

ENDOMETRIAL POLYP WITH ENDOMETRIAL HYPERPLASIA & CHRONIC INFLAMMATION IN RABBITS

Asmaa Sh.Aliawy

Department of internal medicine, College of veterinary medicine, University of
Basrah, Basrah, Iraq

(Received 12 May 2012 , Accepted 9 June 2009)

Keywords; Rabbits, polyp, Uterine.

ABSTRACT

Rabbits were treated with large doses of progesterone for up to 420 days developed numerous cysts of the endometrial, sometimes associated with atypical. Histological examination was performed on uterine biopsy samples of irregular cystic (polyp) masses noted. During caesarean section of a 2 month –old female Rabbits, Microscopically examination revealed dilated hyperplasia gland with focal back to back appearance, surrounded by spindle, fibrocystic-like cells, stroma, heavy plasma cells infiltration of the endometrial by widely scattered viable and degenerate neutrophils, lymphocytes, and plasma cells admixed with mild amounts of cellular debris and hemorrhage. The endometrial was markedly expanded by many irregular polyps and hyperplastic gland. Grossly one uterus was slightly thickened with pale mucous membranes. Whereas the other uterus had numerous small, 4 mm in diameter, translucent cysts diffusely scattered on the endometrial surface. 2x1.5x1 cm polyp oval, hard, gray-blue smooth surface. Shows pink and bluish thin with small cysts.

INTRODUCTION

Endometrial polyps are common nonmalignant pedunculate polyps are more common than sessile ones uterine polyp is a sessile mass in the inner lining of the uterus, They may have a large flat base (sessile) as be attached to the uterus by an elongated pedicle (pedunculated) sessile nodules protruding into the uterine cavity. They originate as focal hyperplasia of the basal is and develop into benign, localized overgrowths of endometrial tissue covered by epithelium and containing variable amounts of glands, stroma, and blood vessels (1). Recurrence as carcinoma has been reported in <0.5% of benign polyps (2), although they are present in 12-34 % of the uteri containing endometrial carcinoma (3). If endometrial hyperplasia represents an obstacle to fertility in rabbit then developing diagnostic modalities for its detection in live animals will be important. Expulsion of endometrial polyps represents an indirect means of diagnosing endometrial disease, but it would be desirable to detect disease before it reaches the advanced state of polypoid hyperplasia (4). Progesterone initially suppresses estrogen receptor alpha (ER α) and oxytocin receptor (OTR) expression in the endometrial, but exposure of the endometrial to progesterone for 8-10 days down-regulates expression of the PR (5). Endometrial glands may actively secrete fluid into the uterine lumen, and CEH can eventually lead to mucometra, hydrometra or pyometra in middle aged, sexually intact bitches. (6,10) Cystic endometrial hyperplasia can lead to permanent infertility in domestic animals by preventing implantation or fertilization. (11) Cystic endometrial hyperplasia has been commonly described in dogs and cats, and is well characterized in Asian and African elephants, but rarely in other species. (10,11) The etiology and pathogenesis of

