Worsening acute respiratory distress syndrome: Is it immune reconstitution inflammatory syndrome?

Sir,

Immune reconstitution inflammatory syndrome (IRIS) results in paradoxical deterioration in the clinical status that is attributable to hyperactivity of the immune system. Although paradoxical reactions have been described previously, they have not been addressed in patients receiving mechanical ventilation. We hereby describe the development of this syndrome following initiation of anti-tubercular treatment (ATT).

A 22-year-old post partum human immunodeficiency virus negative female was intubated and transferred to intensive care unit (ICU) following respiratory distress accompanied by fever, cough and altered sensorium. Ventilatory support was provided with synchronized intermittent mandatory ventilation mode of the ventilator. ATT was commenced in the patient after finding the tracheal secretions positive for acid fast bacilli while being sterile for other bacterial pathogens. After initial clinical and radiographic improvement, marked deterioration was noticed after 24 h of initiation of ATT with high grade fever (39°C), hypoxemia (pO_2-52.3 mmHg, SpO_2-85%, P: F ratio<100), hypercarbia (pCO_2-80.6 mmHg) on FiO_2 of 0.9 along with hypotension and newly developed bilateral infiltrates on chest X-ray suggesting acute respiratory distress syndrome (ARDS) [Figure 1]. Mechanical ventilation was switched to the pressure control mode and patient was managed according to the ARDSnet guidelines. Methylprednisolone infusion was started at the rate of 40mg/day. Transthoracic echocardiography did not reveal any underlying cardiac abnormality. However, the patient did not improve and died on the 14th day of admission to ICU.

Deterioration during ATT in a patient receiving mechanical ventilation remains a clinical challenge for the intensivist. The exact pathogenesis is unclear and may be due to either restoration of the immune responses causing exuberant inflammatory reactions or lack of specific immune response leading to abnormal reaction.[1] Since, clinical deterioration occurs during immune recovery, the phenomenon has been described as immune restoration disease, immune reconstitution syndrome or paradoxical reactions with IRIS being widely accepted. The incidence of 6-30% has been reported in patients on ATT and the syndrome can be elicited by either infectious or non-infectious causes including the auto immune diseases.[2]

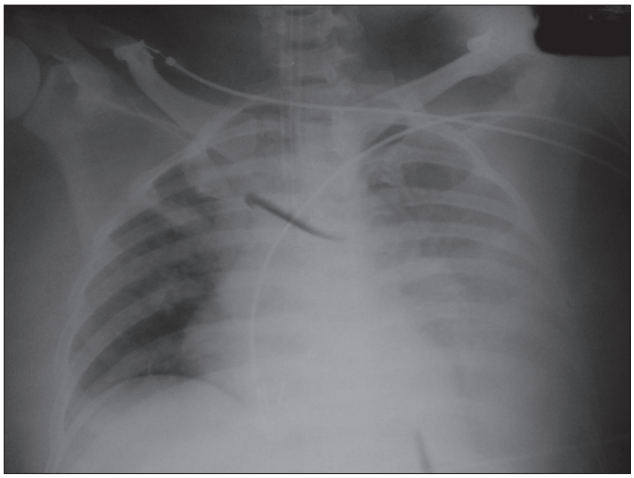

Figure 1: Bilateral infiltrates following initiation of anti-tubercular treatment

Paradoxical responses have varied clinical spectrum with both pulmonary and extra pulmonary manifestations that develop at least 2 weeks after initiation of ATT and usually subside on their own.[3,4]

Reversal of pregnancy induced immunosuppression may also have added to the hyper inflammatory responses in the present case there by worsening the clinical symptoms.[5] Isolation of tubercle bacilli from the cultures after excluding treatment failure, drug resistance, underlying new infection and drug hypersensitivity correlated with development of this syndrome. Interestingly, the features of IRIS manifested at an earlier stage as well following initiation of ATT.

We therefore emphasize maintaining a high degree of vigilance in patients receiving mechanical ventilation and consider the development of this syndrome following ATT in worsening ARDS or newly developed ARDS. Whether paradoxical reactions are common in certain subsets of the population is still unknown. No specific disease criteria have been established as for now.

The research efforts should therefore be directed to identify underlying immunopathological mechanisms triggering this condition to formulate preventive and therapeutic strategies at the earliest to protect the patient against the hyperinflammatory response without compromising antimicrobial therapy.

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