Case:  
A 20-year-old man with CF: genotype F508del homozygous, CF-related liver disease with cirrhosis, and CF-related diabetes on insulin who presented with excessive daytime sleepiness, poor attention, and progressive lung function decline over the previous year. FEV1 had decreased from 78%-predicted to 33%-predicted. Body mass index (BMI) had declined from baseline 24.7 kg/m² to 21.7 kg/m². Polysomnography revealed severe obstructive sleep apnea during rapid eye movement (REM) sleep with an apnea-hypopnea index of 43/hour and a maximal desaturation to SaO2 of 78%. In non-REM sleep, the patient exhibited an elevated ventilatory load with increased respiratory rate, and increased respiratory effort.

Discussion Points:
1. Sleep as a Vulnerable State in CF  
   a. Sleep plays a vital restorative role in all individuals.  
   b. Sleep is a vulnerable state that can induce physiologic stress.  
   c. Sleep architecture and quality in CF patients may be impaired as a result of nocturnal cough, chronic upper airway infection, and increased upper airway obstruction from chronic sinus disease and nasal polyposis.  
2. Typical altered ventilatory mechanics during sleep in CF patients  
   a. CF patients exhibit increased respiratory rates and worsening of gas exchange during sleep.  
   b. Alterations in blood gas exchange are multifactorial and include V/Q mismatching from chronic lung disease, worsened hypoxemia in the supine position, and blunted CO₂ sensitivity leading to hypoventilation, hypercapnea, and disrupted sleep.  
   c. Increased respiratory loads may further contribute to muscle wasting, fatigue, and ongoing pulmonary cachexia.  
3. Sleep disruption impacts metabolic demand and contributes to weight loss  
   a. Compensatory respiratory changes maintain the stability of breathing and defend gas exchange in CF patients.  
   b. However, the necessary increase in caloric expenditure contributes to pulmonary cachexia.  
   c. Therapies to decrease the ventilatory load during sleep may decrease energy expenditure and lead to improvements in BMI.  
4. Potential therapies  
   a. Continuous positive airway pressure (CPAP): often poorly tolerated in CF patients who have chronic, nocturnal, suppurative cough.  
   b. High-flow Nasal insufflation (HFNI): treats mild sleep apnea, provides airway humidification, reduces respiratory load, and potentially reduces energy expenditure.  

Case Follow-up:  
started on HFNI with resolution of sleep apnea, improvement in daytime sleepiness, and lung function.