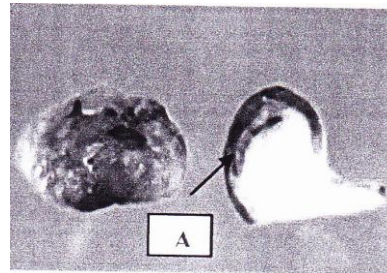
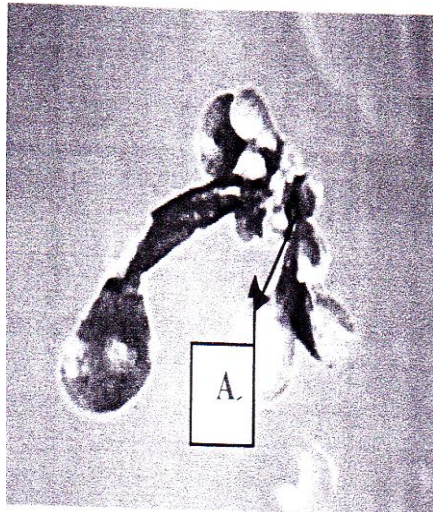
spontaneous cystic endometrial hyperplasia CEH is not fully understood ,although excessive or prolonged hormonal (estrogen or progesterone, or both) stimulation has been shown to play a role in its initiation .In the dogs and cats, progesterone is believed to be the main hormone involved in the pathogenesis of CEH by acting on an estrogen –primed endometrial.(15)Experimentally ,the inoculation of Escherichia coli into the canine uterus at the implantation phase successfully induced CEH and pyometra and CEH was induced in bitches after experimental abrasion of the endometrial .(13,14) in ruminants ,estrogen is usually involved in the pathogenesis of CEH .(9-10)This case report describes a case of endometritis and CEH in a Rabbits endometrial hyperplasia is a condition of excessive proliferation of the cells of the endometrial ,or inner lining of the uterus. Most cases of endometrial hyperplasia result from high levels of estrogens .combined with insufficient levels of the progesterone-like hormones which ordinarily counteract estrogens proliferate effects on this tissue. This may occur in a number of settings ,including polycystic ovary syndrome and certain formulations of estrogen replacement therapy .Endometrial hyperplasia is a significant risk factor for the development of endometrial cancer so careful monitoring and treatment of women with this disorder is essential (16).

Materials and Methods

Female rabbits of mixed breeds were employed .They were obtained commercially ,ostensibly as young virgin adults, averaging slightly over 3Kg in weight .The experiment was started with 11 animals ,5 served as controls, 6 of which were treated with progesterone .They were maintained and fed under identical conditions; and were housed singly .All animals were observed for 10 days beginning injections of hormones. The progesterone preparation was hydroxyl progesterone diluted with sesame oil in a concentration of 125 mg/ml .The i.m. injection of progesterone were given on alternate weeks in doses recommended dose for humans (12.3 mg) .Since the rabbits averaged slightly over 3Kg in weight . the average dose was about 13 mg of the progesterone preparation the uterine biopsy was fixed in 10%neutral buffered formalin and sent for routine histopathologic examination paraffin sections .4µm thick were prepared routinely and stained with hematoxylin and eosin (14).

Results

The duration of treatment to time of death of the animals varied from 172-420 days in the progesterone treated group (Table 1) .The control was followed from 42-283 days .In control animals the tissues were to autolysis to allow interpretation .And 6 progesterone treated animals experimental period the completed all the experiment .Since number of animals died before the termination ,it was possible to study certain changes in various stages of development. Histological examination was performed on two uterine biopsy samples noticed of irregular cystic masses noted during caesarean section of a 2month-old female rabbits in addition ,the uterus contained increased amounts of material viscous fluid .The rabbits were part of a herd of 11 rabbits and had no history of reported abortive or reproductive diseases .All of the endometrial polyps were classical pedunculated nodules protruding into the uterine cavity .The histopathological examination sections show polyploidy endometrial composed of numerous hyperplastic gland ,some with dilatation ,other with mild branching .Squamous metaplasia or Squamous morules is present in a few glands . of all specimens revealed a dense stroma hyperplasia consisting of spindle fibroblast-like cells and abundant collagen fibers in which endometrial gland were underrepresented and pushed toward the periphery of the lesion (Fig 3)



