Case Report

Infertility caused by oophoritis in a dog resolved by hemiovariectomy

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Abstract

Canine oophoritis is a rare ovarian pathology that has been reported to cause infertility. However, diagnostic work-up, treatment options, and prognosis of return to fertility after treatment for oophoritis were not reported. We report oophoritis in a dog that was diagnosed via histopathology after hemiovariectomy; diagnostic tests, treatment, and outcome of fertility are included and compared to other domestic species and women. Additionally, pathophysiology and prognostic outcome of oophoritis in women are discussed in the context of future directions and possible avenues of investigation in canine oophoritis.

Keywords: Canine oophoritis, infertility, ovarian nodule, hemiovariectomy

Background

Canine infertility is oftentimes a heartbreaking issue for breeders and veterinarians to deal with as there can be multiple facets to this problem. In certain cases, 'apparent infertility' may be due to inappropriate breeding time; it can be addressed by breeding at the most fertile window, 4-6 days after luteinizing hormone (LH) surge, depending on the type of semen utilized, and measuring serial blood progesterone concentrations. Most serious breeders utilize a veterinary team for breeding management to determine the optimal day(s) of estrus to breed. If dogs are bred at optimal day(s), the next step in a diagnostic work up for infertility is assessing semen quality. Good semen quality is > 70% normal morphology and progressive motility with at least 200 x 10^6 progressively motile sperm per breeding dose.[1] After addressing appropriate breeding day(s) and semen quality, brucellosis should be considered; in negative brucellosis cases, determining the cause of infertility is challenging. A possible structural cause for female dog infertility is endometrial degeneration due to cystic endometrial hyperplasia (CEH) in dogs > 5 years or subclinical endometritis. Ovarian and/or uterine pathology was noted in 42/76 dogs presenting for elective ovariohysterectomy that were clinically normal.[2] Most common uterine pathologies observed were CEH, periglandular fibrosis, and endometritis. Most common ovarian pathologies observed were hyperplasia of the rete ovarii, follicular cysts, and oophoritis.[2,3]

Canine oophoritis is a rare ovarian pathology that has been reported to cause infertility. In the past 3 decades, 3 cases[4,5] of canine oophoritis have been reported; a prospective study[2] investigated the prevalence of ovarian and uterine pathology in clinically normal dogs at ovariohysterectomy. We report the diagnosis and treatment of a dog with left ovarian granulomatous oophoritis.

Case presentation

A 5-year, maiden German shepherd dog, was presented in August 2020. The referring veterinarian determined ovulation via measuring serial serum progesterone concentrations. During breeding management, abnormal estrous cycles and shortened interestrous intervals were observed. Abnormalities noted were failure of appropriate progesterone increases above ovulation concentrations and split estrus with an interestrous interval of < 2-3 months. Similar to her dam, this dog had estrous cycles lasting for 21 days and cycled every 4 months.

The first breeding attempt was in November 2019 and ovulation was determined via serum progesterone concentrations (Chemiluminescence, IDEXX, Westbrook, ME). The dog

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tested negative for brucellosis (Rapid slide agglutination test; Zoetis, Parsippany, NJ). The estimated LH surge (2.3 ng/ml of progesterone) occurred on November 16, 2019. However, progesterone concentrations did not increase and the cycle was assumed to be a split estrus. The dog came into proestrus in late December 2019, ~ 4 weeks from the end of previous cycle. Progesterone concentrations never increased > 1.1 ng/ml in the following 20 days. The dog was prescribed compounded mibolerone (Safeway Compounding Pharmacy, Newark, DE) to assist in extending her interestrous interval to have a fertile estrous cycle. Mibolerone treatment was initiated on January 13, 2020 and discontinued on May 7, 2020 when the drug availability became limited. Her next estrous cycle began in July 2020, with proestrus starting on July 9, 2020 and followed via determination of serial progesterone concentrations every 2-4 days until they reached 3.2 ng/ml on August 4, 2020. Testosterone concentrations were 0.1 ng/ml (< 0.1 ng/ml normal for a female dog). Vaginal cytology revealed lack of cornification throughout the cycle. Since the dog had another slow increase in progesterone concentrations she was referred.

