CASE REPORT

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Sudden Death Caused by Embolization of Trophoblast from Hydatidiform Mole

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ABSTRACT: A 16-year-old pregnant female presented to a hospital emergency room with vaginal bleeding and uterine cramping. She underwent a hysterotomy and curettage and, during the procedure, her pulse dropped from 130 to 30 beats/minute, her pO_2 fell to 10 mm of mercury, and she could not be resuscitated. At autopsy, she was found to have massive pulmonary embolization of syncytiotrophoblast from a hydatidiform mole of the uterus. This is the sixth reported case of trophoblastic embolization from a hydatidiform mole ending in death. This fatal termination may occur after a period of respiratory symptoms and may occur regardless of the mode of treatment.

KEYWORDS: pathology and biology, embolisms, trophoblast, pregnancy, embolization, hydatidiform mole, pregnancy complications

Hydatidiform mole is a well recognized complication of pregnancy, occurring in from 1/1000 to 1/2000 pregnancies in the United States [*1*]. Two commonly recognized complications of a molar pregnancy include bleeding and malignant transformation. Rarely sudden death occurs as a result of a hydatidiform mole. We present such a case.

History

The patient was a 16-year-old white female, 3 ½ months into her first pregnancy, who presented at 3:15 a.m. to a hospital emergency room with a chief complaint of vaginal bleeding and uterine cramping. Her admission vital signs were pulse rate 138/minute, respirations 22/minute, and blood pressure 128/68. Her hemoglobin was 8.1 g/dL, and her hematocrit was 23.1%. From the vagina 250 mL of blood were evacuated. Over the next 8 h the vaginal bleeding continued and she used seven sanitary pads and five bed pads. Her pulse ranged from 100 to 160/minute, with most measurements between 130 and 140. Her blood pressure was generally 108 to 110 mm Hg and 60 to 66 mm Hg diastolic. Respirations were mostly 20 to 22 min. Over the 8-h period she received 1000 mL each of 5% dextrose in water and lactated Ringer's solu-

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tion, 500 mL each of normal saline and 5% dextrose in water, and two units of packed red blood cells. Hemoglobin and hematocrit at 11:15 a.m., 8 h after admission, were 10.3 g/dL and 28.8%, respectively. At 11:45 a.m. she was taken to the operating room, where she underwent hysterotomy with curettage of the uterine contents. As the incision was being closed, her heart rate suddenly dropped from 130 to 30 beats/minute. Five minutes later her pO_2 was 10 mm Hg despite administration of 100% oxygen and cardiopulmonary resuscitation. She was pronounced dead 1 h 45 min later.

Physical examination revealed the uterine fundus to be at the level of the umbilicus, and was estimated to be five months gestational size.

Autopsy

At autopsy, multinucleated syncytiotrophoblastic giant cells were seen within pulmonary arterioles and capillaries of every microscopic field examined (Fig. 1). These emboli stained positively for human chorionic gonadotropin, using the peroxidase-antiperoxidase technique [2] (rabbit anti-human chorionic gonadotropin, DAKO Immunoglobulins, Copenhagen, Denmark). Occasional alveoli contained deposits of fibrin with entrapped neutrophils and red blood cells. An Attwood stain showed no evidence of amniotic fluid emboli.

The curetted uterine contents consisted of hydropic villi without cellular atypia. No fetus was present. At autopsy, a few hydropic villi were found within the uterine cavity. There was no myometrial invasion by hydropic villi.

Discussion

Embolization of trophoblast following treatment for hydatidiform mole is a well recognized complication among those physicians treating molar pregnancies, with an incidence of 2.1 to

