

Severe Complicated Adenovirus Infection in Previously Healthy Infant

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1. Introduction

Adenovirus are highly contagious viruses that is responsible for febrile illness in children. These viruses group is mostly associated with respiratory tract infections, but also have a role in gastrointestinal, genitourinary, ophthalmologic and to lesser extent neurological manifestations [1]. The spectrum of illness severity of adenovirus ranges from subclinical and self-limited to severe and lethal disease [2, 3]. Adenoviruses has 51 serotypes, out of which, 15 serotypes play a role in human disease. Adenovirus serotypes have a variable clinical and epidemiology presentations, for instances, serotypes 3 and 7 are usually associated with respiratory illness, while serotypes 40 and 41 frequently cause acute gastroenteritis [4-7].

2. Case Presentations

Six months old child, previously healthy, presented to us with history of 3 days fever and cough. He was born by LSCS at term, with uneventful perinatal history, fully vaccinated. His development was appropriate to age. Unremarkable family history. Upon admission his growth parameters showed weight (10th-50th centile), Height; (50th centile) and Head Circumference; (3rd-10th centile). He was feverish with temperature 38°C, tachycardia; pulse was 158 b/m, respiratory rate 36/m, blood pressure 94/44 mmhg and O₂ saturation was 92% on 4L/m oxygen. The child was not active but well perfused, mildly distressed, with intercostal and subcostal recession. His systemic examination was unremarkable apart from chest examination showed crackles and wheezes. Initial investigations

showed mild anemia with hemoglobin 9.9 g/dl (NORMAL VALUE (N); 11.1-14.1 g/dL), WBC: 8×10^3 u/l (N; 6.0-18.0 10^3 /ul), platelet; 276×10^3 ul ($200-550 \times 10^3$ /uL). CRP: 43 mg/l (NORMAL VALUE ≤ 10 mg/L], absolute neutrophils was normal.

Respiratory virology panel PCR showed positive Adenovirus and Bocavirus. Chest x-ray showed opacification of right upper lobe, right lower lobe and left lower lobe–retro-cardiac. Initially, the child was managed with salbutamol and ipratropium nebulization in addition to IV antibiotics amoxicillin clavulanic acid. He was in need for oxygen supplementation to maintain saturation.

On Day 3 of admission the child developed generalized edema with hepatomegaly (liver was 5-6 cm below costal margin). He was tachypneic and tachycardic. On day 4 sputum culture showed MRSA positive antibiotic changed accordingly to vancomycin in addition to ceftriaxone. On day 5, child was sick looking, remained febrile, with shallow breathing, grunting, reduced air entry mainly on the right side and recessions muffled heart sound and hepatomegaly. Abnormal movements in right arm noted. Liver function showed elevated ALT (842 U/L (N; 0-56 U/L) and hypoalbuminemia 2.2 gm/dl (N; 3.8-5.4 g/dL). Disturbed coagulation where PT 17.7 secs (N: 11-14 Secs), PTT: 72 secs (N; 28.0-41.0 Secs). Procalcitonin 60 ng/mL, platelets reduced to 126×10^3 ul. Repeated chest x-ray showed worsen on right side with mild pleural effusion. Abdominal ultrasound showed ascites with hepatomegaly and mild pleural effusion. Child was shifted to PICU, hepatitis markers (Hepatitis A, B and C) were negative, and brain ultrasound was unremarkable. Hemoglobin dropped to 7.2 mg/dl. Child was on 2 liter oxygen by nasal prong received fresh frozen plasma, packed RBCS, albumin and continue on antibiotics. Child developed respiratory acidosis and was ventilated, in view of worsen chest x-ray, child had acute respiratory distress syndrome. He was unresponsive to the above management, so first dose of immunoglobulin was given as well as corticosteroids. Repeated investigations showed coagulopathy PT: 15.1, APTT: 80.5, D-Dimer test; 1.9 (N: 0.9 gm/l), Lipid profile cholesterol: 98 HDL:10, LDL :32, Triglycerides– 232, LDH: 5309 IU/L, ferritin: >40 000 ng/ml, fibrinogen; initial: 115 however repeated one: became normal >200. Blood culture was negative. On day 7, the child was edematous with ascites. He developed hypertension with low urine output. There was obvious acute renal injury. He was managed by furosemide and fluid restriction, in addition to Hydralazine and Amlodipine as per the nephrology.