Complete blood count and serum chemistry findings were normal. Breeding management consisted of progesterone assay (TOSOH Bioscience AIA 360, San Fransico, CA) and vaginal cytology. Progesterone concentrations on initial presentation were 5.91 ng/ml that suggested potential ovulation; however, her vaginal cytology revealed < 10% cornification with low cellularity. Disagreement between progesterone concentrations and vaginal cytology could not be immediately explained. Transabdominal ultrasonography was performed; the uterus was normal with no cystic endometrial changes. Ovaries were heterogeneous and asymmetrical; the right ovary measured 0.8 x 1.9 cm and the left ovary was 1.8 x 2.5 cm. A single anechoic structure on the right ovary measured 0.2 cm and a hypoechoic nodule in the left ovarian parenchyma measured 1.7 cm (Figure 1A); the left ovarian nodule was vascularized, as evidenced on Doppler ultrasonography. The radiologist labeled the anechoic structure on the right ovary as a potential cyst or cystic functional body. Potential differentials for the left ovary nodule were complicated cyst, atypical functioning body, or neoplasia. The decision was for another progesterone concentrations in 1 week to determine if the estrous cycle would continue to progress.

A week later, the dog was presented for follow up breeding management; her progesterone concentrations had decreased to 2.73 ng/ml (similar to findings on repeat vaginal cytology). A follow up ultrasonography was performed on September 9, 2020. Minimal changes were observed in the left ovary (still enlarged with a 1 x 1.7 cm hypoechoic nodule in the cranial aspect). The nodule appeared more cavitated in the center compared to initial ultrasonography. The right ovary appeared normal (no anechoic structure on reexamination). Mild development of mammary tissue was noticed; due to these findings and lack of change in the nodule, among previous differentials, neoplasia (with granulosa-theca cell tumor) appeared more likely. We suspected left ovarian abnormality as the reason for abnormal estrous cycles. Submitting a sample for antiMüllerian hormone (AMH) to UC Davis versus conserving the dog's breeding potential via hemiovariectomy was discussed. Owners decided to have hemiovariectomy with histopathology submission via referring veterinarian and not to submit a serum sample for AMH.

Treatment

Surgery was scheduled via the referring veterinarian; left hemiovariectomy was performed on September 18, 2020. Surgery and recovery were uneventful. When the ovary was bisected, a cavitated center was identified and a black mucous material oozed from the cut surface (Figure 1B). Histopathology revealed that the structure was not neoplastic; diagnosis was granulomatous oophoritis characterized by lymphocytes, macrophages, plasma cells, fibrosis, and hemorrhage (Figure 1C and 1D).

Outcome

After left hemiovariectomy, the dog came into estrus in January 2021. She was naturally bred based on progesterone concentrations that measured > 20 ng/ml near the end of estrus; this time there was no abnormalities in cyclicity. The dog was diagnosed pregnant on February 25, 2021, and whelped 6 healthy pups on March 26, 2021. Since surgery, the dog whelped and reared 3 healthy litters: 6 (all surviving past weaning), 9 (8 surviving past weaning), and 7 pups (all surviving past weaning) before retiring from the breeding program.

Discussion

It is unclear what caused oophoritis in this case. Oophoritis has been reported[2] to be extremely rare with prevalence of 6.6-7.9% in 42/76 clinically healthy dogs with reproductive abnormalities at ovariohysterectomy. In other species (e.g. pigs and cattle) oophoritis has been linked with modified-live vaccinations of pseudorabies,[6] infectious bovine rhinotracheitis,[7] and noncytopathogenic bovine pestivirus (bovine viral diarrhea virus).[8,9] In mares, extremely rare cases of oophoritis or salpingo-oophoritis were reported in repeated transvaginal aspiration of oocytes.[10–12] In dogs, oophoritis was reported in a 3.5-year Rhodesian ridgeback[4] that had prolonged estrus and an abnormal corpus luteal structure with inflammatory invasion leading to luteal insufficiency. Oophoritis[5] causing primary anestrus in 2 dogs has been reported, but none presented ultrasonographic structure as we have described.

