ORIGINAL RESEARCH PAPER
Volume - 13 | Issue - 05 | May - 2024 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

PEDIATRIC CASES OF PERTUSIS WITH LEUKEMOID REACTION TREATED WITH THERAPEUTIC LEUKOCYTAPHERESIS

Transfusion Medicine

Saneha Anjum Shaikh* Assistant Professor, Dept of IHBT at Parul Institute Of Medical Science And Research, Parul University Vadodara Gujarat, India *Corresponding Author

Dr Farzana Kothari Professor and Head in Dept of IHBT at Baroda Medical College, M S University Vadodara Gujarat, India

ABSTRACT

Background and Objectives: Epidemic kind of scenario for Pertussis with leukemoid reaction at a rural area of Gujarat, India. A new indication for therapeutic leukocytapheresis,as limited literature on this topic is available.
Pertussis (Whooping cough) is a respiratory tract infection characterized by paroxysmal cough.]It spreads through airborne droplets and is highly contagious. Risk factors for acquiring pertussis include pregnancy, epidemic exposure, lack of immunization, close contact with an infected individual. **Materials and Methods:** Study was done retrospectively. Follow up of pediatric patients diagnosed with Pertussis on swab with leukemoid reaction was done. Leukocytapheresis was done on Spectra Optia machine with the exchange kit. Clinical and hemodynamic laboratory parameters were evaluated. **Results:** Out of 3 pediatric patient, one survived follow up was done till 6 months post procedure,2 patients died 10-20 days post-procedure. **Conclusion:** we conclude that at present there is no effective treatment for malignant pertussis..Leukocytapheresis have been associated with high mortality and complications. Role of leukocytapheresis can't be established by mere 3 procedures large number of target population is required

KEYWORDS

INTRODUCTION

Pertusis(Whooping cough) is a respiratory tract infection characterized by paroxysmal cough. The most common causative organism is Bordetella Pertusis.[1] It spreads through airborne droplets and is highly contagious. Risk factors for acquiring pertusis includes pregnancy, epidemic exposure, lack of immunization, close contact with an infected individual.[2]

Hyperleucocytosis is arbitarily WBC > 1,00,000/cmm typically seen with same malignancies like AML, CML.This leads to leucostasis damaging mainly CNS, GI and cardiac system.[3]Cytapheresis (removal of cellular components of blood) has been used as modality in infectious treatment.There is insufficient evidence regarding use of Leucocytapheresis as treatment modality in pertusis cases.However, there are guidelines like ASFA 2023 (American Society For Apheresis) which support Leucocytapheresis in Hyperleucocytosis Category 3 GRADE 2B.[4]

Complications results from Hyperleucocytosis includes 1) DIC (Disseminated Intravascular Coagulation) 2) Tumor lysis syndrome and leukostasis.

Here we report 3 cases of pertusis in which Leucocytapheresis was used as treatment modality.The outcome was analysed in form of clinical and hemodynamic changes in the patient.

CASE 1

A 18 month old female weighing 7.7 kg came with chief complains of cough,cold fever for 2 days.On admission her vitals were heart rate 167/min, respiratory rate 26/min and Spo2 was 80% temperature was 102^0 F.She was intubated and admitted to PICU.Her CBC ,Hb 6.4 gm/dl,WBC count 1,20,000/µL,Platelet :3,10,000/µL.Her serum Urea came to be 13 mg/dl,serum creatinine 0.6 mg/dl, sodium was 135 mmol/L, potassium was 3 mEq/L.Her general condition was poor. Respiratory system showed air entry bilaterally equal,bilateral crepts were present.CVS showed S1S2 present,no murmur.CNS: she was alert, concious.ultrasound showed was hepatomegaly no splenomegaly. Patient was stabilized by mechanical ventilation, antibiotics, foley catheter and monitoring of strict input and output. Leucocytapheresis was done on Spectra Optia machine,Total blood volume processed was 1383 ml, procedure lasted for 161 min, Anticoagulant used was 129 ml, priming was done with 305 ml of leukoreduced, AHG compatible red cell concentrate.30 ml of top up transfusion was also done.Post procedure Hb was 8.4 gm/dl,WBC count was 40,500/cmm and platelet count was 74,000/cmm.After 6 months of follow up,patient is healthy.

