What is your diagnosis?

An uncomplicated cesarean section was performed under general anesthesia on a 33-year-old woman with a gestational age of 34 weeks and 2 days due to a valuable pregnancy. At postoperative hour 4 the patient developed dyspnea, tachypnea, hypertension, and agitation, and she was transferred to the intensive care unit due to worsening general condition and alteration in consciousness. At initial assessment, the general condition of the patient was poor, with confusion and agitation, and her Glasgow Coma Scale score was 13. Also, on auscultation, she had rales and rhonchi bilaterally in her lungs, her respiratory rate was 36/min, and her cardiac rate was 160 bpm with arrhythmia. She was intubated without delay and mechanical ventilation was started (Drager Evita 4, Germany, BIPAP mode, lung recruitment maneuver). An antero-posterior chest x-ray showed bilateral diffuse infiltrations, and blood gas analysis indicated oxygen-resistant arterial hypoxemia (PaO_2/FiO_2: 75). A pre-diagnosis of severe acute respiratory distress syndrome (ARDS) was suspected based on Berlin criteria (Figure 1, Table 1). Her central venous pressure was 6 mm Hg. However, based on the presence of risk factors for pulmonary embolism and its clinical resemblance to ADRS, the patient's D-dimer level was measured and contrast-enhanced computed tomography (CT) of the chest was scheduled to rule out pulmonary embolism. The patient's D-dimer level was 2.7 mg/dL. However, CT imaging could not be performed due to her poor medical condition, which precluded transfer to the CT unit from the ICU. Despite this, enoxaparin (Cleaxane 60 mg/0.6 mL, Sanofi Aventis; İstanbul, Turkey) s.c. BID was started due to a possible occurrence of pulmonary embolism after consultation with the departments of pulmonology and obstetrics. A diagnosis of severe ARDS was primarily considered, and midazolam (Demizolam, DEM Medical; İstanbul, Turkey) infusion at a rate of 10 mg/hour was commenced to increase adaptation to mechanical ventilation. Also, esmolol (Brevibloc premiks, Eczacıbasi Baxter; İstanbul, Turkey) infusion was given due to a heart rate of 145 bpm and a blood pressure of 170/110 mmHg, and furosemide (Lasix amp, Sanofi Aventis; İstanbul, Turkey) (4 mg/h) was given due to the presence of bilateral rales on lung auscultation and pinkish-foamy endotracheal aspiration fluid, suggesting pulmonary edema. Additionally, clarithromycin (Uniklar 500 mg, Mustafa Nevzat; İstanbul, Turkey) (2x500 mg) and ceftriaxone (Rocephin 1 gr, Saba Drugs; İstanbul, Turkey)

Table 1. The patient's mechanical ventilation and arterial blood gas analysis

Time (hours)	**0**	**2**	**4**	**10**	**36**	**72**	**96**	**120**
Ventilatory mode	BIPAP	BIPAP	BIPAP	BIPAP	CPAP	CPAP	y-connection	Extubation
FiO_2	1	0.8	0.6	0.5	0.4	0.4	0.3	0.3
P_{insp}	30	30	30	30	-	-	-	-
P_{ASB}	20	20	20	20	10	10	-	-
PEEP	10	10	10	10	5	5	-	-
Respiratory rate	14	14	14	14	0	0	-	-
PaO_2/FiO_2	75	89	101	133	175	272	245	383
pH	6.98	7.07	7.27	7.48	7.53	7.42	7.45	7.47
$PaCO_2$	66	59	41.4	32.6	34.2	42.9	39.9	39.2
PaO_2	75	71.4	60.6	66.7	70.3	109	73.5	115
SaO_2	79	82.7	84.8	94.1	94.9	97.7	93.4	97.7
HCO_3	11.1	13.4	18.3	26.1	30.1	27.7	27.8	28.8
Lactate	6.7	5.7	4	2.4	1.1	1.9	2.1	1.4
Base excess	-14.6	-11.9	-6.8	1.3	6.1	3.8	3.8	4.7

BIPAP: bilevel positive airway pressure; CPAP: continuous positive airway pressure; FiO_2: fraction of inspired oxygen; P_{insp}: inspiration pressure; P_{ASB}: pressure support above PEEP; PEEP: positive end-expiratory pressure; PaO_2: partial arterial oxygen pressure; $PaCO_2$: partial arterial carbon dioxide pressure; SaO_2: arterial oxygen saturation; HCO_3: bicarbonate