In women, oophoritis may be more common, albeit still rare, as there is more information available on lymphoplasmacytic oophoritis in women. The most common presentation and clinical history in women with oophoritis is premature ovarian failure, also known as premature ovarian insufficiency/dysfunction or premature menopause, affecting 1–2% of all women; autoimmune oophoritis is thought to cause 5% of POI cases.[13–18] Clinical signs of premature ovarian insufficiency (POI) in nulligravid to multigravid women < 40 years was amenorrhea (at least for 4 months); women commonly had pelvic pain, hot flashes, low libido, vaginal dryness, infertility, and changes in their menses cycle. Hormonal profiles of these women were hypergonadotropic hypogonadism characterized by hypoestrogenism (< 50 pg/ml), hypoandrogenism, and elevated (> 40 IU/ml) follicle-stimulating hormone (FSH) concentrations were on 2 occasions, 1 month apart. Most women had a medical history of either having autoimmune thyroiditis (Hashimoto's) and adrenal insufficiency (Addison's) known as autoimmune polyendocrine syndrome types I and II.[13–19] Studies suggested that 80% of women that had Addison's disease usually developed autoantibodies against CYP21-α-hydroxylase, CYP11, or CYP17-α-hydroxylase in the adrenal cortex and ovary.[20–26] This caused a selective

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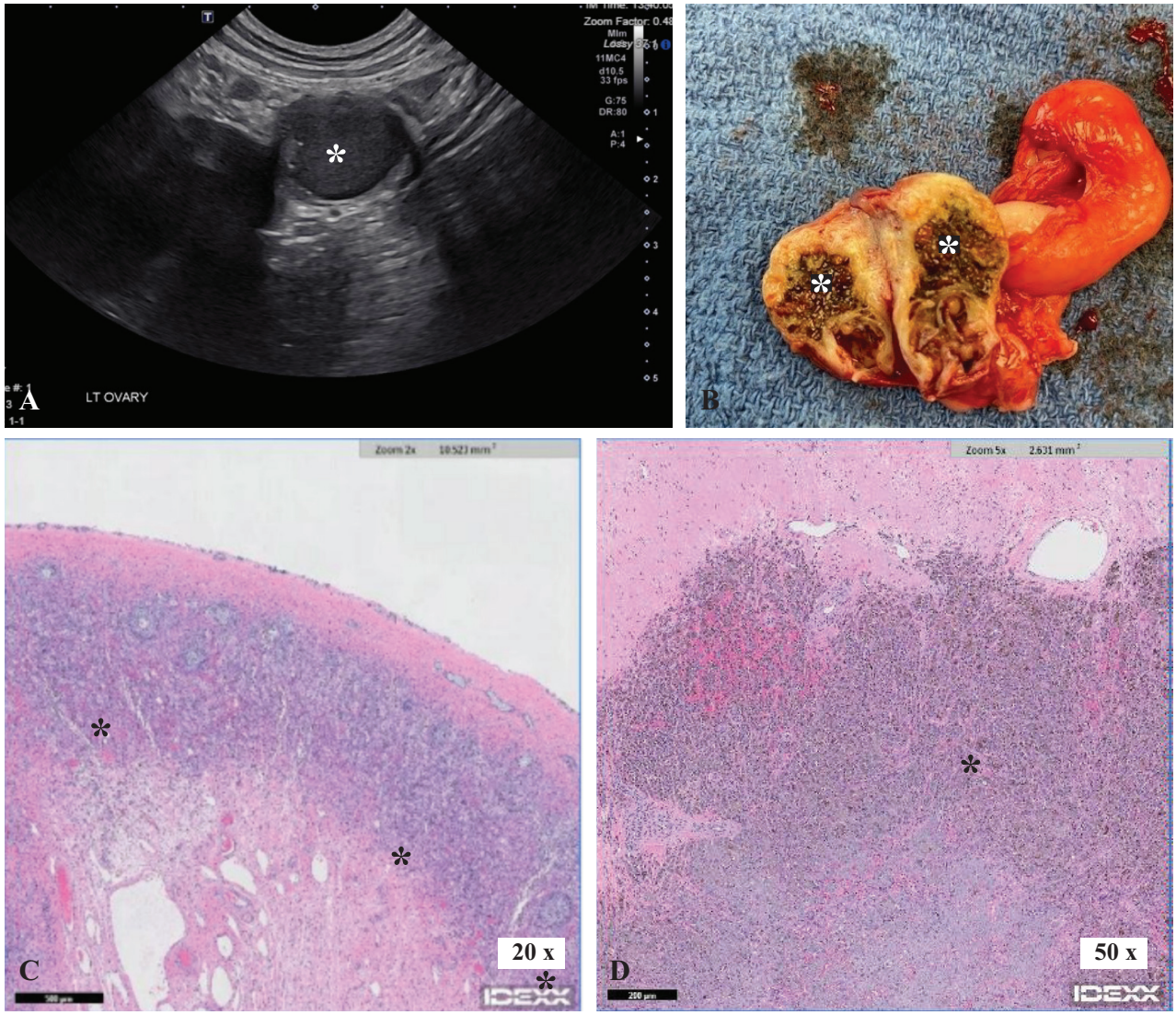

