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HEPATITIS WITH HYPERFERRITINEMIA IN DENGUE FEVER: THE DIFFERENTIAL MARKER OF DENGUE SEVERITY

Clinical Research

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ABSTRACT

Dengue virus infection is an important cause of febrile illness in tropical and subtropical areas. Herein, we present a rare clinical scenario of dengue fever with encephalopathy complicated by Hyperferritinaemia and hepatitis. During course of illness, ferritin and hepatic enzyme levels rose to 90 and 287 folds, respectively. The patient was managed conservatively with adequate supportive care. This case-report highlights utility of serum ferritin and hepatic enzymes for prediction of dengue hepatitis severity.

KEYWORDS

Dengue severity; Hyperferritinaemia; Hepatitis

INTRODUCTION

It is estimated that annually more than 50 million cases of severe dengue are reported which was attributed to 5% fatality rate in Asian countries.(Krishnamoorthy, Bhatt, Mathew, & Ittyachen, 2017) Serum ferritin is disproportionally raised in dengue fever as compare to other viral and bacterial infection and this elevation corroborates with increased risk of developing complication.(van de Weg et al., 2014)

CASE REPORT

A 35-year-old man, presented with five days history of high-grade fever with rigor, generalized myalgia, diffused abdominal pain and non-projectile vomiting. Dengue fever was confirmed with positive NS_1 and IgM serology. His laboratory examinations revealed normal haemogram but elevated total bilirubin (1.88 mg/dl), prothrombin time (19 sec) and international normalized ratio (1.55), lactate dehydrogenase (LDH), serum ferritin and liver enzymes (Figure-1). He was treated with N-acetylcystine and ceftrioxone.

He was found restless, hypoxic, disoriented on 3rd day of hospitalization. His haematological investigation revealed leucocytosis (10300 cells/mm^3) with thrombocytopenia (62000/mm^3), abnormal prothrombin time (24.6 seconds) and ammonia level (97.7 µg/dl). Figure-1 demonstrated elevated liver enzymes, LDH, and ferritin level in figure-2. The patient was diagnosed with dengue encephalopathy complicated by hyperferritinemia and hepatitis. He was treated with oral lactulose, rifaxamin and L–ornithine L– aspartate for dengue encephalopathy along with supportive care. His condition started improving from day-5 of hospitalization. The patient discharged after 11 days of hospital stay. After four weeks, on follow up, his laboratory investigation revealed restored liver function, platelet count and ferritin level.

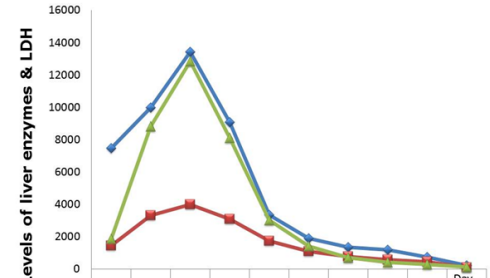
DISCUSSION

Dengue is one of the most common mosquito-borne viral infections. Severe dengue is comprised of three stages. The first febrile stage that lasts for 2 – 7 days followed by toxic stage lasts for 24 – 48 hours, it is most critical period and the third convulsant stage in which rapid recovery occur without precipitation of any sequel. (Chaiyaratana, Chuansumrit, Atamasirikul, & Tangnararatchakit, 2008) Similar to that in our case, we observed higher level of serum ferritin and liver enzymes during all those three stages then they dropped to normal during follow up. The important conclusion of our case report is morbidity related to sever liver impairment and hyperferritinaemia. Transaminases began to rise in first three days and reach at peak (almost 90-fold elevation) during the second week of illness. Krishnamoorthy et al. reported that transaminases elevated ten folds or higher was associated with higher risk of mortality. (Krishnamoorthy et al., 2017)

Ferritin releases from reticuloendothelial system as an acute phase reactant in response to infection or inflammation. Increased serum ferritin in dengue fever was associated with severe disease and a proinflammatory cytokine profile. (van de Weg et al., 2014) Interestingly, level of ferritin is also found to be associated with viral load.(Nadeem, Shafiq, Manzoor, & Ahmed, 2016; van de Weg et al., 2014) Moreover, hyperferritinaemia in dengue infection is associated with thrombocytopenia, increased liver enzymes and activation of coagulation and fibribolytic system.

(Nadeem et al., 2016) Hyperferritinaemia in dengue infected patient indicates highly active disease resulting in immune activation. (Nadeem et al., 2016; van de Weg et al., 2014) Therefore, dengue infected patients with hyperferritinaemia are recommended to clinically monitor carefully. Soundravally R et al. reported that raised ferritin level could predict the dengue severity with sensitivity of 76.9% and specificity 83.3% on the day of admission. (Soundravally, Agieshkumar, Daisy, Sherin, & Cleetus, 2015) Another study by Van de weg, C A et al. reported more than 1500 ng/ml serum ferritin in confirmed dengue fever is associated with dengue severity.(van de Weg et al., 2014) Moreover ferritin level measured at day 4 or 5 may be a good predictor although the above studies find utility of hyperferritenemia for prediction of severity of illness in dengue fever; we observe its utility in patient with dengue hepatitis also. We observed 90 and 287 folds elevated level of hepatic enzymes (ALT: 3976 U/L, AST 12848 U/L on 3rd day) and ferritin (125000ng/ml on 4th day) respectively. These observations suggest that serum ferritin and transaminases level may use as an early predictor of dengue hepatitis severity. However, further large studies may require ascertaining this finding.

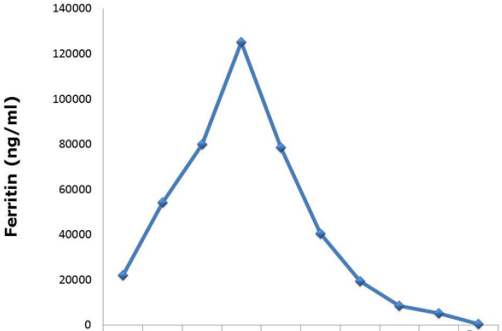
Figure 1: Trandeline of liver function during course of illness



	Day -1	Day-2	Day-3	Day-4	Day-5	Day-6	Day-7	Day-8	Day -9	Day - 11
LDH* (U/L)	7470	9968	13415	9088	3352	1896	1333	1176	722	230
ALT** (U/L)	1450	3295	3976	3083	1735	1096	766	571	450	100
AST*** (U/L)	1860	8825	12848	8093	3020	1400	692	429	289	108

* Lactate dehydrogenase ** Alanine transaminase *** Aspartate transaminase

Figure 2: Trandeline of serum ferritin during course of illness



	Day-1	Day-2	Day-3	Day-4	Day-5	Day-6	Day-7	Day-8	Day-9	Day-11
Ferritin (ng/ml)	22000	54000	80000	125000	78415	40302	19351	8479	5269	520

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