

Immature ovarian teratoma in two heifers

Augusto Carluccio¹, Maria Teresa Zedda², Alberto Contri^{1*}, Alessia Gloria¹,
Domenico Robbe¹, Ippolito De Amicis¹ and Salvatore Pau²

¹Faculty of Veterinary Medicine, University of Teramo, Loc. Piano d'Accio, 64100 Teramo, Italy.

²Department of Veterinary Medicine, University of Sassari, Via Vienna 2, 07100 Sassari, Italy.

*Corresponding author at: Faculty of Veterinary Medicine, University of Teramo, loc. Piano d'Accio, 64100 Teramo, Italy.
e-mail: acontri@unite.it.

Veterinaria Italiana 2017, **53** (4), 327-330. doi: 10.12834/VetIt.738.3603.2

Accepted: 18.01.2017 | Available on line: 29.12.2017

Keywords

Heifer,
Teratoma,
Ovary,
Histochemistry.

Summary

A 15 months-old Simmental heifer (SH) and a 18 months-old Marchigiana heifer (MH) were referred to the Faculty of Veterinary Medicine of Teramo (Italy). In the first heifer, clinical examination of the vulva, vestibulum, and vagina showed no signs of disease and no discharge was detected. Palpation per rectum revealed a mass in the left portion of the abdominal cavity, closely attached to the tip of the left uterine horn. The mass was mainly firm and fibrous and its surface was slightly lobulated. The second heifer had a history of a regular cycle from the 11th to the 14th month of age followed by an anoestrus state. Gynecological examination revealed the presence of a large and firm mass in the caudal left region of the abdomen, soon over the edge of the pelvis floor. In both cases, the histologica examination of the mass revealed an immature ovarian teratoma.

Teratoma ovarico di tipo immaturo in due manze

Parole chiave

Bovina,
Teratoma,
Ovaio,
Immunoistochimica.

Riassunto

Due bovine, una Simmental (SH) di 15 mesi e una Marchigiana (MH) di 18 mesi, sono state condotte alla Facoltà di Medicina Veterinaria, Università di Teramo (Italia), per infertilità legata ad aciclia. L'esame clinico della vulva, del vestibolo e della vagina non ha mostrato segni di malattia apparente nel primo animale. Alla palpazione per via rettale, è stata riscontrata una massa fibrosa a superficie leggermente lobulata nella parte sinistra della cavità addominale, strettamente collegata all'apice del corno uterino sinistro. Nella seconda bovina, l'anamnesi riportava cicli regolari dagli 11 ai 14 mesi di età, seguiti da una fase di anestro. Anche in questo caso, la visita ginecologica ha evidenziato la presenza di una massa grande e di consistenza elevata nella regione sinistra caudale dell'addome, appena oltre il bordo del pavimento del bacino. In entrambi i casi, l'esame istologico ha diagnosticato un teratoma ovarico, classificato di tipo immaturo.

Introduction

Ovarian teratomas are considered a rare neoplasm in any domestic species. Cases of teratoma have been mostly reported in humans, dogs, and cats (Dehner *et al.* 1970, Basaraba *et al.* 1998, Piano *et al.* 2002, Oliveira *et al.* 2004, Yamaguchi *et al.* 2004, Tachibana *et al.* 2010). Teratoma consists of pluripotential, also called totipotential, germ cells that undergo neoplastic transformation into two or more germinal cell types (endoderm, mesoderm, and ectoderm). These different cell types differentiate into different tissues such as adipose, epidermal, musculoskeletal, or nervous tissue.

Teratomas are classified into mature or immature form (Czernobilsky and Lifchitz-Mercer 1990). Whereas the mature form is clearly differentiated, the immature one (teratocarcinoma) contains less well-differentiated embryonal elements in addition to mature structures. Many theories have been proposed to explain the formation of teratomas. The two most widely accepted hypotheses are: 1) the teratoma originated from undifferentiated embryonic cells which maintain their capacity to develop into tissues that are different from those of the organ they are growing in; 2) teratoma is a parthenogenic tumor that develop from a single germ cell that had completed the first but not

the second meiotic. A study on 5 women with benign ovarian teratoma findings supported this hypothesis, since all the teratomas examined presented the 46,XX karyotype (Linder *et al.* 1975). In humans, teratoma is diagnosed shortly after birth or in early infancy, so it is likely that this type of tumor developed in the fetus (Crum 1999). Since the formation of primary oocytes in the bovine fetus starts and is completed between days 80 to 130, teratoma formation in the cow could begin as early as the third month of pregnancy. In human, immature teratoma is considered a rare form of ovarian germ cell tumor, involving about 1% of all teratomas (Tewari *et al.* 2000, Smith *et al.* 2006).