CASE 2

A 12 month old female weighing 5.5 kg came to our hospital with chief complains of cough,cold fever for 3 days also breathing difficulty from 2 days. Patient was a known case of Severe Acute Malnutrition.On admission her vitals were heart rate 150/min, respiratory rate 68/min and Spo2 was 94%,temperature was 97^0 F.Pallor was present, Cyanosis, Icterus was absent and suprasternal retraction was present. She was admitted to PICU.Her CBC ,Hb 9.4 gm/dl,WBC count 1,30,000/µL,Platelet :3,63,000/µL.Her peripheral smear was reported as mild hypochromic, microcytic RBCs, anisopoikilocytosis, and many cellular debris. WBC morphology represented leukemiod reaction.Her serum Urea came to be 12 mg/dl,serum creatinine 0.84mg/dl, sodium was 137 mmol/L,potassium was 4.5 mEq/L,CRP was 79.5 mg/dl.Nasopharyngeal swab was taken and reported as Pertusis positive..Her general condition was poor.Respiratory system showed air entry bilaterally equal,bilateral crepts were present.CVS showed S1S2 present,no murmur.CNS: she was alert, concious. ultrasound showed was hepatomegaly no splenomegaly. Initially High flow nasal oxygen canula was started but patient detoriated so mechanical ventilation was done. Chest X ray showed prominent vascular margings with patches of air space opacities in bilateral mid zone and suprahilar region. Patient was stabilized by mechanical ventilation, antibiotics, foley catheter and monitoring of strict input and output. Exchange Transfusion was done.[6]Post exchange her WBC count reduced to 88,900/µL,Hb 7.5 gml/dl,Platelet count was 5,24,000/µLLeucocytapheresis was done on Spectra Optia machine, Total blood volume processed was 747 ml, procedure lasted for 4 hrs, Anticoagulant used was 83 ml, priming was done with 310 ml of leukoreduced, AHG compatible red cell concentrate.Post procedure Hb was 12.8gm/dl,WBC count was 40,500/cmm and platelet count was 2,50,000/cmm.32 ml of top up transfusion was also done. Patient expired after 20 days of procedure due to cardiac compromise.

CASE 3:

A 12 month old male weighing 7.8 kg came to our hospital with chief complains of cough,cold fever for 4 days and one episode of convulsion. On admission her vitals were heart rate 171/min, respiratory rate 70/min and Spo2 was 91%,temperature was 98^0 F. Pallor was present, Cyanosis, Icterus was absent and suprasternal retraction was present. She was admitted to PICU.Her CBC showed Hb 6.7 gm/dl,WBC count 1,10,000/µL,Platelet 3,53,000/µL.Her peripheral smear was reported as mild hypochromic, microcytic RBCs, anisopoikilocytosis, and many cellular debris.WBC morphology represented leukemiod reaction.Her serum Urea came to be 10 mg/dl,serum creatinine 0.64mg/dl, sodium was 132 mmol/L, potassium was 3.7 mEq/L.Nasopharyngeal swab was taken and reported as Pertusis positive.High flow nasal oxygen canula was started but patient detoriated so mechanical ventilation was done.Leucocytapheresis was done on Spectra Optia machine,Total blood volume processed was 1280 ml, procedure lasted for 155 min, Anticoagulant used was 128 ml, priming was done with 311 ml of

leukoreduced, AHG compatible red cell concentrate. Post procedure Hb was 12.8gm/dl,WBC count was 63,400/cmm and platelet count was 2,25,000/cmm.28 ml of top up transfusion was also done. Patient expired after 10 days of procedure due to cardiac compromise.

DISCUSSION

Hyperleucocytosis is arbitarily WBC > 1,00,000/ cmm typically seen with same malignancies like AML, CML.This leads to leucostasis damaging mainly CNS,GI and cardiac system.[5]This was a rare scenario where in an infective condition total counts roses in lakhs.Particular epidemic was suspected at that time because total of 10-12 children with similar presenation admitted from a rural area, WHO team also went there to collect swab and further manage the scenario, lack of awareness and lack of immunization can be one of the cause in this scenario.Among the most common symptoms of hyperleukocytosis is leukostasis. Tissue hypoxia is caused by vascular blockage caused by a high leukocyte count.Modern therapies for pertussis frequently target lowering the amount of leukocytes since very high levels of leukocytosis are linked to poor outcomes in babies hospitalised with the disease.[3] Although it affects people of all ages, newborn babies are more susceptible to the sickness, which may result in repeated hospital stays and sporadic fatalities (Berger et al. 2013).[7]. The leukocytosis-promoting component of Bordetella pertussis is unquestionably pertussis toxin (PT), which most likely achieves its function via interfering with leukocyte surface adhesion molecules and chemokine receptor signalling.[8] Infants hospitalised with severe pertussis will benefit from a better knowledge of the disease's pathophysiology and from future research into pertussis leukocytosis and other PT consequences. Leukocytosis, an abnormally high concentration of white blood cells in the bloodstream, is another hallmark of pertussis in newborns and young children, with the characteristic paroxysmal coughing (Heininger et al. 1997).[9] Pulmonary hypertension, which is linked to greater infant mortality, is more likely in babies with higher peak WBC levels.[10]One possible explanation is hyperleukocytosis, which causes thrombi rich in intravascular leukocytes in the pulmonary vasculature [11]. Several postmortem histologic examinations of lung tissues from infants who died of pertussis provide credence to this notion, although other comparable investigations have shown inconsistent thrombi presence, pointing to a multifactorial cause.

