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A rare and unusual case of advanced complete molar pregnancy in an Arabian mare: first report

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Abstract

Molar pregnancy is a rare condition in women, referring to the development of fetal membranes with or without an embryo. A 22-year-old mare referred to the veterinary faculty clinic due to the delayed parturition. In the ultrasound examination, the uterine membranes were seen suspended in fluids without any trace of the fetal organs. The mare underwent caesarean section, a mixture of brown fluid with fragments of fetal membranes was removed, but no fetus or any remnants of the fetus were found in the uterus. In the histopathological examinations, the fetal membranes showed severe degenerative changes. Also, the thickness of the endometrium had lost its normal structure and the layers of stratum spongiosum and stratum compactum could not be separated. The contents of the uterus were evacuated as much as possible and the mare regained her full health after the surgery. This is the first case of continued pregnancy without an embryo in a horse, which can be an unusual type of molar pregnancy.

Introduction

Molar pregnancy is a condition of abnormal growth of outer parts of the conceptus known as trophoblastic cells. It is also named hydatidiform mole. When an oocyte without nucleus cooperates with sperm to establish a pregnancy a complete mole is created. Another condition named partial mole is due to the fertilization of a normal oocyte with two sperms.[1,2]

Mole is a very rare condition in human (approximately one *per* 1,000 pregnancies).[3] Reports in animal world are limited to a few cases in cattle.[4-7] In humans, most mole pregnancies are aborted at the age of 3 to 4 months, the age that pregnancy loss may occur without any clinical presentation and abortion materials are lost in feces.[8] Therefore, the dimensions of epidemiology and pathophysiology of this abnormal state in animals are not very clear. In women with mole pregnancy, excretion of bloody fluids, sudden development of irregular tissue mass in the uterine lumen, and elevated levels of human chorionic gonadotropin (hCG) can be seen. In clinical examination, a uterus that is larger than expected gestational age is observed. Cervical os is dilated along with dislocation of trophoblastic mass to anterior vagina. In ultrasonography, no detectable fetus or fetal parts exist in the womb and masses with mixed echotexture containing cystic areas fill the inner space of the uterus.[1] Because of high concentration of hCG produced by trophoblast, multiple large follicles are present inside ovaries.[9] Grossly moles are large tissue mass due to the edema and include multiple cisterns with different sizes. Definitive diagnosis is based on histopathological assessment and demonstration of strange tissue consisting of hyperplastic trophoblast with villi projected outward having cisterns in the central parts. Typical cuboidal trophoblastic cells in outer parts of tissue are evident.[10]

Treatment of molar pregnancy in human includes removal of uterine content using vacuum aspiration or suction curettage. Because of severe hemorrhage after this procedure, an emergency blood transfusion may be necessary for the patient. Sometimes, some of the trophoblastic cells remain inside uterus and multiply again, and sometimes metastasis occurs in peripheral tissues.[1,11] Therefore, in addition to routine treatment protocols, prophylactic chemotherapy can be prescribed. In majority of molar pregnancies in cows, this phenomenon has been reported in parturitions with no later serious complications.[7]

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In animals, there is limited information about molar pregnancy. We did find a weird case of advanced null pregnancy in a mare which was not similar to any other lesions except molar pregnancy.

Case Description

A 22-year-old Arabian mare was referred to the Veterinary Hospital of Shahid Bahonar University of Kerman, Kerman, Iran, for dystocia. The mare was 2 weeks over the approximate time of delivery and she had signs of restlessness and enlarged mammary glands. At clinical examination, body temperature was 38.30 ˚C, heart rate was 48 beat *per* min, breathing rate was 16 breath *per* min, and capillary refill time was 2 sec. Also, the color of mucous membranes (vagina and conjunctiva) and gastrointestinal movements were normal. In the hematology examination, a decrease in hematocrit was observed (Table 1). An increase in serum total protein and fibrinogen and a decrease in sodium, chlorine, and potassium were found in the blood biochemical test (Table 2). In an attempt to obtain peritoneal fluid, no fluid was obtained. Tachycardia was also seen in the electrocardiography (Cardimax FX-2111; Fukuda, Tokyo, Japan). In the examination performed by an obstetrician in rectal palpation, no part of the fetus was touched, which was completely abnormal considering the gestational age. In ultrasonography (ImaGo.S; IMV Technologies, Saint-Ouen-sur-Iton, France), again no part of the fetus could be seen up to a depth of 20.00 cm from rectum or anywhere on the abdominal surface. Pieces of suspended curtains were seen near the inner wall of the uterus and in the central parts (Fig. 1). We suspected to hydrallantois base of these clinical manifestations. In vaginoscopic examination using a speculum, cervix was closed with central cervical plaque. It was decided to perform a cesarean section. After ventral midline laparotomy, a nasogastric tube was inserted through purse string suture on the swollen uterine horn for prevention of hypovolemic shock. About 50.00 L of odorless serosanguineous fluid came out of the uterus. In further investigations, these fluids contained a very small amount of protein and sodium chloride. In addition to fluid, degenerated membrane like tissues were pulled out. In gross examination, the uterine wall had thickened and some of the mentioned degenerated tissues were adhered to the endometrium.