Case description

A 15 months-old Simmental heifer (SH) and a 18 months-old Marchigiana heifer (MH) were referred to the Faculty of Veterinary Medicine of Teramo (Italy) in 1998 and 2009 respectively.

First case

In the SH, the examination of the vulva, vestibulum, and vagina showed no signs of disease and no discharge was detected. The palpation per rectum revealed a large mass which easily moved within the abdomen, and the left uterine horn moved with it. The ultrasound examination of the mass was performed transrectally, and the echotexture of the mass was very variegated, with iperechoic and well defined portions or ipoechoic areas with occasional cysts. Because of the genetic value of the heifer and the mobility of the mass, a therapeutic approach by the surgical removal of the mass. Sedation was performed using xylazine (0.05 mg/kg intramuscular) and local paravertebral anesthesia (T13, L1, L2 and L3) was carried out with 2% lidocaine (Cox 1987). The laparotomy was performed using the approach proposed for the caesarean section (Cox 1987). The surgeon introduced sterile gloved arms within the incision and moved the mass near the laparotomy. The abdominal breach was increased of about 10 cm to allow the extraction of the mass. The mass was isolated by ligation of the dorsal and caudal vessels and removed from the abdomen. The laparotomy was closed by a three-layer suture. Systemic antibiotic therapy (intramuscular penicillin G 1.000.000 UI/100 kg and dyhydrostreptomycin 1 g/100 kg) was administered daily for 5 days. The mass was 41x33x30 cm in size and weighted 36 kg.

Second case

The MH had a history of a regular cycle from the 11th to the 14th month of age followed by an

anoestrus state. In the second heifer through the palpation per rectum, the uterus, the uterine horn and the right ovary were detected, but the identification of the left ovary was not possible. The left horn seemed attached to a mass. On the surface of the right ovary no functional structures were found. No other signs were detected. The ultrasound examination revealed the presence of a mass with heterogeneous echogenicity and areas characterized by an high echogenicity. The results of the gynecological and ultrasound examination suggested the presence of an ovarian tumor. The owner choose to stop diagnostic procedures and the heifer was slaughtered because of the low genetic value. After slaughter, the reproductive tract was collected. The macroscopic examination revealed a normal right ovary, with luteinic formations and follicles at different size. No pathological alterations were detected in the uterus. The left ovary was completely altered, with a size of 45x35x35 cm (40 kg) (Figure 1).

Macroscopic examination of the mass in both cases revealed a thin fibrous capsule. The cut surface showed evident connecting strands spreading from the surface capsule, often for some millimeters and penetrating into the parenchyma in an irregular way. There was an abundance of a whitish component identified as typical bovine adipose tissue. When the tumor was cut, bone tissue was found as laminar bone formations surrounding some nodules. Numerous cystic formations of different size and shape (the smaller circular and the larger of irregular shape) were seen most frequently in the SH, some of them pigmented, and the content was either serous, mucous or caseous.

Histopathological examination

For histopathological examination specimens of the most significant parts of both neoplasms were fixed in 10% buffered formalin, embedded

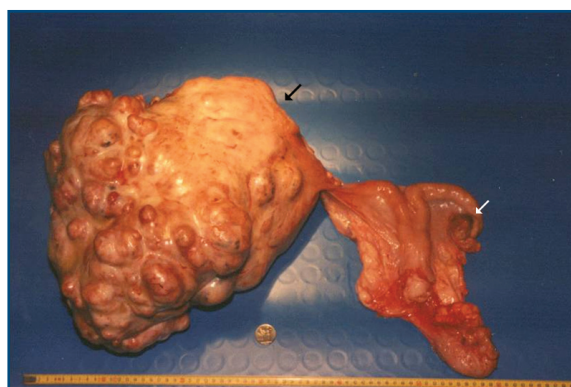


Figure 1. Ovary; heifer, Case No. 2. Macroscopic feature of the right ovary (white arrow), presence of a large follicle; and left ovary (black arrow).

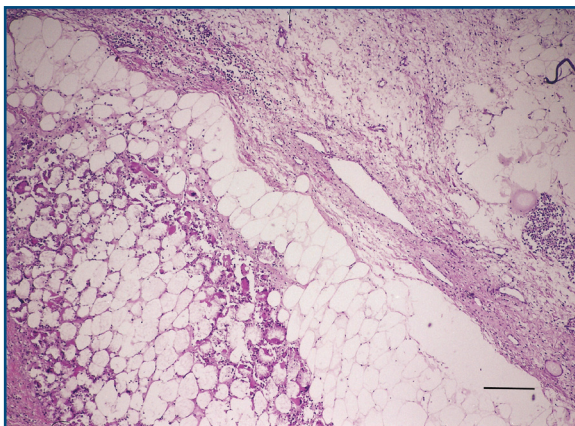


Figure 2. Ovarian teratoma; heifer. Areas of adipo-necrosis (Hematoxylin-Eosin, 4X objective). Bar, 150 μ m.