Figure 1. A. Ultrasonographic image of left ovary (craniocaudal view), note hypoechoic structure measuring 1 x 1.7 cm (asterisk) that remained consistent in size at reexamination; B. left ovary bisected after hemiovariectomy, note dark pedunculated mass containing debris (asterisks); and C and D. histopathologic (H&E stain) confirmation of granulomatous oophoritis (asterisks).

theca cell dysfunction in the ovary leading to decreased steroid production (diminished androstenedione and estrone precursors) and hypoestrogenism. Not only was steroid production affected due to the autoantibodies, lymphoplasmacytic destruction occurred primarily in secondary and Graafian follicles that have theca interna and externa layers, initially sparing primordial and primary follicles. Autoantibodies against oocytes ooplasma were identified in surveillance studies in cattle[27–29] presenting for infertility and in thymectomized mice studies.[30,31] Autoimmune oophoritis was definitively diagnosed solely through ovarian biopsy and histopathology (as in the case). Research to correlate less invasive testing with oophoritis diagnosis suggested testing for autoantibodies against CYP21-α-hydroxylase using enzyme linked immunoassay or indirect immunofluorescence.[19] Others have diagnosed salpingo-oophoritis via laparoscopy,[32] ovarian cytology,[33] and ultrasonography.

Approximately 20% of women with POI and autoimmune oophoritis experience spontaneous ovulations, with 5-10% of these women conceiving naturally and delivering a child.[17,19,34]

Apart from hormonal testing of estrogen, progesterone, testosterone, LH, and FSH, ultrasonography is a key feature in the preliminary diagnostic work-up for oophoritis.[35–37] Ovarian presentations were enlargement, asymmetry, multiple or singular cystic structures, or lack of follicular development;[20] it was theorized that the pathogenesis for women who developed multiple cystic follicles despite low estrogen was due to elevated FSH driving follicular development without estrogen's negative feedback and producing higher concentrations of inhibin B.[20]

Treatment for autoimmune oophoritis is difficult and most often unsuccessful. Most treatment entails assisted reproductive technologies in controlled ovarian hyperstimulation protocols. Protocols utilize gonadotropin-releasing hormone to aid in suppressing FSH, thus increasing ovarian sensitivity and human chorionic gonadotropin[38] for ovulation induction when follicles reach an inducible size (≥ 18 mm). This has limited success as observed in some studies where only 3/15 women ovulated after treatment[38] and might have interfered with spontaneous ovulation in a small subset of women with