No trace of the fetus or fetal parts was found in the uterus. After removing a small piece of the uterine wall at the surgical incision for histopathological examination, this place was stitched, and after completion of surgery mare was recovered normally. In microbial culture, a special effort was made to isolate pathogenic bacteria, such as salmonella, types of clostridiums, and other possible bacteria involved in causing this disease from the uterus, and the result was negative.

Table 1. Hematological indicators in the Arabian mare affected by pregnancy mole.

Parameters	Measurement	Normal range	Variation
Hemoglobin (g dL^{-1})	16.00	11.00 - 19.00	Normal
Hematocrit (%)	23.00	32.00 - 53.00	Decreased
Red blood cells (×10^6 cells μL^{-1})	10.11	6.80 - 12.90	Normal
White blood cells (cells μL^{-1})	12,800	5,400 - 14,300	Normal
Mature neutrophils (cells μL^{-1})	7,500	2,300 - 8,500	Normal
Immature neutrophils (cells μL^{-1})	58.00	0 - 100	Normal
Lymphocytes (cells μL^{-1})	2,200	1,500 - 7,700	Normal
Monocytes (cells μL^{-1})	430	0 - 1,000	Normal
Eosinophils (cells μL^{-1})	250	0 - 1,000	Normal

Table 2. Biochemical indicators in the Arabian mare affected by pregnancy mole.

Parameters	Measurement	Normal range	Variation
Sodium (mEq L^{-1})	125	132 - 146	Decreased
Chlorine (mEq L^{-1})	91.00	98.00 - 110	Decreased
Potassium (mEq L^{-1})	2.00	3.00 - 5.00	Decreased
Calcium (mg dL^{-1})	12.40	2.60 - 11.13	Normal
Phosphorus (mg dL^{-1})	4.40	1.60 - 3.50	Normal
Magnesium (mg dL^{-1})	2.40	2.20 - 2.80	Normal
Iron (µg dL^{-1})	100	91.00 - 199	Normal
Total protein (g dL^{-1})	8.60	0.70 - 6.70	Increased
Albumin (g dL^{-1})	3.40	2.90 - 3.80	Normal
Fibrinogen (mg dL^{-1})	4.50	2.00 - 4.00	Increased
Creatinine (mg dL^{-1})	1.10	0.90 - 1.90	Normal
Lactate dehydrogenase (U L^{-1})	230	160 - 410	Normal
Bicarbonate (mEq L^{-1})	29.00	23.00 - 32.00	Normal
Venous blood pH	7.40	7.35 - 7.45	Normal

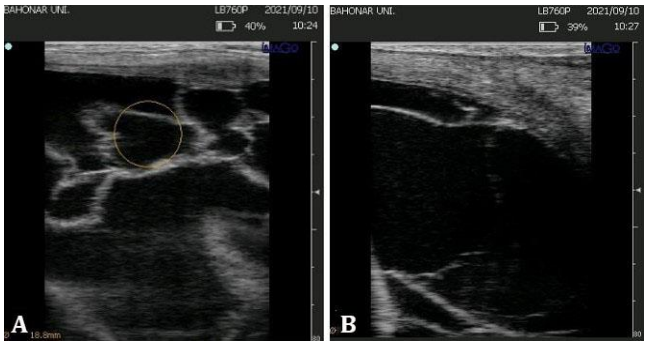

Fig. 1. Ultrasound image of the mare uterus in rectal palpation. **A)** Irregular lines in a fluid-filled space (yellow circle) representing membranes floating in the intra-uterine fluids are evident. **B)** There is no trace of the attachment of the placenta to the endometrium near to external os of cervix. It seems that these membranes have some connections with the inner surface of the uterus.

In the histological sections prepared from the uterus, uniform fibro-vascular tissue was observed in all the endometrium thickness, not having any endometrial glands. It was assumed that the stratum spongiosum layer was gone and only the stratum compactum layer was visible (Fig. 2). A thin layer of squamous cells was seen on the inner surface of the endometrium (Fig. 3A). Completely necrotic fetal membranes had pyknotic nuclei (Fig. 3B).

After the termination of the surgery, the mare stood up in a normal process and was discharged from the hospital 3 days later.