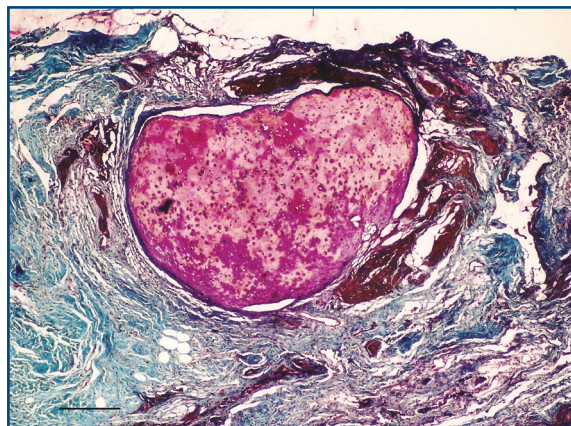


Figure 3. Ovarian teratoma; heifer. Bone enclosed in muscle tissue (Azan-Mallory, 10X). Bar, 100 μ m.

in paraffin, sectioned at 3 μ m and stained with Hematoxylin-Eosin (HE) and Azan Mallory's trichrome stain (AM). Samples with pigmented epithelium was treated with H_2O_2 and potassium permanganate to confirm melanocyte. The histopathological examination revealed in both animals a similar feature. The neoplasm presented a mainly disordered organization with mixture of tissues and an ovarian epithelium that covered surface of tumors. The sections near the ovarian residue confirmed the presence of follicles at different stages of development. Adipose tissue was frequently found, sometimes showing signs of adipo-necrosis with calcification and infiltration of giant cells and lymphoplasmocyte (Figure 2). Connective tissue, at a different stage of maturation, was abundant and with areas of necrosis. Portions of smooth muscle in longitudinal section were often present, the muscle cells predominated over the other components but sometimes they were localized peripherally as cystic structure. In some areas, bone tissue was found embedded in the muscle (Figure 3). Lymphocytic cells were found near glandular or cartilage tissue (Figure 4). Hyaline cartilage was sometimes found near cysts lined by ciliated respiratory epithelium. Some areas showed the presence of nervous tissue, always mixed with other components. Cystic formations lined by skin displayed a differentiated keratinized and stratified squamous epithelium, hair follicle and sebaceous glands. In the lumen, corneous pearls, horny cysts and melanin were found. Ovarian origin was hypothesized accordingly to the anatomic localization. The presence of numerous forms of immature tissue, the necrotic areas around the neoplasm, the infiltration of the fibrous capsule by proliferating tissues, and the thinning in the capsule, supported the diagnosis of malignant tumor in both the heifers. The presence of nervous tissue confirmed the diagnosis of ovarian immature teratoma.

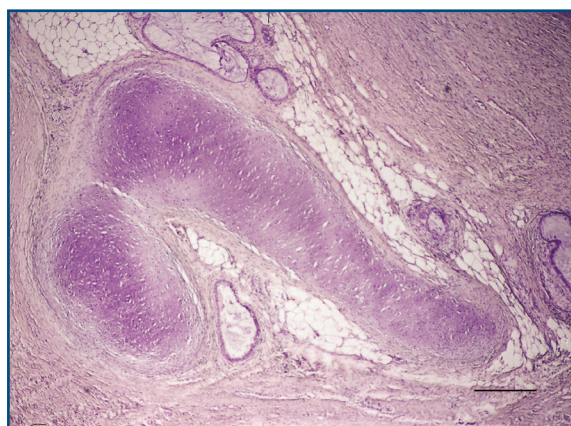


Figure 4. Ovarian teratoma; heifer. Hyaline cartilage with gland formations (Hematoxylin-Eosin, 4X objective). Bar, 200 μ m.

Discussion

In this study two cases of ovarian immature teratoma in heifer was reported. The ovarian origin of these masses was hypothesized accordingly to the anatomic localization and was demonstrated by the presence of ovarian tissue residues, with different degree of follicular development. Ovarian teratoma is a occasional ovarian tumor in domestic animals. However, differently to the human in which the incidence in the female population was reported, in the domestic and non-domestic animals the occasional detection of this neoplasm makes arduous the study of the epidemiology in animals. In a study on 110 zebu cows, in which the age was not reported, two cases of teratomas, one bilateral and the other one on right ovary, were reported (Ali *et al.* 2006), but this percentage (1.8%) could be affected by a selection of the cases recorded. According to other reports, in our study ovarian teratoma was recorded and diagnosed in this study slightly after puberty (Mcintosh 1949, Thiel and Weingartener 1984, Oliveira *et al.* 2004, Tachibana *et al.* 2010),

supporting the hypothesis that this neoplastic degeneration occurs during the fetal stage of the development (Crum 1999).