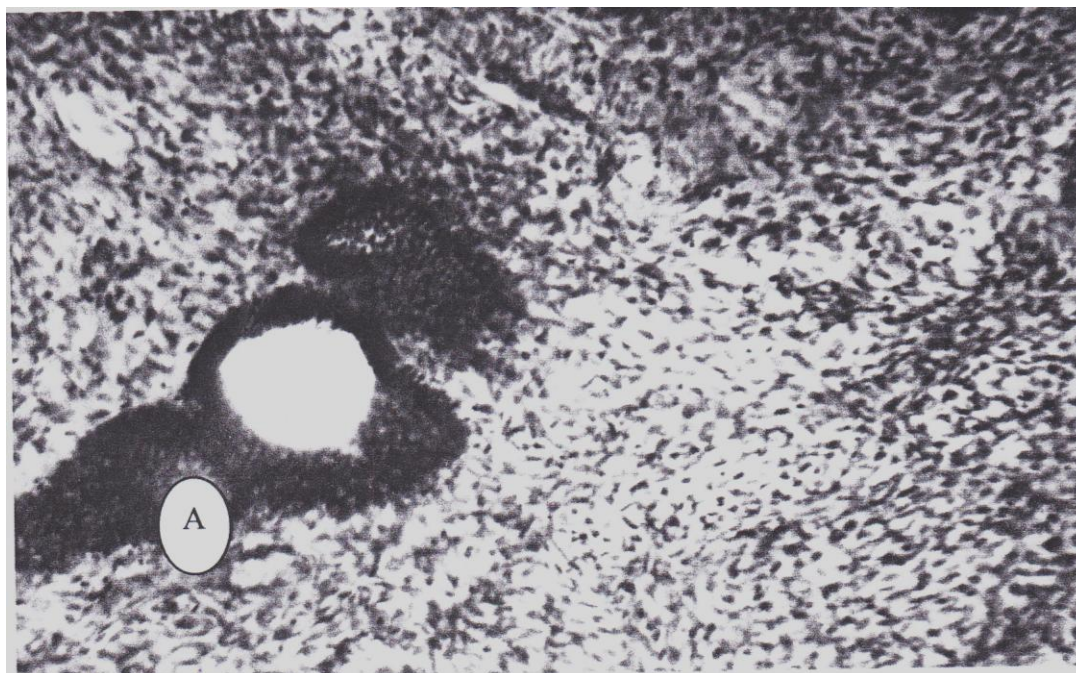
Figures (1) Numerous small ,translucent cysts diffusely scattered .

Histology

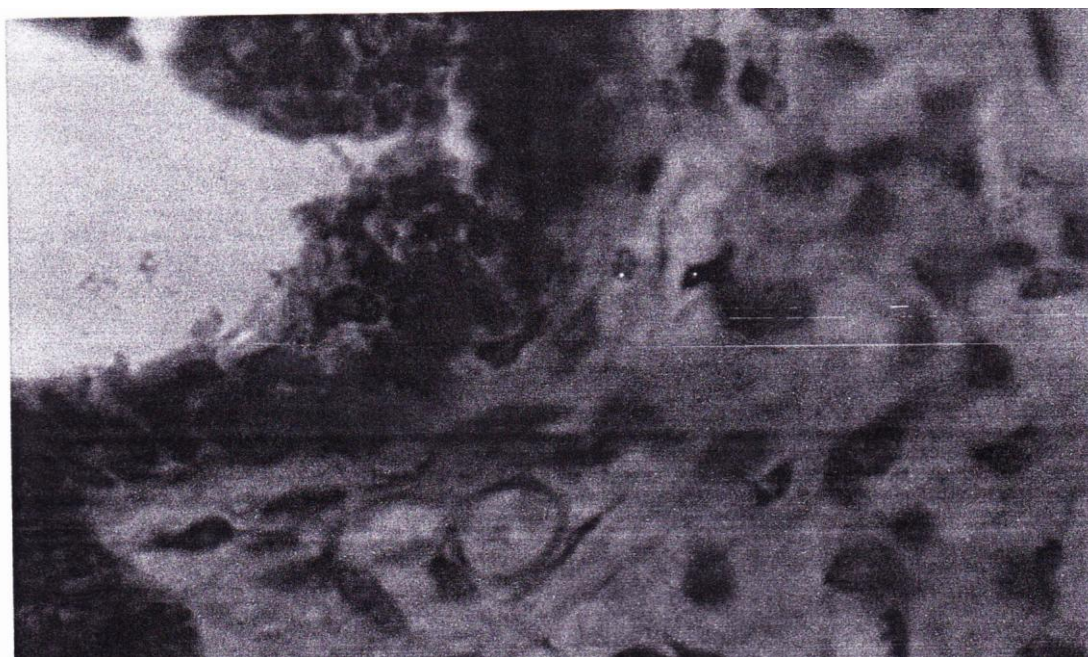
The histological study revealed that endometrial polyp composed are of gland of variable size and shape ,fibro tic stroma and thick –walled blood vessels .The relative amounts of the 3components vary considerably from polyp to polyp .Focal back to tack appearance surrounded by spindle ,fibrocystic –like cells ,stroma ,heavy plasma cells infiltration of the endometrial by widely scattered viable .and degenerate neutrophils, lymphocytes ,and plasma cells admixed with mild amounts of cellular debris and hemorrhage .The endometrial was markedly expanded by many irregular polyp and hyperplasic gland.