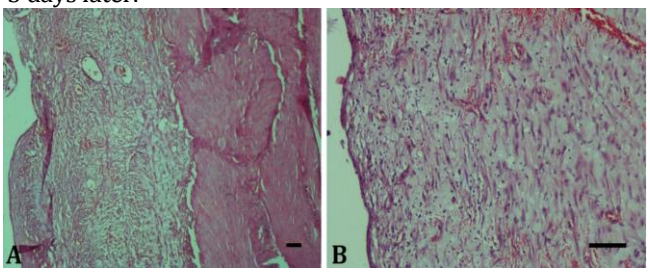

Fig. 2. A) A section of the mare uterus in which the muscular layer and the endometrium are well-defined, and the stratum spongiosum and the stratum compactum layers cannot be separated; **B)** Fibro-vascular tissue of the endometrium of the mare (Hematoxylin and Eosin staining; bars = 100 µm).

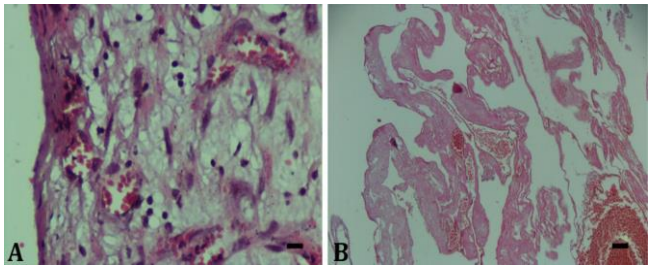

Fig. 3. A) The inner surface of the endometrium of the mare being covered with a layer of squamous cells; **B)** Sections of membranes suspended in uterine fluids of the mare containing a large amount of blood vessels in addition to necrotic cells (Hematoxylin and Eosin staining, bars = 10.00 and 100 µm, respectively).

In the ultrasound examination that was performed 24 hr after the surgery, the uterus contained more than 4.00 cm of secretions in the body, which was resolved (Fig. 4) with the intramuscular administration 20.00 IU oxytocin (Aburaihan, Tehran, Iran). The ovaries were small and had no follicles larger than 1.00 cm, and the remains of the luteal tissue were found on the left ovary.

Fig. 4. An image of the mare uterine wall in body 24 hr after surgery with the presence of intra-uterine secretions. Echogenic spots (arrows) near the inner wall of the endometrium represent remnants of fetal membranes that are still attached to the endometrium.

Discussion

Molar pregnancy is a rare event in humans, occurring due to the chromosomal abnormalities during fertilization in the forms of complete (fertilization of a haploid sperm with an egg lacking chromosomes) or partial (simultaneous fertilization of two sperms with a healthy egg).[12,13] In both forms, the abnormal proliferation of trophoblastic cells without the presence of a healthy embryo causes the formation of a strange cell mass in the uterus. Unfortunately, genetic analysis was not done in the present report, but the dilated uterus with the remnants of the fetal membranes without any trace of the fetus suggests nothing but a molar pregnancy. The present report is the first case of suspected molar pregnancy in horses, which differs from all previous cases reported in animals and humans in terms of clinical features.

One of the characteristics of molar pregnancy in humans is the formation of ovarian cysts with excessive secretion of hCG.[3] In women, the formation of cystic structures on the ovary is due to the excessive secretion of hCG from trophoblastic cells, not existing in animals. In all five recorded reports of molar pregnancy in the animal world, cystic changes have been reported in only one case of molar pregnancy in cat, for which there is no clear mechanism.[14] In four other reports that were in cows, no cystic changes were observed in the ovary.[4-7] In the mare of the present report, no specific cystic changes were observed in the ovaries.

In the ultrasound examination of the mare, fragments of the fetal membranes were seen and there was no trace of the fetus in the depth of the fluids. A similar situation is seen in cases of hydrallantois in horses, but in hydrallantois there is a fetus. The characteristics seen in the ultrasound examination of this case are not similar to any of the reported cases of molar pregnancy in humans and animals. In the previous cases, an accumulation caused by excessive growth of the fetal membranes was seen inside the uterus, which could be a little fluid-layered.[4] In previous humanand animal reports of molar pregnancy, endometrial changes have not been investigated, and in the mare in our report, extensive degenerative changes in the structure of the endometrium were seen in such a way that uterine glands were not seen in the thickness of the endometrium, and different parts of the endometrium were completely occupied by fibrosis. A tight connection between the degenerated embryonic membranes and endometrial wall was not found. Embryonic membranes did not show any distinct structures indicative of microvilli. Microvilli are an important part of the microcotyledonary structure of pregnant mare. Meanwhile, in the pathological studies conducted in some of the previous reports of molar pregnancy in animals, specific villi structures related to the chorioallantois were seen.[7,14] Since this case was presented after the full gestation period in the horse and following the absence of parturition, these changes could have occurred due to the occurrence of programmed cell death.

In none of the previous cases of molar pregnancy the complication was not diagnosed long after the normal pregnancy period. No one can predict what will be the outcome of molar pregnancy in a horse or for example in a cow. Similar to what occurs in humans, endometrial carcinogenic changes following molar pregnancy have not yet been reported in animals. Degenerative changes observed in the endometrium of this mare may be a prelude to the next unpredictable events.

Acknowledgments

Not applicable.

Conflict of interest

The authors declare no competing interests.

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