Hemoperitoneum in a mare following rupture of a granulosa-theca cell tumor

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Summary

An 18-year old Quarter Horse mare with a five-month history of suspected granulosa-theca cell tumor on the right ovary was presented with acute abdominal pain. The mare was displaying signs of cardiovascular shock on arrival so attempts were made to stabilize her while performing further diagnostic tests. Transabdominal ultrasound examination revealed a large, well-demarcated mass in the right caudal abdomen and a significant peritoneal effusion, which was confirmed to be hemorrhagic following abdominocentesis. Transrectal ultrasound examination confirmed a large, multi-loculated right ovarian mass. Despite aggressive medical therapy the mare continued to show signs of cardiovascular deterioration. Serial blood samples and repeated abdominal ultrasonography were consistent with uncontrolled intra-abdominal hemorrhage.

Based on the mare's clinical deterioration euthanasia was elected. Postmortem examination confirmed rupture of a granulosa-theca cell tumor on the right ovary associated with profuse intra-abdominal hemorrhage.

Case presentation

An 18-year-old Quarter Horse mare was presented to the Veterinary Medical Teaching Hospital at the University of California Davis for evaluation of colic. The mare had been examined and treated by the referring veterinarian but no improvement was seen so the mare was referred for further diagnostics and treatment.

The mare had a history of displaying stallion-like behavior and five months prior to presentation a presumptive diagnosis of a granulosa-theca cell tumor on the right ovary had been made based on transrectal palpation and ultrasound examination. The diagnosis was not confirmed by endocrine diagnostic tests and financial limitations had precluded surgical excision at that time.

On presentation the mare displayed signs of depression and cardiovascular shock. Based on history and initial clinical examination, differential diagnoses included gastrointestinal volvulus/strangulation, visceral rupture, and hemoperitoneum following rupture of the previously diagnosed ovarian mass.

A complete blood cell count (CBC), serum biochemistry and venous blood gas analysis were performed. The CBC revealed reduced hematocrit (22.6% [reference range 30-46%]), red blood cell count was 4.15 M/ul (reference range 6.2-10.2) and hemoglobin was 7.8 gm/dl (reference range 11.2-17.2) which were consistent with anemia. The platelet count was 110,000 u/l (reference range100,000-225,000) but a coagulation panel was not performed. Serum biochemistry revealed hypoproteinemia (3.7 g/dl [reference range 5.8-8.7]), and hyperlactemia (12.7 mmol/l [reference range<2mmol/L]).

Transabdominal ultrasound examination revealed a significant peritoneal effusion, with a classical echogenic swirling consistency, suggestive of a hemoabdomen. A large, (approx. 19 x 16 cm), well-demarcated mass was visualized in right caudal abdomen.

Based on ultrasound findings abdominocentesis was performed to characterize the peritoneal effusion. Upon entry into the peritoneal cavity a large volume of hemorrhagic fluid flowed from the cannula. The fluid was collected and submitted for evaluation, which confirmed it to be frank blood.

Transrectal palpation and ultrasound examination revealed a solid, large (>15 cm) mass on the right ovary, which was well demarcated, circular/oval in shape, with a multi-loculated appearance. It was not possible to obtain exact measurements of the mass as both the length and width exceeded the measuring capabilities of a 7.5 MHz transrectal probe. An area of approximately 7 cm on the ventromedial aspect of the mass had a homogenous echogenicity, consistent with fluid/hemorrhage (Figure 1). The mass appeared to be suspended by the broad ligament, but it was not possible to determine whether the source of hemorrhage was from the ovarian parenchyma or pedicle and ovarian

vessels.

Based on the severity of the clinical signs displayed and diagnosis of active intra-abdominal hemorrhage, anemia and hypoproteinemia, a cross-match was performed. Three available blood donors were tested at the teaching hospital and a suitable donor selected.