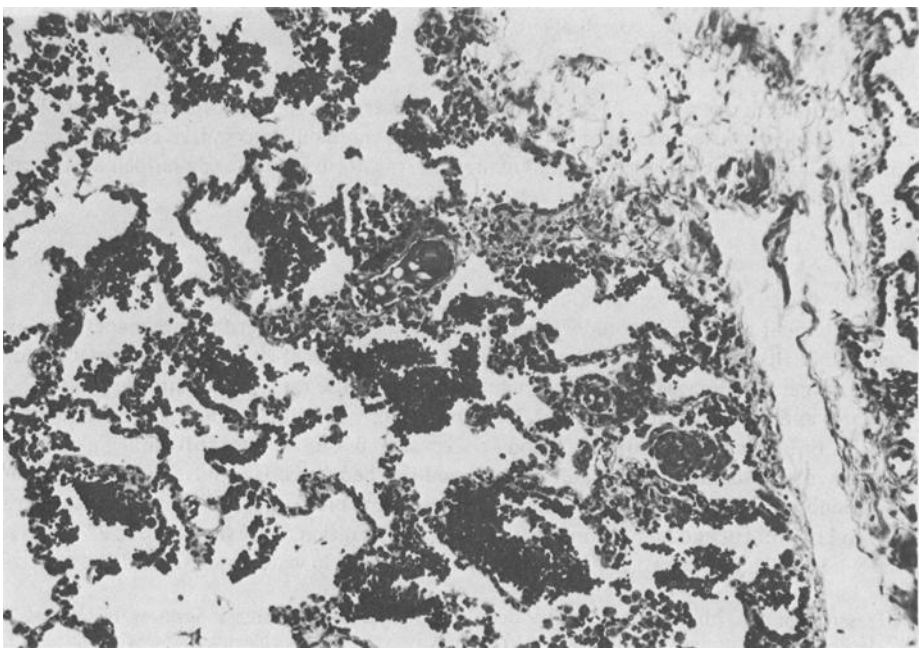

FIG. 1*a*—*Lung section showing trophoblastic emboli and intra-alveolar hemorrhage and fibrin (original magnification ×100).*

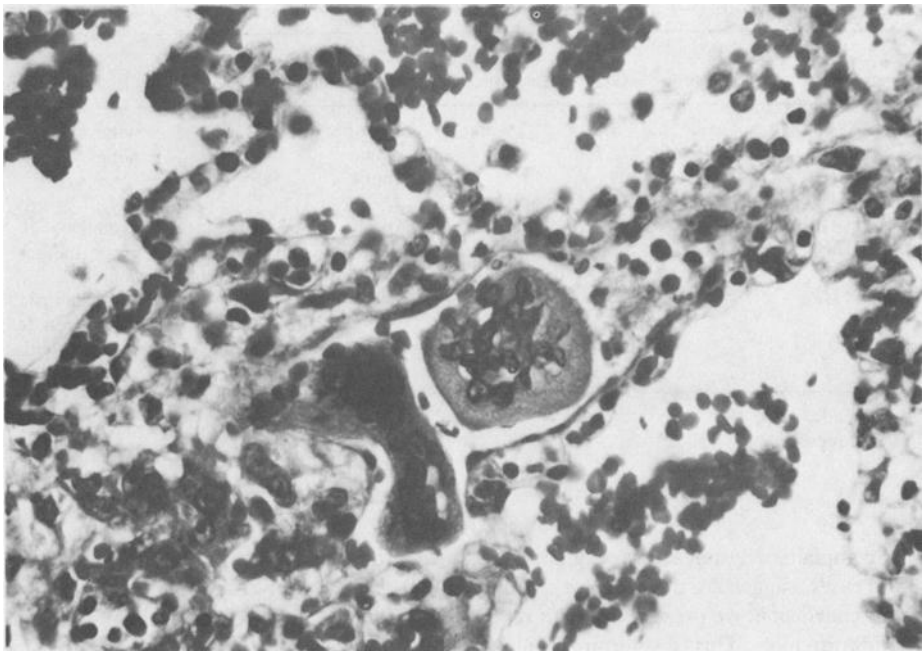

FIG. 1*b*—*Syncytiotrophoblastic cells within pulmonary capillary (original magnification ×400).*

5.6% (Table 1) [*3–5*]. This complication is almost always self-limiting, generally resolving in three days [*4*].

Embolization of trophoblast cells to the lungs occurs in normal pregnancies and is generally asymptomatic. Marcuse [*6*] described a case of sudden death in a woman with a normal, six-month intrauterine pregnancy.

In addition to ours, six other cases of fatal trophoblastic embolization from a hydatidiform mole have been reported (Table 2). In three of those, the patients had respiratory symptoms, presumably related to embolization, for two weeks, four days, and 3 to 4 h, respectively. At autopsy, the two cases with the longer duration of symptoms contained pulmonary infarcts. There were no symptoms suggestive of embolization before removal of the mole in the cases of Hughes [*10*], Smith et al [*11*], or in our case. Our patient did have vaginal bleeding and decreased hemoglobin and hematocrit on admission, but these were probably caused by the "physiologic anemia" caused by human chorionic gonadotropin (hCG)-mediated increase in plasma volume; with the marked hCG levels present in a molar pregnancy [*13*], the hemodilution would be even greater. Her hematocrit and hemoglobin just prior to surgery, after transfusion with two units of packed red blood cells, were higher than they were on admission. Her mild tachypnea and tachycardia might have been due to a small amount of trophoblastic embolization in the hours before her demise, but could also have been caused by anxiety. She did

TABLE 1—*Incidence of trophoblast embolization in hydatidiform mole.*

Twiggs et al [*3*]	7/128	(5.6%)
Kohorn and associates [*4*]	9/376	(2.5%)
Goldstein [*5*]	4/189	(2.1%)

