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CANINE SERTOLI CELL TUMOR: CASE REPORT

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Abstract: A 10-year-old male German shepherd dog was diagnosed with Sertoli cell tumor and paraneoplastic feminization syndrome.

INTRODUCTION

The most widely used classification of testicular tumors is based on the cell type from which the tumor is derived, namely, germinal or stromal (Leydig and Sertoli) cells. The Sertoli cell cannot synthesize steroid hormones *de novo* and is dependent on testosterone that diffuses in from adjacent Leydig cells. Sertoli cells can convert testosterone to estradiol and to dihydrotestosterone. The seminiferous tubules also produce the peptide hormone inhibin that regulates the secretion of FSH by the hypothalamic-pituitary axis. Whether inhibin is the primary physiologic regulator of FSH is unclear; testosterone and estradiol can also inhibit FSH scretion, and altered frequency of LHRH pulses can result in selective increases of FSH.

Elevated estradiol and testosterone production in patients with testicular tumors can arise by at least two mechanisms. In trophoblastic tumors and in tumors of Leydig and Sertoli cells the production of both hormones occurs autonomously in the tumor tissue itself; in these instances plasma gonadotropin levels and hormone production by the uninvolved portions of the testes is depressed and azoospermia is uncommon. When potent estrogens and androgens are formed (directly or indirectly) by the tumors, feminization, virilization, or no obvious change may result, depending on the pattern of hormones produced and the age of the patients involved .

Approximately one third of dogs with Sertoli cell tumor will manifest signs of apparent hyperestrogenism, characterized by any combination of feminization, gynecomastia, atrophy of the contralateral testicle, squamous metaplasia within the prostate gland (often with accompanying suppurative prostatitis), symmetrical alopecia, and bone marrow atrophy. The mechanisms for these clinical syndromes have not been completely described. The incidence of feminization increase from approximately 15% with scrotally located Sertoli cell tumors to 70% in abdominally located Sertoli cell tumors.

The first manifestations of a functional Sertoli cell tumor are usually changes in the skin and hair coat. Bilaterally symmetrical alopecia typically starts at the genital area and extends craniodorsally with time. The skin is usually hyperpigmented and the hair is often easily epilated. Microscopically, the epidermis varies from normal thickness to moderately acanthotic, with follicular atrophy and a thin dermis. Approximately one fourth of dogs with feminizing syndrome are attractive to other male dogs similar to a bitch in heat. Redistribution of body fat, gynecomastia with or without mammary secretions and squamous metaplasia of

the prostate are also frequently apparent. Marked squamous metaplasia of the epithelial lining of the ducts and glands of the prostate can lead to glandular obstruction with secondary cyst formation. Secondary infection frequently develops in these cystic glands, and prostatic abscessation may result. In non-metastasized tumors, most of the signs of hyperestrogenism disappear after castration, however, the effects of severe bone marrow suppression may be irrevocable due to the acquisition of secondary disease. Bone marrow effects are initially characterized by transient increased granulocytopoiesis and neutrophilic leukocytosis, followed by decreased hematopoiesis leading to progressive leukopenia, thrombocytopenia, and nonregenerative anemia. The resulting thrombocytopenia may precipitate a hemorrhagic diathesis and overwhelming bacterial infection may occur subsequent to granulocytopenia. These stages of the syndrome are often refractive to treatment and progress to death.

The Sertoli cell tumor is generally the firmest of the canine testicular tumors. These tumors can become quite large and are typically nodular or multinodular to discrete with a diffuse white or gray appearance. Tan or yellow areas of hemorrhage or fluid-filled cysts are occasionally observed. Tumors are histologically sub-classified as intratubular or diffuse, with the diffuse subtype representing a continued progression of the intratubular type to a more infiltrative pattern. The tumor cells are elongate with indistinct borders and oval or spindle shaped nuclei. Their cytoplasm is typically eosinophilic, vacuolated or dense, with lipochrome pigment granules. Both patterns of neoplastic Sertoli cells elicit a sizable fibrous stromal response which often undergoes hyalinization.

Sertoli cell tumors are almost always benign, with the rate of metastasis reportedly less than 10%. Metastasis is more likely to occur in large tumors of the diffuse subtype. The most common site of metastasis are the regional lymph nodes but metastasis to a wide variety of internal organs has also been reported. Metastatic nodules may be hormonally active and typically have a histological appearance similar to the primary tumor.

CASE REPORT

A 10-year-old male German shepherd dog, which had anorexia, was referred for investigation of a two-month history of progressive alopecia, gynecomastia and hyperpigmented skin.

Physical examination showed a large scrotal tumor, a secondary paraneoplastic feminization syndrome (nipple enlargement, pendulous prepuce) and *acanthosis nigricans*. The dog manifested, also alopecia in the genital area (fig.1), and hair loss to the flanks (fig.2). The skin was thin. In addition, the patient had depression and pyrexia.

Because of negative prognosis, the patient was euthanised.

Anatomopatology. Grossly, the *testicular tumor* (fig.3) was several times larger than the normal testis, which was atrophyated. The cut surface bulges and was grayish-white in color.

Microscopically, the pattern was intratubular type of Sertoli cell tumor. The germinal line cells had disappeared.

Fig.1. Alopecia in the genital area

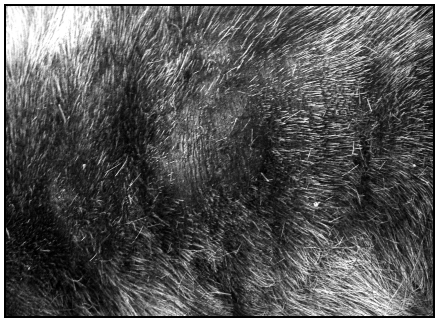

Fig.2. Hair loss to the flanks

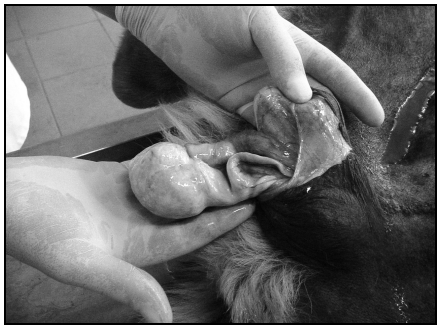

Fig.3. Testicular tumor

Fig.4. Testicular tumor - section

Fig.5. Normal testis - section

The *prostate* showed a characteristic change - marked enlargement (fig.6) owing to the extensive squamous metaplasia of its epithelial elements with the formation of large epiderinoid cysts (estrogen-induced metaplasia) and was infected (pyogranuloma) (fig.7).

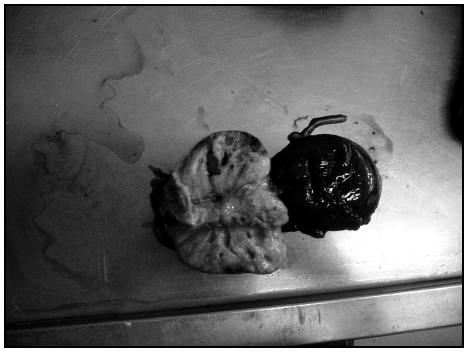

Fig.6. Enlarge of prostate

Fig.7. Prostate - pyogranuloma

Skin biopsy revealed orthokeratotic hyperkeratosis, follicular keratosis and dilatation, follicular atrophy and telogenization of hair follicles, sebaceous gland atrophy.

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