POI.[17] Other reproductive laboratories added adjunct therapy,[39] supplementing women with dehydroepiandrosterone sulfate to improve androgen concentrations and secondary increase in estrogen. This group observed success with 5/6 women having ovarian responses of a single follicle and 3/6 resulting in ovulation. Two of the 3 ovulations were spontaneous resulting in pregnancies and delivery of healthy children in both women. Although results were substantial, the success of treatment can be limited depending on the definition of success. Is the definition of success having follicular development, even of a single follicle leading to ovulation or is it conceiving and delivering a child? These varying definitions of success, if not explicitly stated, can have substantial impacts on a patient's expectations and compliance during treatment. Autoimmune oophoritis has been anecdotally treated successfully using glucocorticoids via immunosuppression in the early stages before complete follicle deprivation occurred. Glucocorticoids worked synergistically with controlled ovarian hyperstimulation and increased the success of treatment or return of menses in the short-term.[40,41]

Possible sequelae to oophoritis reported in women are ovarian torsion from large cysts/follicles,[40] adrenal insufficiency within 9 years of POI, osteoporosis, ischemic heart disease, increased risk of mortality, and psychological distress.[13,15–19] Osteoporosis due to hypoestrogenism necessitates estrogen supplementation until menopausal age (50 years) to reduce pathologic fractures.[13,17] As mentioned, autoantibodies against adrenal CYP21-α-hydroxylase is the main etiology causing autoimmune oophoritis.[19] Women with these autoantibodies should be tested for adrenal insufficiency if not already diagnosed to avoid an adrenal crisis during pregnancy. Fasted baseline cortisol and ACTH stimulation tests are poor screening tools, as women in this population tend to have low sensitivity and specificity to these tests.[17] Appropriate diagnosis and management of adrenal insufficiency have to be referred to an endocrinologist and are not discussed here. There are no reports of these sequelae occurring in dogs; however, they cannot be ruled out as a possible presentation for oophoritis.

Pathogenesis of oophoritis is multifactorial with various genetic and environmental components. In women, a hereditary link has been theorized as similar familial history was observed in some patients.[13–15] Other causes of oophoritis are vaccination against human papilloma virus,[13] galactosemia,[13] chemotherapy,[13,16] smoking,[12] mumps,[42,43] and Zika virus.[43,44] Mumps virus caused gonadal infection in 5% of women and 20% of men, with oophoritis reported more often in women affected before puberty.[42] Interestingly, mumps caused transplacental infection of fetuses resulting in offsprings experiencing oligomenorrhea and ovarian hypoplasia.[42] After the Zika virus epidemic in 2015, acute oophoritis and follicular apoptosis occurred in mice after infection with Zika-virus via T lymphocyte-mediated destruction.[42,43,44] Subsequently this was confirmed; however, no difference in oocyte yield, fertilization rate, or blastulation rate were observed between treated and control mice.[43]

It is unclear in this case how or why this dog developed oophoritis, as no pertinent medical history of hypothyroidism or Addison's was mentioned in the record. Furthermore, there is limited information on canine oophoritis to know if a similar pathogenesis occurs as in women. The only familial history mentioned was short interestrous intervals of 4 months. However, since she was a German shepherd dog, short interestrous intervals are fairly common in this breed.[45–47] Research is needed to determine whether there is a link with oophoritis and other endocrine insufficiencies like autoimmune thyroiditis and Addison's in canine patients. To fully elucidate this, a complete thyroid panel with inclusion of autoantibodies could have been performed in this case. However, the inclination to have this bloodwork without any clinical signs was low at initial presentation. Typical Addison's was also ruled out due to normal electrolytes (serum chemistry) and no clinical signs in the history. Testing for atypical Addison's disease was not performed in our case. Additional serum hormonal testing in this case could have been recommended to describe the dog's hormonal status that would include FSH, LH, estrogen, testosterone, and AMH. This would have provided more information in the disease process and would have allowed comparisons to women. However, other hormonal testing was declined in favor for a definitive diagnosis via histopathology after a hemiovariectomy. Although serum estrogen concentrations were not determined, one can suspect hypoestrogenism due to the indirect bioassay obtained via vaginal cytology. Throughout each bleeding episode, no cornification was observed from November 2019 to September 2020 on vaginal cytology and it was consistent with anestrus (low cellularity and low cornification). This provided preliminary evidence of hypoestrogenism in this dog as observed in women with POI. Progesterone concentrations reported previously were possible because of luteinization of the follicular wall without ovulation in any monitored cycle.