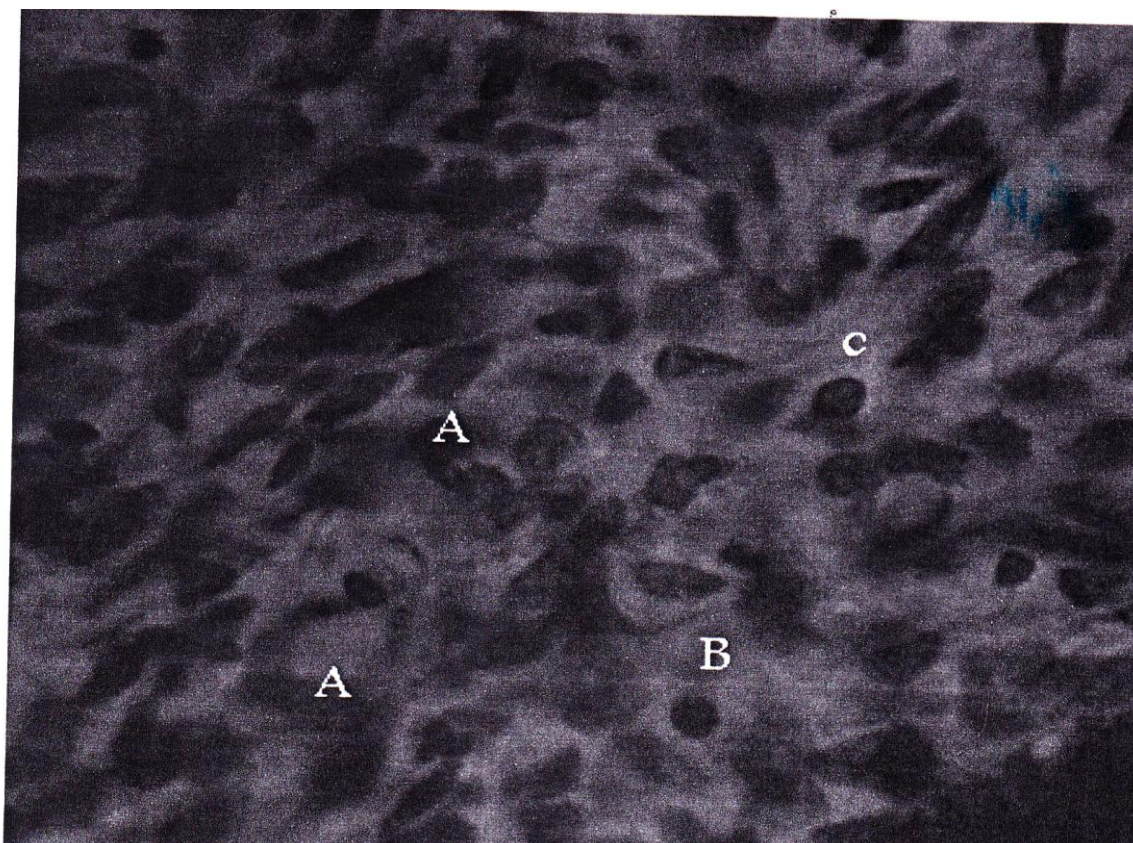
Figures (2) Endometrial polyp many dilated blood vessels are present.



