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Research Article

PHYSIOLOGICAL BASIS OF RADIOLOGICALLY PROVEN EXTRAVASATION OF BODY FLUIDS IN DENGUE

Subhash Singla*, AmitGulrez**, Neeru Mittal***, John Pramod**

**Dept of Radiology, **Dept of Physiology, ***Dept of Chest Medicine*

Christian Medical College, Ludhiana, Punjab, India.

ABSTRACT

Dengue epidemics caused by DEN1, DEN2, DEN3 or DEN4 serotypes in the recent past has shown varied clinical presentations, some of which may be confused with other differential diagnosis and thus delay the treatment. The growing evidence of cases with disequilibrium in body fluids and plasma leakage into potential cavities and spaces within the body as pleural effusion, ascitis and haemorhage prompted the present study which was done on 40 seroconfirmed cases of Dengue to assess the ultrasonographic findings in thorax and abdomen. The commonest findings were of reactionary cholecystitis, hepatomegaly, pleural effusion and ascitis. The study discusses the possible mechanisms of altered physiology in fluid shift mechanisms during dengue and recommends the use of ultrasonography as one of the essential diagnostic tools to assess the severity and progress of the disease in patients with dengue virus infection

Keywords: Dengue, Fluid shift mechanisms, ultrasound

INTRODUCTION

The clinical presentations of Dengue fever have been observed to vary with each fresh epidemic in different parts of the world. While the diagnostic tools are well advanced to establish and confirm the presence of this viral infection, the severity of the symptoms and the underlying fear of complications like haemorrhage has prompted many physicians and consultants to often order radiological imaging according to the presentation and progress of the disease especially in drastically dwindling thrombocytic counts and impending or evolving circulatory shock. Quite often the counts bounce back spontaneously or with platelets transfusion, but what remains baffling for most of the physicians and consultants is the persisting evidence of extravasations of body fluids into extravascular compartment commonly visible as dependent oedema, ascitis , pleural or pericardial effusion on Xray, Ultrasound or CT imaging. These findings often mislead the clinicians into exploring further the other differential diagnosis of presence of these fluids in the extracellular compartment or in the body cavities..Such diagnostic detours result in adding to the cost of the care, not to mention the delay in the management of the disease for which the patient presented to the hospital.

North India has seen frequent revisits of dengue which is a mosquito transmitted viral infection involving any of the serotypes DEN 1, DEN2, DEN3 or DEN4. The signs and symptoms may range from a mild flu like symptoms to serious haemorrhage and shock leading to fatal consequences. Dengue Haemorrhagic Fever (DHF) is know to progress into hypovolumicshock , the Dengue Shock Syndrome (DSS).

Most of the cases of DHF and DSS have been observed to have selective leakage of fluids into pleural and abdominal cavities rather than having generalized oedema.

Ultrasound examinations are useful as an additional diagnostic tool to rule out pssoibility of DHF.1 Association of a thickened gallbladder wall is a useful sonographic finding that may help in the prognosis of DF, but the early abdominal sonographic findings of adult patients with DF have rarely been described.. Radiological imaging, though not specific, are obtained much more rapidly than the serological results. Few published studies by Tai et al 2, Bhamraparvati et al 3 suggest association of Dengue with thickened gall bladder, ascitis, splenomegaly and pleural effusion robably resulting from increased vascular permeability causing leakage and serous effusion with high albumin content in the transudate.4

Many studies in the past(5,6,7,8) have included routine sonography and Xray imaging of chest and abdomen in all febrile illness to find out the incidence and pathophysiology of extravasation of fluids in the body cavities. But the association can not be reliably established in the light of the fact that all febrile illness in the epidemic time can not be attributed to Dengue and the fact that in most cases effective follow up sonography was not done.

The present study, which is a progressive study done in established and confirmed diagnosis of DF,

DHF, DSS is based on consecutive imaging using primarily USG and Xray to explore the possibility and pathophysiology of serous extravasations known to occur in association of or as a complication of Dengue.

Aim of the study:

To examine and document ultrasound findings in the examination of abdomen and thorax in seropositive confirmed cases of Dengue.

To assess possible alterations in physiological factors leading to leakage of fluid into extravascular compartment in confirmed cases of Dengue fever.

MATERIAL AND METHODS

Fifty patients admitted with confirmed diagnosis of Dengue fever, Dengue Haemorrhagic Fever or Dengue Shock Syndrome were included in this prospective study done at Department of Radiology and Department of Physiology at Christian Medical College, Ludhiana. All patients had confirmed serological findings of DNV done at the Microbiology laboratory of CMC Ludhiana. All patients were admitted under the primary teams of medical consultants in the IPD unit. None of the patients had previous history of confirmed dengue fever, or any other illness in the recent past. None of the patients were on prolonged treatment for any illness whatsoever prior to admission for the illness under consideration.

Serial ultrasound examinations of thorax and abdomen were done on all patients using PHILLIPS HDX 11 E COLOR DOPPLER. on day 0, 1,3,5 of the admission. Bedside sonography was done in patients who showed worsening of the disease with either DSS or DHF.