Despite the shortcomings of limited serum hormonal assays or endocrine tests, we have documented oophoritis as the cause for estrous cycle abnormalities and infertility. To the authors' knowledge, for the first time, successful treatment and return to fertility in a dog diagnosed with unilateral granulomatous oophoritis is reported.

Learning points

- Oophoritis is a cause of infertility in dogs
- Hemiovariectomy may be curative in unilateral oophoritis
- Dogs can have a successful breeding career after hemiovariectomy

Conflict of interest

None to report.

References

1. Hollinshead FK, Hanlon DW: Factors affecting the reproductive performance of bitches: a prospective cohort study involving 1203 inseminations with fresh and frozen semen. Theriogenology 2017;101:62-72. doi: 10.1016/j.theriogenology.2017.06.021
2. Maya-Pulgarin D, Gonzalez-Dominguez MS, Aranzazu-Taborda D, et al: Histopathologic findings in uteri and ovaries collected from clinically healthy dogs at elective ovariohysterectomy: a cross-sectional study. J Vet Sci 2017;18:407-414. doi: 10.4142/jvs.2017.18.3.407
3. Sasidharan JK, Patra MK, Singh LK, et al: Ovarian cysts in the bitch: an update. Top Companion Anim Med 2021;43:1-7. doi: 10.1016/j.tcam.2021.100511
4. Nickel R, Okkens AC, van der Gaag I, et al: Oophoritis in a dog with abnormal corpus luteum function. Vet Rec 1991;128: 333-334. doi: 10.1136/vr.128.14.333