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(2x1 gr) were started due to possible pneumonia. Magnesium (Magnesium sulfate amp 15%, Biofarma; İstanbul, Turkey) was infused at a dose of 60 mg/h on the basis of its neuroprotective effects as well as its therapeutic effects on pre-eclampsia. Esmolol infusion was gradually reduced as the patient's blood pressure and heart rate returned to normal values. Mechanical ventilation parameters were adjusted according to serial arterial blood gas measurements and chest x-ray findings (Table 1, Figure 1). Progressive improvement was observed clinically; sedation was stopped on day 4, and the patient was placed on a y-connector. At day 5 she was extubated, and on day 6 she was transferred to the obstetrics ward. On postoperative day 8, contrast-enhanced CT of the chest showed several bilateral pulmonary nodules, the greatest being 6 mm in diameter. The patient was discharged on the same day.

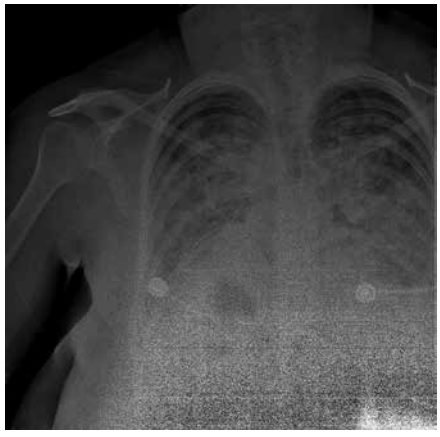

Figure 1. The patient's posterior-anterior chest x-ray immediately before admission to the intensive care unit

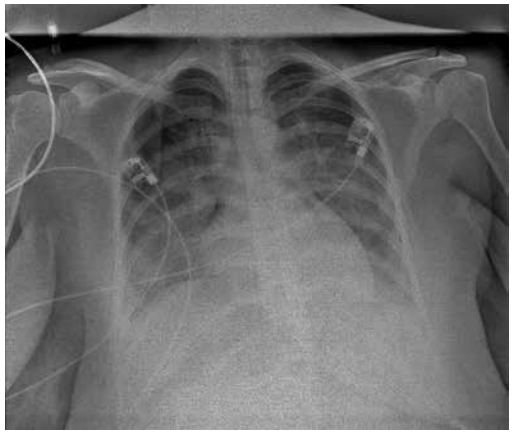

Figure 2. The patient's anterior-posterior chest x-ray on the second day

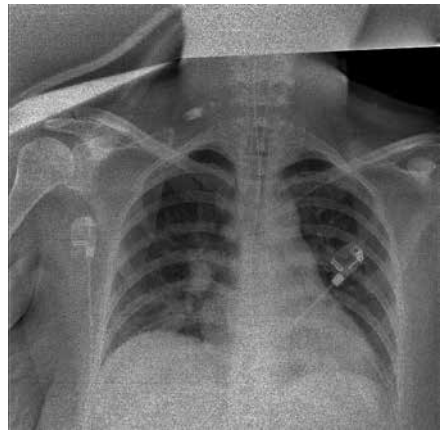

Figure 3. The patient's anterior-posterior chest x-ray on the sixth day

Answer

Acute respiratory distress syndrome is an acute, diffuse, and inflammatory lung disease characterized by increased pulmonary vascular permeability, increased lung weight, and decreased aerated lung tissue. Clinical manifestations of ARDS include hypoxemia and bilateral radiographic opacities, while the pathological manifestations include diffuse alveolar damage associated with alveolar edema and acute inflammation of the alveolar walls and hyaline membranes (1).

Although some risk factors for ARDS during pregnancy are similar to those in the general population (e.g., sepsis, aspiration, pancreatitis, trauma, inhalation injury, drowning, and pneumonia), pregnancy-specific conditions such as amniotic fluid embolism, pre-eclampsia/eclampsia, HELLP syndrome, chorioamnionitis, and endometritis may also play etiological roles in pregnant women (2-5).

Acute respiratory distress syndrome has an annual incidence of 1.5/100,000 and has a fatal outcome in 35% to 50% of cases. Despite the absence of clear data on the incidence of ARDS in obstetric patients, the incidence rate in these patients is thought to be comparable to that in the general population. In the UK and the US, the prevalence of the need for intensive care among pregnant women is around 0.9%; ARDS represents a major cause of maternal death in intensive care units (6).