Figures (3) Endometrial polyp (A) hyperplasic glands H&E 100x



Figures (4) Endometrial polyp Hyperplasia & chronic inflammation H&E 800x.



Figures (5) Endometrial polyp(A) Neutrophils, (B) lymphocytes and (C) plasma cells H&E 1000x

Clinical behavior

Endometrial polyps are benign with no malignant potential but malignant tumors may be found in them .When this occurs the prognosis is more favorable provided the tumor has not extended beyond the base.

Table (1): Observation period (days on female Rabbits treated i.m. with progesterone (n=5).

Control 5 Rabbits untreated	Progesterone 26 mg/month (5 rabbits)
42	172
170	260
205	350
226	390(2 animals)
283	420

Progesterone- Treated animals

The endometrial showed dilated blood vessels are present changes in the great majority. Secretary droplets in the cells decreased progressively with the duration of treatment up to 420 days after which secretion in individual cells was no longer found .5 of the 6 cases showed cyst formation .The endometrial cysts were found as early as the 260 days at which time they were small and resembled those seen in the control animals. With increasing duration of treatment, the cysts became progressively larger and more numerous (Fig 2).

In 6 of the animals there was an associated atypical hyperplasia of the epithelium in the endometrial between the cysts .This occurred mostly in older animals ,but was present once after 390 days of therapy (Fig 3) with focal back to tack appearance surrounded by spindly ,fibrocystic –like cells ,stroma ,heavy plasma cell infiltration of the endometrium by widely scattered viable and degenerate neutrophils, lymphocytes and plasma cells admixed with mild amounts of cellular debris and hemorrhage .The endometrial was markedly expanded by many irregular polyps and hyperplasic gland.

DISCUSSION

The most significant finding was the development of prominent endometrial cysts after prolonged progesterone administration .The cysts themselves did not appear either hyper plastic or precancerous but the endometrial between the cysts often showed either mild or atypical hyper plasia .The cystic changes produced in rabbits resembled somewhat the senile endometrial cystic atrophy found in woman (6) ,termed retrogressive polyploidy hrperplasia by Novak and Richardson (7). Although the cystic endometrial changes produced by progesterone therapy were striking ,they were induced only after continuous treatment with depot injections over long period of time and involving large doses the distribution of elastic ,reticular and collagen fibers and their significance in uteri of goats with acute and chronic endometritis has also been investigated (5) In acute endometritis, the reticular and elastic fibers were either few or absent where as in chronic endometritis, the elastic and reticular fibers were less in numbers as compared with controls (8) This change in fiber distribution could possibly be due to bacterial toxins (8).

الأورام الأنبوبية لبطانة الرحم وفرط التنسج والالتهاب المزمن لبطانة الرحم في الأرانب أسماء شرهان زبون العليوي

فرع الطب الباطني والجراحة والتوليد -الطب البيطري،جامعة البصرة،البصرة، العراق.

