FIGURE 9

Management of Immune-Related Pneumonitis[1,7,9,14,23,31,34]

Background: Pneumonitis is a non-infectious lung inflammation with interstitial and alveolar infiltrates. Although pneumonitis is rare (<5%) it can be life threatening; fortunately, the incidence of grade 3 or 4 toxicity is low (<1%) for both CTLA-4 and PD-1 blocking antibodies. Clinical presentation includes dry, unproductive cough, tachypnea, dyspnea, tachycardia, cyanosis, and fatigue. Oxygen saturation may fall with progression, especially after exercise. Chest imaging typically shows ground glass opacities or patchy nodular infiltrates, particularly in lower lobes. The median time of onset of pneumonitis is 19 weeks (range 0.3-84 weeks) for pembrolizumab, 9 weeks (range 4-26 weeks) for nivolumab and 11 weeks when on combination therapy.

PNEUMONITIS

MANAGEMENT (First rule out infectious causes)

	Description	Referral	Corticosteroids	Supportive Therapy	Immune Therapy
GRADE 1	Asymptomatic; diagnostic radiological observations only; no intervention needed.	Monitor oxygen saturation and chest x-ray or CT every cycle and consider pulmonary and infectious disease consults.	Consider 1 mg/kg/day PO prednisone or 1 mg/kg/day IV methylprednisolone.	Not required.	If patient is on steroids, consider withholding treatment until resolution.
GRADE 2	Symptomatic; medical intervention indicated; limiting instrumental ADL.	Pulmonary and infectious disease consults.	Start 1-2 mg/kg/day PO prednisone or IV equivalent, taper over ≥4 weeks. If no improvement after 48 to 72 hours or worsening, treat as grade 3-4.	Consider hospitalization for daily monitoring of symptoms and re-imaging every 1-3 days. Start empiric antibiotics if suspicious for infection.	Withhold therapy until resolution to grade 0-1 without complications & prednisone dose tapered to <10 mg/day. Discontinue immune therapy if toxicity recurs.
GRADE 3	Severe symptoms; limiting self care ADL; oxygen indicated.	Pulmonary and infectious disease consults. Consider bronchoscopy & lung biopsy to investigate for pulmonary infection.	Start 2-4 mg/kg/day methylprednisolone IV then taper over ≥6 weeks; if no improvement after 48 hours or worsening, additional immunosuppression such infliximab 5 mg/kg IV once q2weeks can be administered (avoid if contraindicated*).	Admit to hospital and start prophylactic antibiotics for opportunistic infections. Oxygen and ventilation support if necessary.	Permanently discontinue therapy.
GRADE 4	Life-threatening respiratory compromise; urgent intervention indicated (e.g. intubation and ventilation).				

* If infliximab is contraindicated (possibility of perforation, sepsis, TB, NYHA 3/4 CHF), consider mycophenolate mofetil (500-1000 mg BID) or other immunosuppressive agents