Observations:

Serial ultrasound revealed varied findings in these forty patients admitted with confirmed diagnosis of Dengue. All the findings were not seen on the first day of admission. Generally the findings evolved as the disease progressed over the length of the inpatient department stay. None of the patients had mortality in our study. We could not find definite correlation between the thrombocyte count at admission and the presence of sonographic findings. More than one finding was present in a number of patients. The commonest finding was that of hepatomegaly and associated reactionary cholecycstitis. However, there were equally significant numbers of ascitis seen in this study. The findings were seen as follows :

Hepatomegaly	15	37.5%
Hepatospenomegaly	4	10%
Splenomegaly	3	7.5%
Reactionary cholecystitis	15	37.5%
Ascitis	14	35%
Bilateral pleural effusion	8	20%
Unilateral pleural effusion	1	2.5%
Normal	6	15%
Fatty liver	2	5%

Hepatomegaly and reactionary cholecystitis were invariably found in the same patient and was generally associated with development of ascitis or pleaural effusion. No abnormality on ultrasound of abdomen or chest was found in 15% of the patients while the presence of fatty liver in 5% of the patients seems coincidental and not related to dengue.

DISCUSSION

Normal physiological mechanisms of fluid distribution and possible changes in dengue or any other illness altering the forces driving the fluid in and out of the vessels and capillaries is a fairly well understood phenomenon. The transport of fluids across the microvascularentholium is regulated by the net Starling foces (9). Excess of proteins in plasma as compared to its content in interstitial fluid is critical in maintaining this dynamic equilibrium across the semipermeable membrane of the capillaries. The transit of macromolecules would depend on their size, configuration and electrical charge on their surface (10,11). Solute particles less than ~42 Å are not restricted within plasma and can move out of the capillary pores. Albumin carries a strong negative charge, although is smaller than the permissible size , is less readily filtered than neutral proteins like transferring (12,13,14). negatively charged polysaccharides complexes known as Glycosaminoglycans (GAGs) are distributed on cell surfaces and are incorporated into the glycocalyx layer on the luminal surface of the vascular endothelium (15,16). The orderly arrangement of fibres and adherent proteins creates a mess extending throughout the vascular bed limiting the selective filtration through this physical barrier in the capillaries(10,17). Disruption of the GAG components of the glycocalyx layer is thought to to increase the clearance of proteins seen in animal models of capillary leak (18,19) and in the pathogenesis of renal protein-losing disorders, such as steroid responsive-nephrotic syndrome (SRNS), and generalized vascular leak

syndromes(20,21). The alteration and disruption of the function of the endothelial glycocalyx during dengue infection is one of the possible mechanisms for leakage of fluid.

The cells of the immune system are also known to play a role in altering the physiology of fluid equilibrium. It is presumed that the epidermal and dermal spillover of mosquito bite results in infection of immature Langerhans cells or the dendritic cells in the epidermis(22,23). These infected cells then result in recruiting macrophages and monocytes in the lymphnodes . This amplifies the viremia as it results in dissemination of the virus throughout the lymphatic system. DENV has also been seen to show tropism for circulating mononuclear cells and for cells in lymphnodes, spleen and bone marrow in infected animal models (24). Following infection, mononuclear cells predominantly die by apoptosis (25,26), while abortively infected or bystander Dendritic cells are stimulated to produce the bulk of mediators that are involved in inflammatory (27,28,29,30,31) and hemostatic (32,33,34,35,36) responses of the host.

The dreadful signs of plasma leakage and haemorrhage are the two main factors considered in assessing the severity of the Dengue fever. It has been suggested that cytokines and other mediators, which are released during the immune response to dengue virus infection, may form the underlying mechanism (37). Cross reactive antibodies formation in the wake of a secondary infection by a different serotype which was not involved in the primary infection promote viral replication in phagocytic cells of the host (38). A host of interleukins and tumour necrosis factors are also known to be produced in response to inflammatory changes due to dengue virus (39). Earlier studies have reported a relationship between high levels of TNF-a, IL-6 and disease severity (40,41).The cytokine storm sometimes associated with this acute interleukin response may drive the patient faster to DSS and mortality.

Ultrasonographic evidence of plasma leakage was detected in DHF in studies carried out by the Department of Child Health in Indonesia (42) and by Joshi et al (43) in Army Hospital, Delhi Cantt.who reported similar findings of Gall bladder thickening, pleural effusion, ascitis and serous exudates besides organomegaly in some of the cases. Since serotypes of the incriminating virus as known to be different, it is quite possible that the evolution of the findings of its occurrence may not be uniformally seen. Absence of serous leakage in no way should be regarded as immunity to DSS. The clinicians and the diagnostic team should be on alert to such phenomenon and should avoid concurrent investigation of other causes of this leakage not attributable to the confirmed diagnosis of dengue viremia.

CONCLUSION

The finding of polyserosities with or without gall bladder thickening is a useful diagnostic indicator which rapidly gives the possibility of existing or impending pathology in febrile illness due to dengue virus infection. We recommend serial Ultrasonography in all admitted patients with confirmed diagnosis to prevent

catastrophic results of DHF and DSS.

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