TABLE 2—*Fatal cases of trophoblast embolization from hydatidiform mole.*

First Author	Age	G/P[a]	Resp. Symptoms	Treatment	Other Conditions
Lipp [7]	30	3/2	2 weeks	dilation & curettage	none
Trotter [8]	19	2/0	4 days	none	none
Llewellyn-Jones [9]	NR[b]	NR	NR	none ...	NR
Hughes [10]	24		none	probe passed into uterus	toxemia
Smith [11]	19	2/0	none	suction & curettage	exophthalmos
Cohle	16	1/0	none	hysterotomy & curettage	none
Tsakok [12]	25	2/1	hours	suction curettage	pre-eclampsia, disseminated intravascular coagulation

[a]Gravida/para.
[b]Not reported.

not complain of dyspnea. It is of further interest that treatment was different in six of the seven fatal cases, suggesting that massive, fatal embolization can occur despite the treatment used.

In conclusion, we present the sixth reported case of trophoblastic embolization from a hydatidiform mole. This fatal termination may occur after a period of respiratory symptoms and may occur regardless of the mode of treatment. Furthermore, symptomatic embolization of trophoblast occurs in a significant percentage of all patients treated for hydatidiform mole.

References

[1] Hammond, C. B., Weed, J. C., Barnard, D. E. and Tyrey, L., "Gestational Trophoblastic Neoplasia," *Cancer Journal for Clinicians*, Vol. 31, No. 6, Nov./Dec. 1981, pp. 322-332.

[2] Sternberger, L. A., *Immunocytochemistry*, 2nd ed., John Wiley and Sons, New York, 1979.

[3] Twiggs, L. B., Morrow, C. P., and Schlaerth, J. B., "Acute Pulmonary Complications of Molar Pregnancy," *American Journal of Obstetrics and Gynecology*, Vol. 135, No. 2, 15 Sept. 1979, pp. 189-194.

[4] Kohorn, E. I., McGinn, R. C., Gee, B. L., Goldstein, D. P., and Osathanondth, R., "Pulmonary Embolization of Trophoblastic Tissue in Molar Pregnancy," *Obstetrics and Gynecology*, Vol. 51, No. 1, Suppl., Jan. 1978, pp. 16S-20S.

[5] Goldstein, P. "Five Years Experience with the Prevention of Trophoblastic Tumors by the Prophylactic Use of Chemotherapy in Patients with Molar Pregnancy," *Clinical Obstetrics and Gynecology*, Vol. 13, 1970, pp. 945-961.

[6] Marcuse, P. M., "Pulmonary Syncytial Giant Cell Embolism," *Obstetrics and Gynecology*, Vol. 3, No. 2, Feb. 1954, pp. 210-213.

[7] Lipp, R. G., Kindschi, J. D., and Schmitz, R., "Death from Pulmonary Embolism Associated with Hydatidiform Mole," *American Journal of Obstetrics and Gynecology*, Vol. 83, No. 12, 15 June 1962, pp. 1644-1647.

[8] Trotter, R. F. and Tieche, H. L., "Maternal Death Due to Pulmonary Embolism of Trophoblastic Cells," *American Journal of Obstetrics and Gynecology*, Vol. 71, No. 5, May 1956, pp. 1114-1118.

[9] Llewellyn-Jones, D., "Management of Benign Trophoblastic Tumors," *American Journal of Obstetrics and Gynecology*, Vol. 99, No. 4, 15 Oct. 1967, pp. 589-594.

[10] Hughes, J. E., "A Case of Hydatidiform Mole with Multiple Small Syncytial Infarctions of the Lungs," *Proceedings of the Royal Society of Medicine*, Vol. 23, Sect. O-W, 30 June 1929-1930, pp. 33-35.

[11] Smith, J. C., Alsuleiman, A., Bishop, H., Kassar, N. S., and Jonas, H. S., "Trophoblastic Pulmonary Embolism," *Southern Medical Journal*, Vol. 74, No. 8, Aug. 1981, pp. 916-919.

[12] Tsakok, F. H. M., Koh, S., Ilancheran, A., Pok, W. F., and Ratnam, S. S., "Maternal Death Asso-

ciated with Hydatidiform Molar Pregnancy," *International Journal of Gynecology and Obstetrics*, Vol. 21, No. 6, Dec. 1983, pp. 485-490.

[*13*] Twiggs, L. B., Non-Neoplastic Complications of Molar Pregnancy," *Clinical Obstetrics and Gynecology*, Vol. 27, No. 1, March 1984, pp. 199-210.

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