Continuous NIPPV in Pneumocystis carinii pneumonia with acute severe hypoxaemic respiratory failure in an immunocompromised cancer patient: A case report

A Prakash, R Jain, M Srikanti, S Mishra, S Bhatnagar

Citation

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Abstract

Pneumocystis carinii pneumonia (PCP) is very common cause of acute respiratory failure in patients with hematological malignancy. The role of non-invasive ventilation in moderate to severe respiratory failure due to PCP is controversial. We report a case of PCP with acute severe hypoxaemic respiratory failure well managed with prolonged continuous non-invasive positive pressure ventilation (NIPPV) and other specific treatment in a patient with acute lymphoblastic leukemia (ALL), on consolidation chemotherapy.

INTRODUCTION

Patients with malignancies have a greater tendency to acquire infections than the general population. The cause is altered immunity either due to underlying neoplasm or antineoplastic therapy. The organisms in this setting can range from normal skin flora such as Candida species, the normally nonpathogenic saprophyte like Pneumocystis carinii (PC) to commensal organism like dematiaceous fungi.[1] Pneumonia is a common cause of morbidity and mortality in these type of patients and the incidence of Pneumocystis carinii pneumonia (PCP) as high as 47% have been observed in patients with hematological malignancy.[2] Mortality is even higher in patients who need intubation and mechanical ventilation for acute respiratory failure in PCP.[3] Noninvasive ventilatory support may be considered, although the rapid progression to respiratory failure often necessitates intubation at the time of presentation. We report a case of PCP with acute severe hypoxaemic respiratory failure well managed with continuous non-invasive positive pressure ventilation (NIPPV) and other specific treatment in a patient of acute lymphoblastic leukemia (ALL), on consolidation chemotherapy.

CASE HISTORY

A 26 year old male with body surface area of 1.64 m^2, diagnosed case of pre B-cell ALL, came to the emergency department with presenting complaints of high grade fever, dry cough, and black tarry stool for 4 days and worsening dyspnoea for 5-6 days. Two months back he had been given induction chemotherapy according to Hoelzer's protocol (Vincristine, 1.4 mg m^{-2}; daunorubicin, 45 mg m^{-2}; L-asparagine, 6000 u m^{-2}; and prednisolone 40 mg m^{-2}). After induction he was on consolidation chemotherapy (cyclophosphmide, 600 mg m^{-2}; cytosine-arabinoside, 60 mg m^{-2}; intrathecal methotrexate, 10 ng m^{-2} and purinethal 60 mg m^{-2}) which was withheld seven days back due to low total leukocyte count(TLC) and absolute neutrophil count(ANC) . He was evaluated in the emergency and was found to have pulse rate of 140 beats min^{-1}, BP 100/80 mm of Hg, bilateral basal crepts on auscultation of chest and finger pulse oximetry (SpO_2) showing 80-85 % on room air. On investigation his Hb was 3.8 gm%, total leukocyte count (TLC) 2000 cmm^{-1}, absolute neutrophil count (ANC) 400, platelet count 38,000 cmm^{-1}, bilirubin 1.6 mg dl^{-1}, creatinine1.2 mg dl^{-1} and predominantly bilateral perihilar interstitial infiltrates in chest X-ray. He was immediately shifted to high dependency unit (HDU). 40% oxygen was supplemented via venturi mask and right femoral vein was cannulated with 16 Fr Seclon-T (Becton-Dickinson SA, Spain). Peripheral blood was sent for culture and awake fibreoptic bronchoscopy was done with ease. Bronchoalveolar lavage (BAL) fluid of both lungs was sent for fungal elements and cytological examination which revealed a bilateral fungal profile of Pneumocystis carinii.

I.V. sulphamethoxazole-trimethoprim (TMP-SMZ), hydrocortisone, vancomycin and granulocyte- colony stimulating factor (G-CSF) was started based on BAL fluid report, suspected superadded bacterial infection and low ANC. Two units of packed red blood cells and one unit of single donor platelets (SDP) were transfused.