The prevalence of hyperleukocytosis and pulmonary hypertension seems to be highest in newborns under 120 days old, indicating that GPCR expression and function, including PT, may vary throughout development [12]. For instance, research has shown that the angiotensin-II receptor AT2 is strongly expressed in foetal tissue, but that this is balanced off in childhood by AT1 receptors. The AT2 receptor is involved in the regulation of vascular smooth muscle cell formation. Pulmonary artery thickening, vasoconstriction, and pulmonary hypertension may occur if pertussis toxin inhibits AT2. It is possible that this process occurs because unopposed smooth muscle cell proliferation occurs [12]. Four of five neonates in a Winter and Harriman histopathologic investigation of newborns who died from pertussis due to pulmonary hypertension had medial thickening of the pulmonary arteries [13]. Leukapheresis had an 86% complication rate in a case series of 102 children with acute leukaemia and hyper-leukocytosis, according to Abla et al. Dietary imbalances, hemodynamic instability, and coagulopathy were the most common adverse events in this research [14]. Given its extensive usage in treating other disorders, exchange transfusion offers a safer and more practical option. Any transfusion has the same risk of problems [15]. Leukodepletion treatment, whether by leukapheresis or exchange transfusion, rapidly improves hypoxemia after a pertussis infection, according to many studies. Ten infants less than three months old who had hyperviscosity syndrome as a result of a pertussis infection and who subsequently experienced cardiovascular, pulmonary, and neurological complications benefited from a rapid leukoreduction approach, according to research by Rowlands et al. [16]. From 2005 to 2009, a total of ten patients had either exchange transfusions or leukapheresis while five others received ECMO. Around 90% of people made it. Similarly, a research conducted from 2001 to 2004 on 9 patients, 6 of whom had ECMO, found a 55% survival rate in the absence of any leukocyte reduction technique[16]. The survival rates for patients with malignant pertussis who had exchange transfusions ranged from 54% to 92% in other small case studies [17]. Since exchange transfusion eliminates pertussis toxin at the same time as it replenishes white blood cells, some writers argue that it is preferable to leukodepletion procedures. [18].

CONCLUSION

Thus, we draw the conclusion that there is currently no curative measures for malignant pertussis. Most of the time, these patients are managed in a supportive manner.Complications and high death rates have been linked to leukocytapheresis. Role of leukocytapheresis can't be established by mere 3 procedures large number of target population is required.Complication needs to be investigated.

CASE 1 CASE 2 CASE 3
Age/Sex 18 month /F 12 month / F 12 month/M
Weight 7.7 kg 5.5 kg 7.8 kg
Preprocedure
Hb(g/dl) 6.4 9.4 6.7
TLC(/µL) 1,20,000 1,30,000 1,10,000
PLT(/µL) 3,10,000 3,63,000 3,53,000
Postprocedure
Hb(g/dl) 8.4 12.8 12.4
TLC(/µL) 40,500 40,800 63,400
PLT(/µL) 1,74,000 2,50,000 2,25,000
Transfusion
Preprocedure(Exchange) No Yes No
Postprocedure Yes Yes Yes
Procedure Related Complication No Yes(Tachycardia) No
Hydroxyurea Yes Yes Yes
Follow up Status Healthy(6months) Died(20 days postprocedure) Died (10 days postprocedure)