Patients with acute hypoxemic respiratory failure frequently have dyspnea, tachypnea, and tachycardia. Auscultation may reveal diffuse bilateral rales in the basal lung zones and wheezing, and the patient may be cyanotic. Bilateral diffuse alveolar and interstitial infiltrations are typical in lung x-rays, although it may be challenging to differentiate these from x-ray images of patients with congestive heart failure or fluid overload (7). Our patient with a history of pre-eclampsia had dyspnea, tachypnea, and cyanosis at postoperative hour 4, followed by alteration in her mental state. She was intubated without delay due to her worsening clinical status and blood gas results, and mechanical ventilation was initiated. The patient's central venous pressure was measured to rule out hypervolemia, as the patient had bilateral rales on auscultation of the lungs and a small amount of pinkish-foamy endotracheal aspiration fluid. Central venous pressure between 4 and 7 mmHg was measured during her clinical course; this was indicative of the absence of hypervolemia. Furosemide infusion was given for possible pulmonary edema.

Adequate disinfection of the surgical field and absence of foul-smelling vaginal discharge suggested that endometritis and chorioamnionitis had no triggering roles in ARDS. A diagnosis of HELLP was also largely out of consideration due to the patient's normal bleeding-clotting time, platelet count, and liver enzyme levels. Delayed gastric emptying in pregnant women is associated with increased risk of aspiration during general anesthesia. Our patient, who had a history of panic disorder, received general anesthesia, which may have resulted in aspiration as a potential cause of ARDS. However, analysis of the endotracheal aspiration fluid showed no material suggestive of active aspiration. Also, no vomiting occurred during anesthesia or during the post-operative period. Furthermore, a diagnosis of sepsis could be readily ruled out due to the absence of a causative microbial agent in the patient's endotracheal aspiration fluid, urine, and blood samples, and also due to the absence of any foci of infection.

Acute respiratory distress syndrome induced by tocolytic agents may occur during beta-adrenoceptor agonist infusion or within 12 hours of its discontinuation. The clinical manifestations may be resolved after 12 hours with diuretics, supportive treatment, and discontinuation of the causative agent (7). However, our patient had a more severe clinical course, and no rapid improvement was observed after stopping the tocolytic agent.

Amniotic fluid embolism, however, classically presents with ARDS, hemodynamic collapse, and disseminated intravascular coagulation (7). Our patient only had ARDS; also, contrary to hemodynamic collapse, hypertension and tachycardia were detected. Also, the patient's bleeding-clotting parameters were normal.

Pre-existing pre-eclampsia was considered as the etiological factor responsible for the development of ARDS in our patient. In a study by Mabie et al. (4), 16 patients were admitted to the intensive care unit due to a diagnosis of ARDS during a 6-year period; only 4 of these cases were related to eclampsia/pre-eclampsia. Among these four cases, additional comorbidities (aspiration pneumonia, lupus nephritis, sepsis, massive transfusion, etc.) were present that could be associated with the occurrence of ARDS. Meyer and Schmidt reported a pre-eclamptic patient in whom ARDS persisted during the postpartum period despite labor and treatment of pre-eclampsia (8). No other possible causes of ARDS were present in our patient; therefore, the most likely cause of her condition was pre-eclampsia.

Treatment of ARDS during pregnancy or the postpartum period is similar to that in non-pregnant individuals. In patients admitted to the intensive care unit due to acute hypoxia and diffuse lung infiltrates during pregnancy or the postpartum period, an etiological search should be undertaken; hypervolemia and congestive heart failure should be ruled out, and amniocentesis should be conducted. For diagnostic purposes, bronchoalveolar lavage aspiration and even lung biopsy may be performed (2). Because the most probable cause of ARDS was pre-eclampsia in our patient, additional diagnostic work-up was not performed. For the management of these patients, the underlying condition should be corrected, and conventional mechanical ventilation should be performed (Vt<6 mL/kg, p plat<30 cm H_2O). Recommended strategies when this treatment is insufficient include airway pressure release ventilation (APRV), high frequency oscillatory ventilation (HFOV), prone positioning, inhaled nitric oxide, and additional lung recruitment maneuvers (2, 7). Magnesium infusion and intermittent recruitment therapy with mechanical ventilation were used therapeutically in our patient.

Acute respiratory distress syndrome may occur during pregnancy or the postpartum period, may be either associated or not associated with pregnancy, and may threaten maternal and

fetal health. Based on our experience with this patient, who had ARDS induced by pre-eclampsia, we wish to emphasize the fact that these patients may be successfully managed by early recognition, pressure-controlled ventilation and supported treatment in the intensive care unit, and with other supportive measures.

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