Two intravenous catheters had been placed upon presentation to facilitate intravenous fluid therapy with a balanced electrolyte solution (Plasma-Lyte A, Abbott Animal Health, Abbott Park, IL) and 4 L of commercial plasma (Equiplas J, Plasvacc USA INC., Templeton, CA) both at a rate of 2-4 ml/kg/hr. Treatment with aminocaproic acid was also started, with a loading dose of 40 g in 1 L saline IV followed by 20 g in 1 L saline IV, q 6 h. Following cross-matching and identification of a suitable donor, 4 L of blood was transfused initially at a rate of 0.1 ml/kg/hr; no transfusion reactions were noted so the rate was increased to 15 ml/kg/hr. A further 4 L of blood was transfused over the course of the treatment. Flunixin meglumine (1.1mg/kg, IV, q 24 h) was continued for its anti-endotoxic, anti-inflammatory, and analgesic properties.

The goal was to perform surgical resection once the mare was hemodynamically stable enough for surgery, however despite aggressive treatment the mare continued to show signs of cardiovascular deterioration. The mare remained persistently tachycardic and became tachypneic. Serial blood samples revealed both the hematocrit (13%) and total protein levels (3.1 g/dl) to be falling and repeat abdominal ultrasonography was consistent with uncontrolled intra-abdominal hemorrhage.

Further treatment options were discussed with the owner, including laparoscopic exploration with the hope to ligate the ovarian pedicle and a second blood transfusion, but based on the mare's clinical deterioration despite aggressive medical therapy, the fact that she was a poor surgical candidate due to cardiovascular instability, and the financial implications of continued treatment, euthanasia was elected.

Postmortem examination revealed the right ovary consisted of a large (~20 cm diameter), spherical, encapsulated mass (b). On cut section, the mass was composed of dozens of variably-sized (1 to 11 cm diameter), cystic spaces separated by dense bands of firm, pale yellow to white, fibrous tissue (Figure 3). The cysts were filled with yellow, watery fluid and blood clots. A 0.5 cm thick, fibrous, white capsule circumscribed the majority of the ovarian mass. At the rostral aspect of the mass, however, a 10 x 5 cm region of the capsule overlying a large blood-filled cyst was ruptured. This was presumed to be the site of profuse hemorrhage into the abdominal cavity, as was severe, hemorrhagic effusion within the peritoneal cavity (Figure 4).

Histopathological examination confirmed a granulosa-theca cell tumor of the right ovary with an atrophied left ovary (Figure 5**)**.

Discussion

Granulosa cell tumors are the most commonly reported ovarian neoplasia in the mare[1-3] and account for more than 85% of equine reproductive tract tumors.[4] They are typically diagnosed based on a combination of clinical signs, transrectal palpation and ultrasound examination, and endocrine assays. Histopathological examination of the ovary provides a definitive diagnosis. Clinical signs reported include stallion-like behavior, aggression and persistent or irregular estrous cycles.[3,5] Taken alone these signs can be misleading, as they may be manifestations of other problems such as musculoskeletal pain or behavioral issues. Transrectal palpation and examination via ultrasound cannot be used to definitely diagnose a granulosa cell tumor, as tumor appearance can be quite variable and not always consistent with the classical mixed "honey-combed" echogenicity on ultrasound examination. Other causes of ovarian enlargement such as an ovarian hematoma, teratoma or hemangiosarcoma may have a similar appearance and so cannot be ruled out based on ultrasound examination alone.[1,4-6] In contrast to granulosa cell tumors, ovarian hematomas typically regress rather than grow with time, the ovulation fossa will still be palpable on the ovary, and the mare will continue to cycle.[7] Endocrine assays used to diagnose granulosa cell tumors include inhibin, testosterone, progesterone, and anti-Müllerian hormone (AMH). Anti-Müllerian hormone in particular has been shown to be highly sensitive for the detection of granulosa cell tumors, being elevated in 98% of cases compared to elevations in inhibin (80% of cases), testosterone (48% of cases) or a combination of both inhibin and testosterone (84% of cases).[3] Endocrine diagnostic

tests were not carried out in this case due initially to financial constrictions and later because concerns regarding treatment of the hemoperitoneum outweighed the necessity to diagnose the tumor type.