REFERENCES

[1] Skoff TH, Hadler S, Hariri S. The epidemiology of nationally reported pertussis in the United States, 2000–2016. Clinical Infectious Diseases. 2019 May 2;68(10):1634-40.
[2] Pierce C, Klein N, Peters M. Is leukocytosis a predictor of mortality in severe pertussis infection? Intensive Care Med. (2000) 26:1512–4. doi: 10.1007/s001340000587
[3] Oñoro G, Salido AG, Martínez IM, Cabeza B, Gillén M, de Azagra AM. Leukoreduction in patients with severe pertussis with hyperleukocytosis. The Pediatric infectious disease journal. 2012 Aug 1;31(8):873-6.
[4] Connelly-Smith L, Alquist CR, Aqui NA, Hofmann JC, Klingel R, Onwuemene OA, Patriquin CJ, Pham HP, Sanchez AP, Schneiderman J, Witt V, Zantek ND, Dunbar NM. Guidelines on the Use of Therapeutic Apheresis in Clinical Practice - Evidence-Based Approach from the Writing Committee of the American Society for Apheresis: The Ninth Special Issue. J Clin Apher. 2023 Apr;38(2):77-278. doi: 10.1002/jca.22043. PMID: 37017433.
[5] Desjardins M, Iachimov D, Mousseau S, Doyon-Plourde P, Brousseau N, Rallu F, Quach C. Respiratory Infections: Clinical characteristics of pediatric pertussis cases, Quebec 2015–2017. Canada Communicable Disease Report. 2018 Sep 9;44(9):190.
[6] Martinez M, Rochat I, Corbelli R, Tissières P, Rimensberger PC, Barazzone-Argiroffo C. Early blood exchange transfusion in malignant pertussis: a case report. Pediatric Critical Care Medicine. 2011 Mar 1;12(2):e107-9.
[7] Berger JT, Carcillo JA, Shanley TP, Wessel DL, Clark A, Holubkov R, et al. Critical pertussis illness in children: a multicenter prospective cohort study. Pediatr Crit Care Med. (2013) 14:356–65. doi: 10.1097/PCC.0b013e31828a70fe
[8] Palvo F, Fabro AT, Cervi MC, Aragon DC, Ramalho FS, Carlotti AP. Severe pertussis infection: A clinicopathological study. Medicine. 2017 Dec;96(48).
[9] Carbonetti NH. Pertussis leukocytosis: mechanisms, clinical relevance and treatment. FEMS Pathogens and Disease. 2016 Oct 1;74(7):ftw087.
[10] Nieves DJ, Singh J, Ashouri N, McGuire T, Adler-Shohet FC, Arrieta AC. Clinical and laboratory features of pertussis in infants at the onset of a California epidemic. The Journal of pediatrics. 2011 Dec 1;159(6):1044-6.
[11] Paddock CD, Sanden GN, Cherry JD, Gal AA, Langston C, Tatti KM, Wu KH, Goldsmith CS, Greer PW, Montague JL, Eliason MT. Pathology and pathogenesis of fatal Bordetella pertussis infection in infants. Clinical infectious diseases. 2008 Aug 1;47(3):328-38.
[12] Scanlon K, Skerry C, Carbonetti N. Association of pertussis toxin with severe pertussis disease. Toxins. 2019 Jun 27;11(7):373.
[13] Murray EL, Nieves D, Bradley JS, Gargas J, Mason WH, Lehman D, et al. Characteristics of severe Bordetella pertussis infection among infants ≤ 90 days of age admitted to pediatric intensive care Units-Southern California, September 2009-June 2011. J Pediatric Infect Dis Soc. 2:1–6 (2013) doi: 10.1093/jpids/pis105
[14] Abla O, Angelini P, Di Giuseppe G, Kanani MF, Lau W, Hitzler J, Sung L, Naqvi A. Early complications of hyperleukocytosis and leukapheresis in childhood acute leukemias. Journal of Pediatric Hematology/Oncology. 2016 Mar 1;38(2):111-7.
[15] Kuperman A, Hoffmann Y, Glikman D, Dabbah H, Zonis Z. Severe pertussis and hyperleukocytosis: is it time to change for exchange? Transfusion (2014) 54:1630–3. doi: 10.1111/trf.12519
[16] Rowlands HE, Goldman AP, Harrington K, Karimova A, Brierley J, Cross N, et al. Impact of rapid leukodepletion on the outcome of severe clinical pertussis in young infants. Pediatrics (2010) 126:e816–27. doi: 10.1542/peds.2009-2860
[17] Donoso F, Cruces PI, Camacho JF, León JA, Kong JA. Exchange transfusion to reverse severe pertussis-induced cardiogenic shock. Pediatr Infect Dis J. (2006) 25:846–8. doi: 10.1097/01.inf.0000232630.70138.a2
[18] Winter K, Zipprich J, Harriman K, Murray EL, Gornbein J, Hammer SJ, et al. Risk factors associated with infant deaths from pertussis: a case-control study. Clin Infect Dis. (2015) 61:1099–106. doi: 10.1093/cid/civ472