5. Johnston S: Premature gonadal failure in female dogs and cats. J Reprod Fertil 1989;39:65-72.
6. Parker RF, Foley GL, Dangler CA, et al: Necrotic oophoritis in gilts associated with experimental inoculation of a viral gene-deletion mutant pseudorabies vaccine. Vet Pathol 1997;34:199-203. doi: 10.1177/030098589703400304
7. Smith P, Nusbaum KE, Kwapien RP, et al: Necrotic oophoritis in heifers vaccinated intravenously with infectious bovine rhinotracheitis virus vaccine during estrus. Am J Vet Res 1990;51:969-972. doi: 10.2460/ajvr.1990.51.07.969
8. Grooms DL, Brock KV, Ward LA: Detection of bovine viral diarrhea virus in the ovaries of cattle acutely infected with bovine viral diarrhea virus. J Vet Diagn Invest 1998;10:125-129. doi: 10.1177/104063879801000201
9. McGowan MR, Kafi M, Kirkland PD, et al: Studies of the pathogenesis of bovine pestivirus-induced ovarian dysfunction in superovulated dairy cattle. Theriogenology 2003;59:1051-1066. doi: 10.1016/S0093-691X(02)01136-6
10. Bogh IB, Brink P, Jensen HE, et al: Ovarian function and morphology in the mare after multiple follicular punctures. Equine Vet J 2003;35:575-579. doi: 10.2746/042516403775467243
11. Hawkins K: Bilateral salpingitis, hydrosalpinx and oophoritis in a mare. Cornell Vet 1986;76:38-48.
12. Velez IC, Arnold C, Jacobson CC, et al: Effects of repeated transvaginal aspiration of immature follicles on mare health and ovarian status. Equine Vet J 2012;44:78-83. doi: 10.1111/j.2042-3306.2012.00606.x
13. Jankowska K: Premature ovarian failure. Menopause Rev 2017;16:51-56. doi: 10.5114/pm.2017.68592
14. Alekberova Z, Goloeva R, Popkova T, et al: Pregnancy outcomes in systemic lupus erythematosus (SLE). BMJ Sci Abstr 2021; 9:1072 AB0086.
15. Silva CA, Yamakami LYS, Aikawa NE, et al: Autoimmune primary ovarian insufficiency. Autoimmun Rev 2014;13:427-430. doi: 10.1016/j.autrev.2014.01.003
16. Luborsky JL, Tung KS: Oophoritis. In: Rose NR, Mckay IR: editors. The Autoimmune Diseases. 4th edition, Cambridge; Academic Press: 2006. p. 849-859. doi: 10.1016/B978-012595961-2/50064-0
17. Nelson LM, Covington SN, Rebar RW: An update: spontaneous premature ovarian failure is not an early menopause. Fertil Steril 2005;83:1327-1332. doi: 10.1016/j.fertnstert.2004.11.059
18. Welt CK: Autoimmune oophoritis in the adolescent. Ann NY Acad Sci 2008;1135:118-122. doi: 10.1196/annals.1429.006
19. Warren BD, Kinsey WK, McGinnis LK, et al: Ovarian autoimmune disease: clinical concepts and animal models. Cell Mol Immunol 2014;14:510-521. doi: 10.1038/cmi.2014.97
20. Welt CK, Falorni A, Taylor AE, et al: Selective theca cell dysfunction in autoimmune oophoritis results in multifollicular development, decreased estradiol, and elevated inhibin B levels. J Clin Endocrinol Metab 2005;90:3069-3076. doi: 10.1210/jc.2004-1985
21. Tong ZB, Otsuka N, Tu W, et al: P450 side-chain cleavage enzyme (P450-scc) is an ovarian autoantigen in a mouse model for autoimmune oophoritis. Reprod Sci 2022;29:2391-2400. doi: 10.1007/s43032-022-00970-7
22. Bagavant H, Adams S, Terranova P, et al: Autoimmune ovarian inflammation triggered by proinflammatory (Th1) T cells is compatible with normal ovarian function in mice. Biol Reprod 1999;61:635-642. doi: 10.1095/biolreprod61.3.635
23. Altuntas CZ, Johnson JM, Touhy VK: Autoimmune targeted disruption of the pituitary-ovarian axis causes premature ovarian failure. J Immunol 2006;177:1988-1996. doi: 10.4049/jimmunol.177.3.1988
24. Ebrahimi M, Asbagh FA: The role of autoimmunity in premature ovarian failure. Iran J Reprod Med 2015;13:461-472.
25. Bakalov VK, Anasti JN, Calis KA, et al: Autoimmune oophoritis as a mechanism of follicular dysfunction in women with 46, XX spontaneous premature ovarian failure. Fertil Steril 2005;84:958-965. doi: 10.1016/j.fertnstert.2005.04.060
26. Damjanovic MA, Jankovic BD: Experimental autoimmune oophoritis. I. Inhibition of fertility in rats isoimmunized with homogenates of ovary. Am J Reprod Immunol 1989;20:1-8. doi: 10.1111/j.1600-0897.1989.tb00628.x
27. Hunter AG: Immunology and fertility in the bovine. J Dairy Sci 1989;72:3353-3362. doi: 10.3168/jds.S0022-0302(89)79498-4
28. Farin PW, Estill CT: Infertility due to abnormalities of the ovaries in cattle. Vet Clin North Am Food Anim Pract 1993;9:291-308. doi: 10.1016/S0749-0720(15)30647-2
29. Summers PM, Campbell RSF, Dennett DP: Herd studies on the genital pathology of infertile beef cows. Aust Vet J 1974;50:150-154. doi: 10.1111/j.1751-0813.1974.tb06881.x
30. Nishizuka Y, Sakakura T: Thymus and reproduction: sex-linked dysgenesia of the gonad after neonatal thymectomy in mice. Science 1969;166:753-755. doi: 10.1126/science.166.3906.753
31. Taguchi O, Nishizuka Y, Sakakura T, et al: Autoimmune oophoritis in thymectomized mice: detection of circulating antibodies against oocytes. Clin Exp Immunol 1980;40:540-534.
32. Ledger WJ: Laparoscopy in diagnosing and managing patients with suspected salpingo-oophoritis. Am J Obstet Gynecol 1980;138:1012-1016. doi: 10.1016/0002-9378(80)91098-4
33. Piseddu E, Masserdotti C, Milesi C, et al: Cytologic features of normal canine ovaries in different stages of estrus with histologic comparison. Vet Clin Pathol 2012;41:396-404. doi: 10.1111/j.1939-165X.2012.00453.x
34. Ayala C, Celis ME: Experimental autoimmune oophoritis and α-melanocyte-stimulating hormone. Expert Rev Endocr Metab 2010;5:539-547. doi: 10.1586/eem.10.11
35. Patrelli T, Franchi L, Gizzo S, et al: Can the impact of pelvic inflammatory disease on fertility be prevented? Epidemiology, clinical features and surgical treatment: evolution over 8 years. J Reprod Med 2013;58:425-433.
36. Singh N, Tripathi R, Mala YM, et al: Xanthomatous oophoritis following uterine artery embolization: successful conservative surgical management with favourable outcome. BMJ Case Rep 2013;2013:1-5. doi: 10.1136/bcr-2013-010184
37. Torre A, Amado A, Joao D, et al: Xanthogranulomatous salpingo-oophoritis presenting as an ovarian tumor. BMJ Case Rep 2022;15:1-4. doi: 10.1136/bcr-2021-248197
38. Van Kasteren Y, Hoek A, Schoemaker J: Ovulation induction in premature ovarian failure: a placebo-controlled randomized trial combining pituitary suppression with gonadal stimulation. Fertil Steril 1995;64:273-278. doi: 10.1016/S0015-0282(16)57722-X
39. Gleicher N, Darmon S, Molinari E, et al: A form of secondary ovarian insufficiency (SOI) due to adrenal hypoandrogenism as

