Capillary leak syndrome in dengue fever

Sudhir Kumar Verma,[a] ***Manish Gutch,***[a] ***Abhishek Agarwal***[b] ***& A.K. Vaish***[a#]

[a]*Department of Medicine, Chhatrapati Shahuji Maharaj Medical University (CSMMU), Chowk, Lucknow-226003, Uttar Pradesh, India.*

[b]*Department of Pulmonary Medicine, Chhatrapati Shahuji Maharaj Medical University (CSMMU), Chowk, Lucknow-226003, Uttar Pradesh, India.*

Abstract

Capillary leak syndrome (CLS) has been described in dengue fever but its exact features have not been clearly defined. We present here the findings in 25 cases of CLS recently seen by us during an outbreak of dengue fever in northern India. Besides fever, body ache and bleeding manifestations, ascites was present in 84% cases, pleural effusion in 76% cases, and both ascites and pleural effusion in 60% of cases. The pleural effusion was right-sided in 52.6% cases, bilateral in 47.4% cases and only left-sided in none of the cases. The fluid accumulation seen was moderate and frequently involved both abdomen and pleural cavity. The fluid rapidly cleared in a week's time without any specific treatment. These cases can pose considerable diagnostic challenge which is discussed here.

Keywords: Dengue fever; Pleural effusion; Ascites; Capillary leak syndrome.

Introduction

Capillary leak syndrome (CLS) can be due to diverse causes.[1] There are several reports of CLS in dengue fever but its precise manifestations have not been clearly defined.[2,3] Recently, in an outbreak of dengue fever in northern India, we encountered several cases of CLS. The detailed findings of CLS in these cases are being presented here.

Materials and methods

Out of the 127 cases seen in one month at the Chhatrapati Shahuji Maharaj Medical University (Erstwhile King George Medical College), Chowk, Lucknow, Uttar Pradesh, India, 25 cases had features of CLS. All the cases of dengue fever with CLS were positive for NS1 antigen (Dengue NS1 Antigen Microlisa Kit marketed by J. Mitra & Co., India) or IgM antibodies (IVD IgM dengue kit marketed by IVD Research Inc., USA) or both (Table 1).

[#]*E-mail: vaish12@rediffmail.com*

Table 1: Results of testing for dengue fever (NS1 & IgM antibody)

Test	Positive (%) (n=25)
NS1 antigen	4 (16%)
IgM dengue antibody	17 (68%)
Both	4 (16%)

The other investigations performed in these cases were complete haemogram including platelet count, urine routine examination, blood urea nitrogen, blood sugar, total serum protein & serum albumin, ultrasonographic examination of abdomen and X-ray chest (PA) view. In a few (4) cases, we could aspirate the pleural/ascitic fluid for cytochemical examination.

Results

The mean age of the 25 cases of dengue fever with CLS was 30.5 ± 15 years, and the male-female ratio was 1:1.27. The results of testing for dengue fever (NS1 & IgM antibody) are shown in Table 1. The main clinical findings on admission in the cases of CLS are shown in Table 2. Fever was present in all (100% cases), generalized body pain in 84% cases, and bleeding manifestations in 56% cases. Pedal oedema was not present in any of the cases. All the cases had some degree of thrombocytopenia. The platelet count became normal in all cases in 4-5 days. No deaths occurred in these cases. The serum albumin levels were mildly reduced (3.0–3.5 gm/dl) in 80% of cases and significantly reduced (<3.0 gm/dl) in 12% of cases (Table 2). Urine examination was normal in all the cases.

The findings of the ultrasonographic examination in these cases are shown in Table 3. Ascites was present in 21 out of 25 cases (84%), pleural effusion in 19 cases (76%) and both ascites and pleural effusion in 15 cases (60%). The pleural effusion was present on the right side only in 10 cases (52.6%) (Figure), and both right-sided and left-sided in 9 cases (47.4%). None of the cases had only left-sided pleural effusion. Mild hepatomegaly and edematous gall bladder wall was present in 48% and 20% of cases respectively. Pericardial effusion was not seen in any case.

The estimated fluid volume in peritoneal cavity and pleural space assessed by ultrasonography are shown in Table 4. In 20 out of 21 cases with ascites, the fluid volume was less than 1000 ml, and in 18 out of 19 cases with pleural effusion, the volume of fluid was also below 1000 ml. Therefore, in a majority of cases, the fluid accumulation was mild to moderate.

In four cases the pleural fluid was aspirated and the findings are shown in Table 5. The pleural fluid was exudative in all the four cases. There were increased numbers of WBCs with a preponderance of lymphocytes in all cases and the sugar level in fluid was normal.

Ultrasonography was repeated in all cases after one week. The fluid collection had completely cleared in 12 cases (48%) and decreased by more than 50% in the remaining cases.