الخلاصة

عولجت الأرانب بجرعة عالية من البروجسترون لأكثر من 420 يوم لتطور تكيسات متعددة لبطانة الرحم بعض الأحيان تتقرن مع فرط تنسج واضح .الاختبار النسيجي اجري على عينة مستأصلة من الرحم لأكياس غير منتظمة (أورام أنبوبية) كتل واضحة.
أظهر الاختبار بعد عملية قيصرية للأنثى أرنب بعمر 2 شهر ظهور تنسج غدي واسع مع بؤرة سوداء مسمارية الشكل يحاط بخلايا ليفية مغزلية الشكل وانتشاح ثقيل أو كثيف لبلازما خلايا بطانة الرحم متوفر بشكل واسع ومنتشر وتنكس الخلايا القاعدية والمفاوية وخلايا البلازما ممزوجة مع كميات طفيفة لحطام الخلايا ونزف بطانة الرحم معلمة بكثرة ببعض الأورام الأنبوبية (زوائد لحمية) غير المنتظمة وفرط تنسج غدي . ولوحظ عياناً وجود واحد متضخم قليلاً مع غشاء مخاطي شاحب بينما امتلكت الأرحام الأخرى أكياساً متعددة صغيرة بالقطر 4 ملم شفاقة منتشرة بشكل واسع على سطح بطانة الرحم وبأبعاد 1x1.5x2 سم أورام أنبوبية بيضاوية خشنة ذات سطح أملس رصاصي مزرق مع أكياس رقيقة.

REFERENCES

- 1- Kurman ,R.J.,and Mazur, M.T (1987): Benign diseases of the endometrium in .A .Blaustein (ed), Pathology of the female Genital Tract,Ed .3.PP.305-307.New York :Springer-Verlag.
- 2-Salm ,R. (1972): The incidence and significance of early carcinomas in endometrial polyps .J.Pathol., 108:47.

- 3- Gray , L.A.,Rbertson .R.W.,and Christopherson w.M.(1974): Atypical endometrial changes associated with carcinoma .Gynecol.Oncol.,2:93.
- 4- Flatt, R.E. (1969): Pyometra and uterine adenocarcinoma in a rabbits .Lab Anim care .19(3):398-401.
- 5-Spencer ,T.E.;Mirando ,M.A.Mayes ,J.S.;Watson ,G.H.;Ott,T.L.;Bazer, F.w.(1996): Effects of interferon-J and progesterone on estrogen-stimulated expression of receptors for estrogen , progesterone and oxytocin in the endometrium of ovariectomized ewes .Reprod Fertil .Dev.;8:843-853.
- 6-Noer,T.(1961): The Histology of the senile Endometrium.Acta pathol.Microbiol.Scand .,51:193-205.
- 7- Novak,E.,and Richardson ,E.H.(1941):Proliferative changes in the senile Endometrium .Am.J.Obstet/Gynecol.,45:564-79.
- 8- Chand ,S.and Chauhan H.V.S(1975):Distribution of elastic reticular and collagen fibers in uteri of sheep and goats under normal and some pathological conditions .Haryana Agric Univ J Res 1:66-70.
- 9- Feldman ,E.C.and Nelson ,R.W.(1996): Cystic endometrial hyperplasia /pyometra complex In:Canine and Feline endocrinology and reproduction ,ed.Feldman EC,Nelson RW, 2nd ed.,PP.605-618.WB saunders ,Philadelphia ,PA.
- 10- McENtee, K.(1990): Reproductive pathology of domestic animals .Academic press, San Diego, CA.
- 11- Agnew DW, Munson L,Ramsay EC(2003):Cystic endometrial hyperplasia in elephants .Vet pathol 41:179-183.
- 12-Blendinger ,K.;Bostedt, H.and Hoffmann B (1997):Hormonal state and effects of the use of an antiprogesterin in bitches with pyometra.J Reprod Fertil Suppl 51:317-325.
- 13- Nomura ,K.(1983):Canine pyometra with cystic endometrial hyperplasia experimentally induced by E.Coli inoculation .Jpnj Vet Sci 45:237-240.
- 14-Nomura,K.,Kawasoe,K.Shimada,Y.(1990)
:Histological observations of canine endometrial hyperplasia induced by intrauterine scratching .Jpn JVet Sci 52:979-983.
- 15- Yamashita,S.(1998):Localization and functions of steroid hormone receptors.Histol Histopathol 13:255-270.
- 16-Richard,C.;Saul,S.;Lawrence,W.and Noel ,W.(2006):Modern surgical pathology 2 Volum 0:7216-7253-1.