CASE REPORT

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Maternal Death Associated with Intravenous Methylphenidate (Ritalin®) and Pentazocine (Talwin®) Abuse

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ABSTRACT: A case of maternal death from pulmonary hypertension secondary to pulmonary granulomatosis is presented. The granulomas are associated with a history of intravenous injection of medications (Ritalin® and Talwin®) intended for oral use.

KEYWORDS: toxicology, methylphenidate, pentazocine, death, pulmonary granulomatosis

When oral medications are injected intravenously, many of the insoluble fillers, such as talc, lodge in the small pulmonary vessels and produce foreign body granulomas. Pulmonary hypertension has been associated with these granulomas, occasionally resulting in death. To our knowledge, this is the first reported case of a maternal death from granulomatosis associated pulmonary hypertension.

Case Report

The patient was a 25-year-old female, gravida 4, para 3, with a history of drug abuse which included intravenous (IV) injection of Ritalin® (methylphenidate) and Talwin® (pentazocine). She was pregnant at 37-38 weeks gestation and had been followed in prenatal clinic, at which time the urine drug screen was positive for caffeine only. She was admitted via the Emergency Room for shortness of breath, lower back pain, lower abdominal pain, and hypotension (systolic 75 to 90 mm Hg). Her most recent drug use was Ritalin and Talwin on the day before admission. The patient showed a lack of peripheral veins with numerous needle tracks and was undergoing uterine contractions approximately every 2 to 4 min. Blood gas analysis on 4 L of oxygen showed pH 7.42, partial pressure of carbon dioxide

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(PCO_2) 14.5 torr, partial pressure of oxygen (PO_2) 82 torr, and bicarbonate (HCO_3) 9.5 meq/L. Laboratory values for prothrombin time (PT), partial thromboplastin time (PTT), fibrinogen, and platelets were normal; fibrin split products were greater than 10 μg/mL but less than 40 μg/mL. Chest X-ray was normal. The electrocardiogram (EKG) showed sinus tachycardia and incomplete right bundle branch block. She was taken to labor and delivery where an amniotomy was performed, and a scalp electrode placed. The fetus was showing late decelerations with every contraction, and no variability. An emergency Cesarean-section was performed under general anesthesia. The procedure was uncomplicated and the estimated blood loss was 500 cm^3. The fetus had an Apgar score of 0 and 6. While closing the peritoneum, the patient's blood pressure began dropping, and cardiopulmonary resuscitation (CPR) was started. The patient developed electromechanical dissociation, and death was pronounced 45 min after CPR was started. The clinical impression was that death was due to amniotic fluid embolism. The female baby weighed 3200 g and was released after 2 weeks with the diagnosis of severe birth asphyxia and narcotic withdrawal syndrome.

Autopsy Findings

The heart was enlarged at 400 g and showed biventricular hypertrophy (right ventricle 0.6 cm, left 1.6 cm). The right ventricle showed dilatation with flattening of the trabeculae carneae. The lungs weighed 1240 g and showed a diffuse fine granularity without consolidation or thromboemboli. The liver weighed 2050 g and was slightly pale. The spleen weighed 370 g. The postpartum uterus weighed 850 g and contained clotted blood.

Histologically, the heart showed hypertrophy in both ventricles, along with an occasional small talc granuloma. The lungs showed numerous foreign body granulomas with birefringent talc particles, many involving small arteries and arterioles with partial or complete compromise of the lumina (Fig. 1). The liver also showed many portal granulomas with smaller talc particles than in the lungs. Additional talc granulomas were seen in the subcutaneous tissue at the injection sites.

Toxicology Studies

A drug screen performed on a urine sample from the Emergency Room was positive for methylphenidate (Ritalin), pentazocine (Talwin), propoxyphene (Darvon®), and acetaminophen. Quantitative levels performed on autopsy serum showed methylphenidate 9 ng/mL (up to 58 ng/mL expected after 20-mg oral dose), pentazocine less than 5 ng/mL, and propoxyphene 0.49 μg/mL (typical therapeutic level 0.42 μg/mL).

Discussion

Chemically, talc is hydrous magnesium silicate [*1,2*]. It is present along with other insoluble filler substances in tablets and capsules intended for oral consumption, where it is used to hold the components of the medication together [*2–4*]. The talc emboli which occur from illicit intravenous use of such oral preparations have been previously reported as a cause of pulmonary foreign body granulomas [*2,3,5*]. Two of the drugs involved in this case, Ritalin [*4,6,7*] and Talwin [*3,8,9*], have been specifically mentioned in such reports. Opiates are generally diluted with more soluble substances and usually do not cause pulmonary granulomas by themselves [*3,4*]. Pulmonary hypertension is often associated with the pulmonary granulomas [*4,6–9*]. The pulmonary granulomas in such cases are usually perivascular or intravascular, and the resulting compromise to pulmonary blood flow is thought to be the mechanism for the pulmonary hypertension [*3,10*]. A few deaths have been reported from or associated with such pulmonary hypertension [*4–7*].

This patient showed clinical and pathologic evidence of pulmonary hypertension with pul-

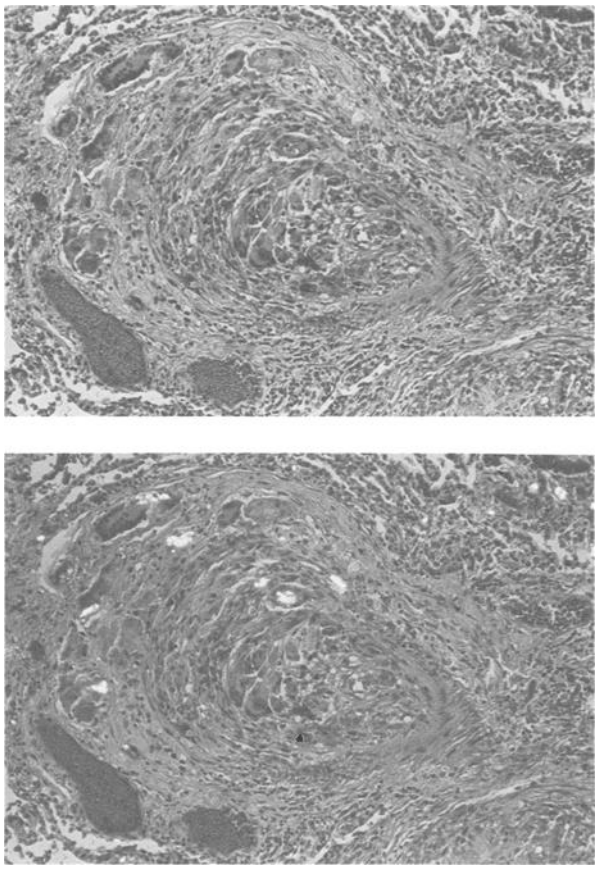

FIG. 1—*Pulmonary granulomatous arteritis. Complete obstruction of the lumen:* (top) ×*125, hematoxylin and eosin stain and* (bottom) ×*125 (polarized light).*

monary granulomatosis and a history of intravenous injection of oral medications. The pulmonary granulomas were extensive and primarily perivascular, often with compromise of the vascular lumina. The quantitative levels of the illicit drugs in this case were sufficiently low that they probably did not directly contribute to the patient's death.

The possibility of significant pulmonary granulomatosis and resulting pulmonary hypertension should be kept in mind when dealing with patients who have a history of intravenous abuse of oral medication.

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