new infertility diagnosis. Endocrine 2021;72:260-267. doi: 10.1007/s12020-020-02512-0
40. Bradbury R, McLean M, Smith H: Successful live birth following a short course of glucocorticoid suppression in a patient with autoimmune polyglandular syndrome type 2 and premature ovarian insufficiency: A case report. J Obstet Gynaecol Res 2023;49:2194-2198. doi: 10.1111/jog.15684
41. Kalantaridou SN, Braddock DT, Patronas NJ, et al: Treatment of autoimmune premature ovarian failure. Hum Reprod 1999;14: 1777-1782. doi: 10.1093/humrep/14.7.1777
42. Morrison J, Givens JR, Wiser WL, et al: Mumps oophoritis: a cause of premature menopause. Fertil Steril 1975;26:655-659. doi: 10.1016/S0015-0282(16)41233-1
43. Caine EA, Scheaffer SM, Broughton DE, et al: Zika virus causes acute infection and inflammation in the ovary of mice without apparent defects in fertility. J Infect Dis 2019;220:1904-1914. doi: 10.1093/infdis/jiz239
44. Broughton DE, Schaeffer S, Halabi J, et al: Zika virus causes acute oophoritis mediated by T lymphocytes in a mouse model. Fertil Steril PCRS Abstracts 2018;109:e4-e5. doi: 10.1016/j.fertnstert. 2018.02.019
45. Sokolowski JH, Stover DG, Van Ravenswaay OF: Seasonal incidence of estrus and interestrous interval for bitches of seven breeds. J Am Vet Med Assoc 1970;171:271-273.
46. Christie DW, Bell ET: Some observations on the seasonal incidence and frequency of oestrus in breeding bitches in Britain. J Small Anim Pract 1971;12:159-167. doi: 10.1111/j.1748-5827. 1971.tb06213.x
47. Sokolowski JH: Reproductive patterns in the bitch. Vet Clin North Am 1977;7:653-666. doi: 10.1016/S0091-0279(77)50076-7