e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2024; 16(1); 434-437

Case Series

Acute Respiratory Distress Syndrome Associated with Dengue Fever in Children - A Case Series

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Received: 04-12-2023 / Revised: 30-12-2023 / Accepted: 15-01-2024
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Conflict of interest: Nil

Abstract:

Pulmonary manifestations of dengue fever such as pleural effusion and respiratory distress due to fluid accumulation are known; however acute respiratory distress syndrome (ARDS) as the inaugural presentation of dengue infection is uncommon[1-3]. ARDS albeit rare, is a potentially fatal complication of dengue infection. Treatment of ARDS associated with dengue is challenging ; it requires a different fluid strategy in contrary to the standard fluid protocols for severe dengue[4]. Literature regarding paediatric ARDS in dengue is scarce[4-6].We present a series of eight paediatric patients of severe dengue who presented with acute onset of dyspnoea and hypoxemia refractory to oxygen therapy , diagnosed to be due to ARDS . Early institution of non -invasive ventilatory support in conjunction with a conservative fluid strategy led to a favourable outcome in all our patients; except one with severe disease who succumbed to the illness.

Keywords: Pulmonary, ARDS, Dengue, Rare Complication.

Introduction

With the rising incidence of dengue virus infections, unusual manifestations involving various organs are increasingly being recognized, without evidence of plasma leakage or shock [7]. Pulmonary manifestations in dengue such as pneumonitis, pulmonary haemorrhage and acute respiratory distress syndrome(ARDS) are less common [1-3]. ARDS is a dreadful complication of dengue fever, the treatment of which remains challenging and may require a different fluid management strategy[6]. Very limited number of studies have been published in the existing literature pertaining to ARDS associated with dengue fever in paediatric patients [4-6].

We describe eight paediatric patients of severe dengue who presented with ARDS at onset, in the absence of features of dengue shock syndrome (DSS) .

Patients and Methods

Medical records of patients aged <=18 years diagnosed with dengue who presented with ARDS to the paediatric emergency of a tertiary care teaching hospital in Northern India between July and December 2023 were analysed. Detection of non-structural protein (NS1 antigen) and IgM antibodies against dengue virus by enzyme linked immunosorbent assay (ELISA) were used to confirm the diagnosis. ARDS was diagnosed on the basis of Berlin's definition[8]: acute onset of respiratory distress within one week of a known clinical insult, bilateral lung opacities on chest radiograph that are not due to effusions, lobar/ lung collapse or nodules; respiratory failure not fully explained by cardiac failure or fluid overload and presence of severe hypoxemia, characterized by a PaO_2/FiO_2 ratio <= 300 with PEEP or CPAP>=5 cm H_2O. Bedside echocardiography was done in all patients to exclude cardiac origin of oedema. Patients of ARDS secondary to sepsis, pneumonia, malaria, scrub typhus or other aetiologies were excluded. Clinical, laboratory and radiological details were noted with evaluation of associated complications, oxygen requirement, treatment administered including duration of ventilatory support and outcomes attained. The study was approved by the Institutional Ethics Committee.

Results

A total of eight patients of severe dengue presented with ARDS; their demographics, clinical features, laboratory findings, treatment details and outcomes are summarised in Table 1.

All patients presented with acute onset of tachypnea and severe hypoxemia refractory to usual oxygen therapy; additional symptoms reported were pain in

abdomen, vomiting and petechial rash. None of the patients were found to have hypotension on admission. The most common laboratory abnormalities observed were thrombocytopenia and elevated aminotransferases (AST >ALT). Skiagram of the chest showed bilateral pulmonary opacities consistent with acute lung injury /ARDS; bedside echocardiogram was unremarkable in all patients. Initial mode of oxygen delivery was non-rebreathing mask (NRBM); however most of the patients required admission to the paediatric intensive care unit (PICU) on account of worsening oxygenation and need for mechanical ventilation.

Two patients developed marked respiratory distress with increased work of breathing rapidly progressing to hypoxemic respiratory failure requiring intubation and mechanical ventilation. Respiratory support using non-invasive ventilation helped to avoid intubation in remaining patients. Crystalloids were administered as the initial maintenance fluid. In contrast to the usual volumes of fluid, a restrictive fluid strategy was adopted. All patients showed gradual improvement in oxygenation with reducing oxygen requirement (improving PaO_2/FiO_2 ratios) and were weaned from ventilator support except one who had a fatal outcome. The median duration of mechanical ventilation was 6 (interquartile range 2-8) days. Ventilator associated pneumonia developed in one patient; one patient developed sepsis requiring escalation of antibiotic regimen (carbapenem and vancomycin) while two patients developed gross hematuria over the disease course necessitating platelet transfusion. None of the patients developed other organ dysfunction or shock. The median hospital stay was 8 (interquartile range 8-10) days.