During the following day, his respiratory distress continued to increase. On investigation, his Hb was 5.9 gm%, TLC 2100 cmm^{-1}, ANC 400, platelets 48,000 cmm^{-1}, bilirubin 1.2 mg dl^{-1} and creatinine 1.8 mg dl^{-1}. Contrast enhanced CT scan of thorax was done which demonstrated bilateral diffuse ground glass opacity with consolidation in posterior segments of lung suggestive of interstitial pneumonia secondary to pneumocystis carinii infection or impending adult respiratory distress syndrome (ARDS). Two more units of packed red blood cells were given. Gastroenterology consultation was taken for gastro-intestinal bleed and intravenous pantoprazole 8 mg hr^{-1} was started after 40 mg of bolus injection.

On the third day of admission, his Hb increased to 9.5 gm% and stool color became normal but his respiratory distress increased. His saturation fell down to 60% even after receiving oxygen 15 L min^{-1} via face mask. His ventilatory frequency increased to 50/min, BP decreased to 80/50 mm of Hg and he became irritable. Dopamine infusion was started 5 mcg $kg^{-1}min^{-1}$ and gradually increased to 10 mcg $kg^{-1}min^{-1}$ and his respiration was supported with non-invasive positive pressure ventilation (NIPPV). He was kept on synchronized intermittent mandatory ventilation (SIMV) mode [rate, 6 min^{-1}; tidal volume, 600 ml; pressure support (PS), 8cm of water; positive end expiratory pressure (PEEP), 5 cm of water; FiO_2, 50%] on Pulmonetic LTV 1000 ventilator. Before starting NIPPV his arterial blood gas (ABG) analysis results were, PaO_2, 45 mm of Hg; $PaCO_2$, 24.1 mm of Hg; pH, 7.507 and HCO_3, 18.5mmol l^{-1} suggestive of mixed respiratory alkalosis and metabolic acidosis. Two hours later, his oxygen saturation was 92-94% and BP increased to 90/70 mm of Hg. His PaO_2 was 60 mm of Hg in ABG and respiratory rate decreased to 35 min^{-1}. Due to intolerance of noninvasive mask, he was tried for intermittent NIPPV two times but as soon as NIPPV mask was removed and his respiration was supported via simple face mask with supplemental oxygen, his oxygen saturation started to fall and dropped to 50%. Finally his respiration was supported with continuous NIPPV and intravenous midazolam infusion was given 1 mg hr^{-1} keeping his Ramsay's sedation score ≤ 2. His PS was increased to 15 cm of water and PEEP 6 cm of water keeping SpO_2 > 90%. Systolic BP not being improved with dopamine alone, nor-adrenaline infusion 0.04 mcg $kg^{-1}min^{-1}$ was started and after that his BP started to increase. A 16-Fr nasogastric tube was inserted and enteral feeding was started.

The next seven days he tolerated NIPPV mask well with wide fluctuation in pulse oximetry (SpO2) between 70-96% which was managed by adjusting FiO_2 between 50- 100% and PEEP 5 to 10 cm of water. His BP increased to 140/80 mm of Hg and radio logically chest X-ray started improving on sixth day after NIPPV support. Blood culture report was sterile and I.V. vancomycin was withdrawn. Dopamine and nor-adrenaline infusion tapered down and NIPPV mode changed to continuous positive airway pressure (CPAP) with PS of 8 cm of water and PEEP of 5 cm of water. Midazolam and pantoprazole infusion was stopped and I.V single daily dose of pantoprazole was started. 12 hour after changing the ventilatory mode to CPAP his ABG was done which showed PaO_2, 78 mm of Hg; $PaCO_2$, 35 mm of Hg; HCO_3, 22 mmol lit^{-1} and BE -2 mmol lit^{-1}. Between day 8 and 9 after commencement of NIPPV, he tolerated CPAP and periods breathing via a high flow oxygen delivery facemask.

On day 10, his ventilation was supported with simple face mask with oxygen 5 L min^{-1} and ABG repeated after 2 hour was same as last report. On auscultation, his chest was bilateral clear; respiratory rate, 18-20 min^{-1}; HR, 90 beats min^{-1}; BP, 120/80 mm of Hg and SpO_2, 96%. On investigation his Hb was 9.3 gm%; platelets 98,000 cmm^{-1}; TLC, 8100 cmm^{-1}; ANC, 5800; bilirubin, 1.2 mg% and creatinine 1.0 mg dl^{-1}. Peripheral blood smear was done and revealed no blast cell and bone marrow aspirate suggested remission phase. He was shifted to ward and SpO_2 monitoring was done. Next two days he was observed in the ward without any deterioration. Finally he was discharged and reviewed in ophthalmic OPD to exclude extra pulmonary complication of P.carinii and in medical oncology for further management of ALL.