T. spot tuberculosis test was not reactive, no acid fast bacilli in the sputum was detected. HIV was negative, Immune status showed; IgA: 0.69 g/l (N; 0.08-0.67 g/L), IgG 19.24 g/l (N:2.06-6.76 g/L), IgM: 0.97 g/l (N; 0.33-0.97 g/L). AI-total IgE 17.2 KU/L (N: 0-64 KU/l. Pneumococcal abs. (vacc. 96.1+ mg/l (N: up to 3.3 Antigen/IgG). IgG subclasses IgG 1 11.10+ g/l (N; 1.40-6.20), IgG 2 4.60+ g/l (N: 0.41-1.30), IgG 3 0.78 g/l (N; 0.11-0.85, IgG 4 0.365+ g/l (N: up to 0.008). There was moderately reduced of CD4 cell count. CD8 cell count, NK cell count were severely suppressed. CD 19 cell count was normal, there was pan T cell suppression.

NK Cells CD16 And CD56: 1.2, NK Cells CD16 and CD56 Abs CELL/uL: 17, CD19 Total Absolute 706 cell/ul (N; 99-426 CELL/uL), CD20 PRE B Cell Absolute 609 CELL/uL, CD4 T-Helper Absolute 388 cell/ul (N:583-1505

CELL/uL), CD8 T Suppressor Cytotoxic Absolute: 97 cell/ul (N; 325-995 CELL/uL), CD3 Total T Cell Absolute: 484 (N; 812-2318 CELL/uL), CD4:CD8 Ratio: 4.0 (N; 1.20-2.40%), (CD19) Total B CELLS: 51 (N; 5.00-20.0%), CD20 PRE B Cell Percentage: 44 (N; 4.00-19.0%), (CD3) Total T Cell 35%, (N; 59.0-85.0%) CD4: 28% (N; 31.0-55.0%), (CD8) T Cell Suppressor Cytotoxic 7% (N; 17.0-38.0%). Common variable immunodeficiency was considered but the repeated investigations showed T cell repertoire was within normal, B cells count (CD 19 and CD 20 was normal. (CD19+226 cell /ul, CD 20 pre B cell absolute 223 cell/ul). T cells was recovered.

On day 9 the child was put on high frequency ventilator, corticosteroid was discontinued in view of persistent hypertension. Second dose of IVIG was given on day 11. On day 17, sputum culture showed negative MRSA, and stenotrophomonas maltophilia was present. Boca virus negative, but adenovirus PCR was still positive. Chest X-ray was worsen. At this point: Meropenam and Linezolid added in addition to fluconazole. On day 27, there were moderate improvement in chest x-ray but the child was drowsy, brain ultrasound was unremarkable. Although the patient stay in the hospital, parents refused to do CT chest. On day 30, the child had muffled heart sound, with increased ascites and edema. ECHO showed pulmonary hypertension with moderate ventricular dysfunction. Milirine and sildenafil were added. Repeated ECHO showed volume overload dopamine was added in addition to peritoneal dialysis which was kept for 13 days.

Adenovirus was the only persistent organism to be positive, with the clinical manifestation of ARDS and multisystem involvement. Child started to gradually improved was extubated on day 49, he was started on oral feeds, which was increased gradually, he was shifted to general ward on day 57. On day 69, the child discharged home in a stable; he continued to have mild tachypnea with bilateral diffuse wheezes and crackles. So he was kept on nebulization, with tapered prednisolone. One month after discharge, the child had mild tachypnea, with bilateral rhonchi. Chest x-ray was improving with only residual bilateral consolidation. Still parents refused to go for CT chest.

3. Discussion

In view of the above-mentioned condition, severe unresolved complicated adenovirus infection was the first possible diagnosis. Our patient has the clinical criteria which highly suggestive of Hemophagocytic lymphohistocytosis (HLH), most probably secondary to severe adenovirus infection. These include the fever, low hemoglobin and platelets, initial fibrinogen was low, triglycerides were mildly elevated (232 mg/dl), high ferritin level, initial low NK activity which was improved. Though it is difficult to know whether a patient has primary or secondary HLH on the basis of symptoms, which may be very similar. Therefore, genetic testing is usually recommended in order to make the proper diagnosis, regardless of age, which was not done. But secondary HLH was considered, or viral associated hemophagocytic syndrome. Oncology team was involved who suggested steroid course.

Tuberculosis was ruled out the child was previously healthy, no history of contact with tuberculous patient, no weight loss, Loss of appetite or night sweats. As well as, sputum acid-fast bacilli and T. Spot test: negative. Primary

immune deficiency could be a possibility but it was ruled out as B and T lymphocytes revealed CD4 cell count moderately reduced. CD8 cell count and NK cells severely suppressed. Pan T cell suppression: suggesting common variable immune deficiency REPEATED: showed improvement in T, B, NK cells.

4. Conclusion

Adenovirus is a common viral pathogen affecting the respiratory tract in pediatric age group, which is usually self-limiting. Severe adenovirus complications unusual in immunocompetent children yet they have been rarely reported. Herein we are reporting an unusual sequelae of the adenovirus infection to draw the attention of the pediatrician to such complications for early interference and management.

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