopenia with normal hemoglobin and hematocrit. The total leucocyte count was raised at 15600/mm^3 . The liver enzymes were within normal limits, but the albumin was low at 2.5g/dL. Peripheral smear did not show presence of malarial parasite however the rapid kit test was positive for Dengue NS1 as well as IgM. The ELISA report which followed showed the same. Blood and urine cultures were sterile. Ultrasound examination of the abdomen showed presence of minimal free fluid in the peritoneal as well as bilateral pleural cavities.

The child was started on intravenous fluids and antipyretics. Her vital parameters and urine output were monitored strictly as per Dengue protocols. Over the next few days, the child's rash resolved significantly, and her activity and appetite improved. However, the fever remained persistent, and the platelet count had improved very marginally. The possibility of secondary bacterial infection was considered; however, investigations did not support this. Nevertheless, the child was started on Ceftriaxone. A fresh clinical examination revealed an unexpected finding. The child had an eschar on the scalp which appeared to have healing margins. Scrub Typhus IgM was sent in view of this pathognomonic finding and turned out to be positive with a tire of 15 units (more than 11 units being positive). The child was started on oral Doxycycline and responded beautifully with defervescence setting in by 48 hours. The platelet counts also showed improvement. She showed an uneventful recovery thereafter and was discharged after 4 days. On follow up she was doing reasonably well, and the eschar appeared to be almost healed.

Fig 1- Eschar of Scrub Typhus visible on the child's scalp after shaving surrounding hair.

III. Discussion

Scrub Typhus is a common tropical infection presenting like many others, with fever, maculopapular rash, myalgia, headache, and often gastrointestinal symptoms like abdominal pain and vomiting. A pathognomonic sign is the presence of an eschar usually present in the folds of the skin, typically having a blackish center of necrosis surrounded by a red rim of inflammation. It is usually accompanied by regional lymphadenopathy and mild hepatosplenomegaly. Aseptic meningitis, pneumonia, and encephalitis are some known complications. The laboratory features show thrombocytopenia with or without anaemia, leucocytosis, elevated liver enzymes, and positive serology.

Dengue fever usually presents with a similar spectrum of clinical features like fever with headache, retroorbital pain, joint pain, and a blanching maculopapular rash typically appearing on the sixth day of fever. Serositis may be seen in the critical or 'leaky' phase in the form of ascites and pleural effusions. Complications include the dreaded dengue haemorrhagic fever and dengue shock syndrome, both of which are life threatening. The laboratory picture usually shows hemoconcentration, thrombocytopenia, and positive serology for NS1 or IgM in the first few and next few days respectively. This may be demonstrated by a rapid test kit or Enzyme Immunosorbent Assay. Viraemia may also be confirmed with molecular diagnostic techniques like PCR[1].

The management of uncomplicated dengue fever is predominantly conservative. Strict input output monitoring with serial charting of hemograms can help in anticipation of complications. Hemorrhagic manifestations are managed with platelet and plasma transfusions. Shock often requires inotropic support. In absence of a specific antiviral agent, a successful outcome rests on these measures. Scrub typhus on the other hand responds very well to doxycycline. Even with concerns about the safety of tetracyclines in the pediatric population, Doxycycline remains the drug of choice after weighing risks and benefits. Azithromycin may be an alternative option which is also reasonable effective.[2]

There have been several studies comparing scrub typhus with dengue highlighting how they behave as close clinical mimics of each other. The clinical diagnosis may be further complicated by cross reactivity between the serological tests for Dengue IgM and Scrub typhus IgM. Chandra et al reported a case very similar to ours, wherein initial treatment for dengue fever did not lead to much clinical improvement in their 65-year-old patient[3]. The diagnosis was revised to Scrub typhus after an eschar was spotted. It was only when the patient was started on Doxycycline, that defervescence took place. A few more isolated cases of scrub typhus[6] and dengue co-infection have been reported with two case series, one comprising of 6 cases from South India reported by Basheer et al[4], and the other by Raina et al[6] comprising of 10 cases from Himachal Pradesh, Noth India.

Reported cases of dengue and scrub typhus co-infection are rare. A predominance of cytopenias, serositis, bleeding manifestations, and the typical rash of 'lakes of white in a sea of red' may tip the scales towards dengue fever. Whereas, presence of lymphadenopathy, hepatosplenomegaly, maculopapular rash, and the pathognomonic eschar will favor scrub typhus as the diagnosis.

Therefore, a high index of clinical suspicion for scrub typhus in cases of fever with rash is often rewarded with early diagnosis and successful treatment outcomes. In a limited resource setting, a syndromic approach is often considered to keep up with the high case load of febrile illnesses especially in the monsoon months.

IV. Conclusion

Dengue and Scrub typhus co-infection though rare, must be kept in mind due to their similarities in clinical and laboratory presentations. A revision of diagnosis is definitely warranted in cases who do not show significant improvement after starting treatment.

Co-infection with these two infections may definitely result in prolonged hospital stay, multiple organ involvement, and even life-threatening complications in case of diagnostic and therapeutic delay. A clinician may have to rely on his diagnostic skills and knowledge about the endemicity of his area of practice to catch cues early.

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