DISCUSSION

The nature of immunological abnormality present in a case has a major bearing on the nature of the infective processes likely to be present. The major categories of immunological abnormality include deficient humoral immunity (agammaglobulinaemia, multiple myeloma or chronic lymphocytic leukemia), deficient phagocytic cell function or

number (chemotherapy induced granulocytopenia) and deficient cell-mediated immune function (patient on chronic corticosteroid, less intensive chemotherapy). Cancer patients have usually mixed immune dysfunction. The incidence of fungal infection of the lungs is increasing in immunocompromised individuals in spite of advances in antifungal prophylaxis and therapy.[4] The incidence of PCP is around 47% among hematological malignancies.[2]

The presentation in our case was typical for PCP with dry cough, fever and progressive dyspnoea accompanied by signs of respiratory distress with basal crepts. His chest X-ray showed typical bilateral predominantly symmetrical interstitial infiltrates which progressed to diffuse lesion later on (Figure.1). Diagnosis was confirmed by BAL fluid examination which illustrated excellent diagnostic yield for PCP.

Initial management included supplemental oxygen, antimicrobial agents and corticosteroid. Earlier role of corticosteroid was uncertain but now its role for the treatment of moderate to severe PCP is well established.[5, 6] In our case corticosteroid treatment was started immediately after confirmation of diagnosis to reduce the risk of early deterioration and acute respiratory failure. Even after prompt diagnosis and no delay in starting treatment patient went into acute severe hypoxaemic respiratory failure and his respiration was supported with NIPPV. Initially he was not tolerating non-invasive mask but after few hours he was comfortable. This might be because of midazolam which had caused mild anxiolysis and improved oxygen saturation with NIPPV which had decreased neurological deterioration. An alternative management strategy would be intubation and mechanical ventilation. But considering the risk of infection due to low ANC and chance of bleeding due to low platelets count, NIPPV was tried and it showed good improvement in patient's condition. Mechanisms of improvement included beneficial effect of PEEP leading to alveolar recruitment and redistribution of extra vascular fluid, and pressure support (PS) reduced the work of breathing, allowing respiratory muscle to regain efficacy.

Non-invasive ventilation was also used intermittently by Tognet and co-workers in patient with hematological cancers.[7] In the study by Gille and co-workers[8] intermittent non-invasive ventilation was used in immunocompromised hematological cancer patients with PaO_2:FiO_2 >85% and showed better outcome when compared with standard medical treatment with supplemental oxygen and no ventilatory support (53% vs. 93% mortality in hospital). In present case we used NIPPV at PaO_2 45 mm of Hg on oxygen via face mask at 15 L min^{-1} (maximum FiO_2 can be delivered 0.8) and PaO_2:FiO_2 < 75% . Not usual in other studies and reports we used continuous NIPPV for >170 hours. During this period pulse oximetry showed wide fluctuation in SpO_2 between 70-96% and tracheal intubation had been considered several times but this invasive intervention had been successfully avoided by increasing FiO_2 and PEEP transiently. Festic and co-workers[9] in their study used NIPPV in 16 non- HIV related PCP with respiratory failure, out of which 75% patient died in whom median duration of ventilation used was 49 hours and 25% patient survived till discharge with median duration of ventilation of 10.5 hours.

We concluded, NIPPV can be used continuously even in severe respiratory failure in an immunocompromised patient for several hours with good outcome by doing minor adjustment in ventilatory variables when appropriate therapy is being given for the precipitating factor. It should be vied as alternative to invasive ventilation rather than a complimentary technique in immunocompromised patients.

CORRESPONDENCE TO

Dr Seema Mishra, F-33, AIIMS, Residential Campus (West), Ansari Nagar New Delhi. India. e-mail: mseema17@yahoo.co.in

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Author Information

Amit Prakash, M.D.
Senior Resident, Anaesthesia, IRCH, AIIMS

Roopesh Jain, M.D.
Senior Resident, Anaesthesia, IRCH, AIIMS

Madhurima Srikanti, M.D.
Senior Resident, Anaesthesia, IRCH, AIIMS

Seema Mishra, M.D.
Assistant Professor, Anaesthesia, IRCH, AIIMS

Sushma Bhatnagar, M.D.
Associate Professor, Anaesthesia, IRCH, AIIMS