Although reports exist,[8] colic is not a typical sign associated with granulosa cell tumors. In a review of 67 cases of hemoperitoneum, however, colic was the most reported associated clinical sign (79% of cases)[9] and hence in addition to the mare's history, hemoperitoneum was high on the list of concerns. While a granulosa cell tumor was suspected based on clinical signs and the external appearance of the mass, histopathological diagnosis was performed for a definitive diagnosis and to rule out other causes of ovarian enlargement and hemorrhage, such as hemangiosarcoma or hematoma.

Treatment was initiated with the aims of restoring circulating fluid/blood volume, enhancing coagulation, controlling pain and reducing the effects of endotoxemia. In spite of aggressive treatment, however, the degree of hemodynamic compromise was irreversible, hence the decision to euthanize the mare. Interestingly a significant difference between survivors and non-survivors in terms of treatment was not reported in two reviews of hemoperitoneum.[9,10]

The prognosis for both survival and future fertility following surgical excision of granulosa cell tumors is good.[1,6] This is in contrast to reported short-term survival rates in cases of hemoperitoneum.[9,10] In a review by Dechant et al. approximately three quarters of the horses that did not survive were euthanized because of the severity of hemodynamic compromise (as in this case) or due to the underlying disease process.[9] Unfortunately it was not possible in this case to stabilize the mare's cardiovascular parameters to a level where she would have been a good surgical candidate.

While the vast majority of cases of granulosa cell tumors in the horse are benign neoplasms, the growth rate of these tumors cannot be predicted. This case highlights the importance of surgical removal following initial detection to avoid catastrophic complications. Hemoperitoneum following rupture of a granulosa cell tumor is a rarely reported but life-threatening complication associated with this neoplasm[6,9,11-13] that could have been avoided in this case with early and appropriate treatment.

Learning points

- Growth of granulosa-theca cell tumors is unpredictable
- Surgical removal following detection should not be delayed as potential complications are life-threatening

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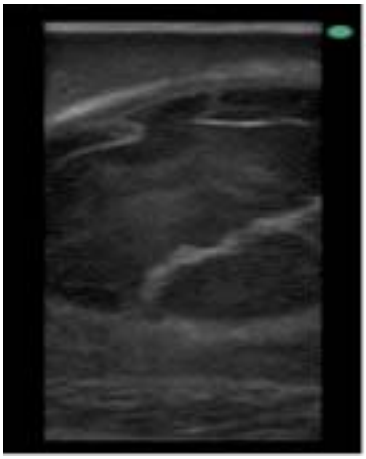

Figure 1. Transrectal ultrasound image of the right ovary revealing echogenic fluid consistent with hemorrhage both within the mass and the peritoneal cavity.

Figure 2. Photograph of the right ovarian mass revealing the ruptured capsule.

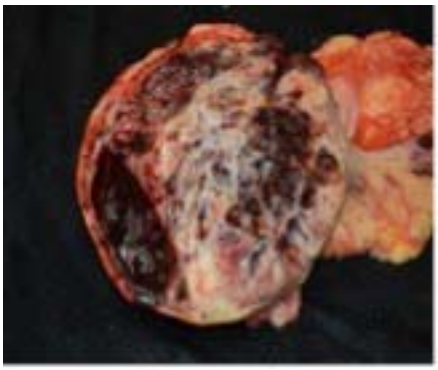

Figure 3. Photograph of the cut surface of granulosa-theca cell tumor of right ovary revealing multiple cystic structures filled with blood clots.

Figure 4. Photograph at necropsy of the hemoabdomen following rupture of the granulosa-theca cell tumor.

Figure 5. Photograph at necropsy of the granulosa-theca cell tumor of the right ovary and atrophied left ovary in situ.

(Editor's note: Photographs in this manuscript are available in color in the online edition of Clinical Theriogenology.)