Table 1: Clinical characteristics , PICU course, duration of mechanical ventilation and outcomes

Parameter	Case1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8
Age(years)	8	11	17	15	2	6	10	5
Gender	F	F	F	F	F	M	M	M
Illness duration prior to admission (days)	5	2	4	5	5	4	5	6
Initial symptoms	Fever, pain abdomen, vomiting, respiratory distress	Fever, difficulty in breathing	Fever, vomiting, Difficulty in breathing	Fever, abdominal distension, difficulty in breathing	Fever, Respiratory distress	Fever, difficulty in breathing	Fever, vomiting and respiratory distress	Fever, pain in abdomen, vomiting
Blood pressure at admission(mmHg)	86/60	116/72	114/80	110/70	80/60	90/60	108/64	92/64
RR (per minute)	46	56	30	30	56	36	54	40
Chest radiograph	B/l ground glass opacities in lower fields	b/l ground glass haziness in lower fields	White out lung	White out lung	b/l infiltrates	b/l infiltrates	b/l opacities	b/l ground glass opacities
Dengue serology	IgM +	-----	IgM positive	IgM positive	IgM positive	IgM positive	IgG positive	----
NS1 Antigen	-----	Reactive	---	Reactive	----	-------	Reactive	Reactive
TLC ($\times 10^3$/L)	12200	14600	6400	8000	14990	6900	7200	7700
Platelets($\times 10^3$/L)	0.4	0.9	0.15	0.75	0.25	1.76	0.15	0.24
ALT (IU/L)	302	72	244	62	102	115	157	103
AST (IU/L)	462	199	340	195	265	161	392	110
Albumin(g/dL)	2.9	2.8	3.0	2.6	2.8	3.0	3.2	3.2
PaO_2/FiO_2 ratio	96(severe ARDS)	182(moderate ARDS)	143(moderate ARDS)	162(moderate ARDS)	252(acute lung injury)	280(mild ARDS)	92(severe ARDS)	234(mild ARDS)
Duration(days) Oxygen support NRBM	15 hrs	2	2	3	5	6	1	8
NIV /BiPAP	---	8	6	8	3	2	3	-------
Days ventilated (SIMV)	8	-----	-----	----	-----	------	2	-------
Organ dysfunction	None	None	None	None	None	-----	------	None
Complications	VAP, hematuria	Sepsis	hematuria, epistaxis	None	None	---	Pulmonary haemorrhage	--
Blood Component transfusion	Yes, platelets	None	Platelets	None	None	None	Platelets	None
Inotrope use	None	None	None	None	None	None	Epinephrine	None
Outcome	Improved	Discharged	Discharged	Discharged	Discharged	Discharged	Expired	discharged

RR: respiratory rate; TLC: total leukocyte count; ALT: alanine aminotransferase; AST: aspartate aminotransferase; NRBM: non-rebreathing mask; NIV: non-invasive ventilation; BiPAP: bilevel positive airway pressure; SIMV: synchronized intermittent mandatory ventilation; VAP: ventilator associated pneumonia.

Discussion

A myriad of atypical manifestations of dengue infection involving various organs such as liver, brain, heart, pancreas and kidney have increasingly being recognized in recent years which do not have the usual features of either DSS or DHF and designated as "expanded dengue syndrome" by WHO [7]. Pulmonary complications in dengue are less common and can present as pleural effusion (occurring as a part of polyserositis), pneumonitis , pulmonary haemorrhage and dyspnoea due to fluid accumulation[1-3] in the resorptive phase of illness. ARDS (non-cardiogenic pulmonary oedema) as the initial presentation of dengue infection is rare [3]; the incidence has been reported to be 1.7-2.4% [4].

The exact pathogenesis of ARDS in dengue remains unknown. Postulated mechanisms include increased permeability of the alveolar-capillary membrane caused by the virus due to endothelial injury resulting in oedema of the alveoli and interstitial spaces [2] and consequent hypoxemia. Dengue virus antigen is found in alveolar cells of the lung. Viral replication primarily takes place in the lung epithelium.

Early recognition of ARDS is of crucial importance since it has therapeutic implications as it requires a different fluid strategy [6] than the usual volumes of fluids recommended in severe dengue.

Treatment of ARDS in dengue fever is similar to ARDS of any other aetiology [2]. Maintaining adequate oxygenation through mechanical ventilation and judicious fluid administration is the mainstay of management [5,9]. Most of the patients in our series were managed with early use of non-invasive ventilatory support resulting in improved oxygenation and outcome, thereby averting the need of intubation and invasive mechanical ventilation. Recent studies also suggest the role of non-invasive respiratory support in early ARDS with good outcomes [10].

Studies have demonstrated lower extra-vascular lung water, reduced need of mechanical ventilation and improved survival with fluid restriction in ARDS associated with dengue in comparison to the usual fluid recommendations [4]. Fluid therapy in ARDS should be targeted to achieve adequate tissue perfusion while avoiding excess fluid infusion to prevent inadvertent increase in lung oedema which may further impair gas exchange [5]. None of the patients in our series had hypotension or evidence of poor perfusion; hence a restrictive fluid strategy was adopted resulting in early recovery using non-invasive ventilation in majority of the patients.

Maintaining a negative fluid balance has been shown to improve respiratory parameters and outcomes in patients with ARDS [6]. Few studies have also suggested fluid removal using diuretic infusion can result in improved survival in patients of dengue fever with ARDS [4].

Although ARDS is associated with a high mortality [11], early recognition and use of NIV along with judicious fluid management led to a favourable outcome in majority of our patients.

Conclusion

To summarize, ARDS although rare, is a life-threatening complication of dengue infection. Dengue fever should be considered as a potential cause of ARDS in dengue endemic areas. Early recognition of ARDS is paramount; careful assessment of volume status and strict monitoring of vital parameters is critical to guide fluid strategy. Appropriate fluid management and early use of non-invasive ventilatory support is the key to decrease mortality and improve patient outcomes.

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