The ovarian immature teratoma is a rare form of germ cell tumor in the female. In human, it was estimated that only the 1% of the teratomas, the 1% of the all ovarian cancer and the 35.6-40.3% of the malignant ovarian germ cell tumors (Tewari et al. 2000, Smith et al. 2006).

As previously reported in human (Woodroff et al. 1968, Norris et al. 1976, Schlafer and Miller 2008, Alwazzan et al. 2015), the mass of both heifers contained three primary embryonic germ cell layers (endoderm, ectoderm and mesoderm).

In human the immature teratoma is the unique ovarian germ cell tumor in which a grading was proposed, based mainly on the proportion of tissue with immature neural tissue (Norris et al. 1976). In

our study the portion of the mass with neural tissue was limited in both the heifers, however the amount of different immature tissue, the necrotic areas around the neoplasm, the infiltration of the fibrous capsule by proliferating tissues, and the thinning of the capsule, strongly suggested the presence of an immature form. Although the occurrence of metastasis was sporadic, immature teratoma is considered malignant in human (Amsalem et al. 2004). In this study no evidence of metastatic diffusion of the tumor were found in other organs in the slaughtered heifer, while in the SH no evident signs of disease in other organs were found. In the authors knowledge, this is the first report of immature teratoma in the bovine. However, the size and the macroscopic aspect of the masses were unable to distinguish between mature and immature teratoma, and an histological evaluation is required to formulate a correct diagnosis.

References

- Ali R., Raza H.A., Jabbar A. & Rasool M.H. 2006. Pathological studies on reproductive organs of zebu cow. *Journal of Agriculture and Social Science*, **2**, 91-95.
- Basaraba R.J., Kraft S.L., Andrews G.A., Leipold H.W. & Small D. 1998. An ovarian teratoma in a cat. *Veterinary Pathology*, **35**, 141-144.
- Cox J.E. 1987. Surgery of the reproductive tract in large animals. 3rd ed. Liverpool University Press, Liverpool, 145-169.
- Crum C.P. 1999. Female genital tract-ovarian tumors. In Cohan RS, Kumar V, Collins T, eds. *Robbins Pathologic Basis of Disease*. 6th ed. Philadelphia: WB Saunders Co, 963-964.
- Czernobilsky B. & Lifchitz-Mercer B. 1990. The ovary and fallopian tube. In Silverberg SG, ed. *Principles and Practice of Surgical Pathology*. New York: Churchill Livingstone, 1806-1808.
- Dehner L.P., Norris H.J., Garner F.M. & Taylor H.B. 1970. Comparative pathology of ovarian neoplasm. III. Germ cell tumor of canine, bovine, feline, rodent and human species. *Journal of Comparative Pathology*, **80**, 299-306.
- Linder D., McCaw B.K. & Hecht F. 1975. Parthenogenic origin of benign ovarian teratomas. *The New England Journal of Medicine*, **292**, 63-66.
- Mcintosh R.A. 1949. An enormous ovarian teratoma (Hereford heifer). *Representative Ontario Veterinary College*, **29**, 128-130.
- Oliveira F.G., Dozortsev D., Diamond M.P., Fracasso A., Abdelmassih S., Abdelmassih V., Goncalves S.P., Abdelmassih R. & Nagy Z.P. 2004. Evidence of parthenogenetic origin of ovarian teratoma: case report. *Human Reproduction*, **19**, 1867-1870.
- Piano G., Raimondi V. & Piras M. 2002. Teratoma ovarico mature in una cagna. *Veterinaria*, **16**, 101-104.
- Schlafer D.H. & Miller R.B. 2008. Female genital system. In Maxie MG (Ed) *Jubb, Kennedy and Palmer's Pathology of Domestic Animals* (5th ed). London: Saunders Elsevier, **3**, 431-564.
- Tachibana N., Shirakawa T., Ishii K., Takahashi Y., Tanaka K., Arima K., Yoshida T. & Ikeda S. 2010. Expression of various glutamate receptors including N-Methyl-D-Aspartate receptor (NMDAR) in an ovarian teratoma removed from a young woman with anti-NMDAR encephalitis. *Internal Medicine*, **49**, 2167-2173.
- Thiel W. & Weingartner E. 1984. Teratoma in a heifer. *Tierärztliche Praxis*, **12**, 163-166.
- Yamaguchi Y., Sato T., Shibuya H., Tsumagari S. & Suzuki T. 2004. Ovarian teratoma with a formed lent and nonsuppurative inflammation in an old dog. *Pathology*, **66**, 861-864.