Table 2: Clinical findings on presentation in the CLS cases

Finding	Number of patients (%) (n=25)
Fever	25 (100%)
Generalized body pain	21 (84%)
Bleeding manifestations	14 (56%)
(a) Petechiae	7 (50%)
(b) Menorrhagia	3 (21.43%)
(c) Malaena	2 (14.29%)
(d) Haematuria	1 (7.14%)
(e) Gum bleeding	1 (7.14%)
Hypotension	2 (8%)
Altered sensorium (Glasgow coma score = 11)	1 (4%)
Platelet count on admission	
(a) 50 000–100 000/mm3	3 (12%)
(b) 20 000–50 000/mm3	15 (60%)
(c) <20,000/mm3	7 (28%)
Serum albumin	
(a) >3.5 gm/dl	2 (8%)
(b) 3.0–3.5 gm/dl	20 (80%)
(c) <3.0 gm/dl	3 (12%)

Table 3: Ultrasonographic findings in cases with CLS

Finding	Number of cases (%) (n=25)
Ascitis	21 (84%)
Pleural effusion	19 (76%)
Both	15 (60%)
Pleural effusion (n=19)	
• Right-sided	10 (52.6%)
• Left-sided	Nil (0%)
• Bilateral	9 (47.4%)

Figure: X-ray chest PA view of a patient with CLS showing right-sided pleural effusion

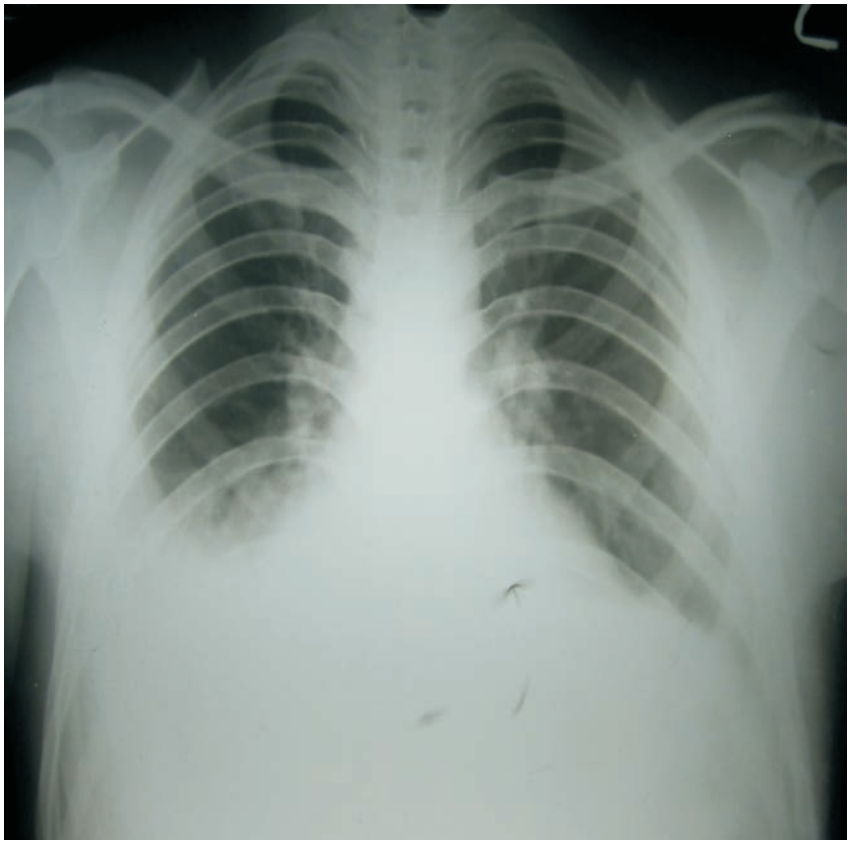

Table 4: Volume of ascitis/pleural effusion in the CLS cases (by ultrasonography)

Volume of fluid	Number of patients (%)
Ascitis (n=21)	
• <500 ml	11 (52.4%)
• 500–1000ml	9 (42.9%)
• >1000 ml	1 (4.7%)
Pleural effusion (n=19)	
• <500 ml	16 (84.2%)
• 500–1000 ml	2 (10.5%)
• >1000 ml	1 (5.3%)

Table 5: Findings of pleural fluid examination in cases with CLS

Pleural fluids findings	Case-1	Case-2	Case-3	Case-4
Colour	Straw coloured	Straw coloured	Straw coloured	Straw coloured
Proteins (gm/dl)	3.3	3.3	3.1	3.4
Total cells/mm3	365	290	320	260
Differential counts				
• Polymorphs	27	10	24	18
• Lymphocytes	69	75	73	76
• Monocytes	4	15	3	6
• Eosinophils	Nil	Nil	Nil	Nil
• Sugar	82	112.6	96	108

Discussion

Our results indicate that CLS is not uncommon in dengue fever, being present in approximately 19.7% of cases. Technological advances such as ultrasonography have probably facilitated the recognition of these cases.[4,5]

The occurrence of fever with ascites/pleural effusion as in our cases can throw up several diagnostic challenges. Similar findings may occur in tuberculosis and collagen disorders. In tuberculosis pleural effusion, sometimes the fever may be moderate to high.[6] In collagen disorders, thrombocytopenia can also occur.

Furthermore, as in tuberculosis pleural effusion, there was lymphocytosis in the fluid in our cases of CLS. Tuberculosis pleural effusion is common in India and hence many of these cases can be misdiagnosed and inappropriately given antitubercular treatment. This distinction is important to be made. Certain points which would favour CLS and help in distinguishing are as follows:

(1) In CLS, collection of fluid frequently involves multiple sites.

(2) The fluid accumulation is mild to moderate and rarely more than 1000 ml.

(3) The pleural effusion is mainly right-sided and never occurs alone on the left side.[7]

The fluid accumulation in our cases rapidly resolved in a week's time without any treatment. In doubtful cases, it would, therefore, be advisable to wait and repeat ultrasound examination after one week before starting any specific therapy. Appreciation of the manifestations of CLS due to dengue fever would help in preventing misdiagnosis and unnecessary treatment.

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