

## CASE REPORT

## Atypical cytomorphologic description of a seminoma in a rabbit

Flavio H. Alonso<sup>1,2</sup> 

<sup>1</sup> Veterinary Medical Teaching Hospital and Department of Pathology, Microbiology and Immunology, School of Veterinary Medicine, University of California, Davis, California, USA

<sup>2</sup> Department of Biomedical Sciences, Ross University School of Veterinary Medicine, Saint Kitts, West Indies

**Correspondence**

Flavio H. Alonso, Department of Biomedical Sciences, Ross University School of Veterinary Medicine, Basseterre, Saint Kitts, West Indies. Email: [flaviohalonso@gmail.com](mailto:flaviohalonso@gmail.com)

Seminoma is reported as a rare disease associated with specific micro-morphologic findings. In the present report, we describe the case of a testicular seminoma in a 7-year-old Holland Lop rabbit, in which the cytology presented an atypical pattern. Upon presentation, the left testicle was severely enlarged, and the patient also had a history of radiation therapy for a previously diagnosed thymoma. Following excision and histopathology of the abnormal organ, results showed a mixed intratubular-diffuse pattern with evidence of torsion. Moreover, cytology revealed a cohesive pattern with multiple malignancy criteria. To our knowledge, this is the first published report of a seminoma with these cytologic features.

**KEYWORDS**

histopathology, lagomorph, malignancy, neoplasia, testicle

**1 | INTRODUCTION**

Seminomas are tumours that arise from germ cells in the testicles. The cause for its development is considered unknown, but cryptorchidism has been reported as a predisposing factor (Hutson et al., 2010; Liao et al., 2009) and other environmental conditions are also speculated to play a role. It is considered a rare disease in any species, but the most common testicular neoplasia in humans and stallions (Agnew & MacLachlan, 2016; Albers et al., 2015). In rabbits, it represents the second most common testicular cancer, after interstitial tumours. (Banco et al., 2012). A total of 10 reported cases in rabbits have been found (Alexandre et al., 2010; Anderson et al., 1990; Banco et al., 2012, 2017; Brown & Stafford, 1989; Rao Veeramachaneni & Vandewoude, 1999; Roccabianca et al., 1999). Breeds included mini Lop, lionhead, Dutch-Belted, New Zealand white, crossbred dwarf and ages upon diagnosis varied from 3 to 10 years. Histopathology divides seminomas into intratubular and diffuse forms based on distribution of neoplastic cells (Agnew & MacLachlan, 2016).

This is, to the best of the author's knowledge, the description of a novel cytomorphologic presentation of seminoma in rabbits or other mammalian species.

**2 | CASE HISTORY**

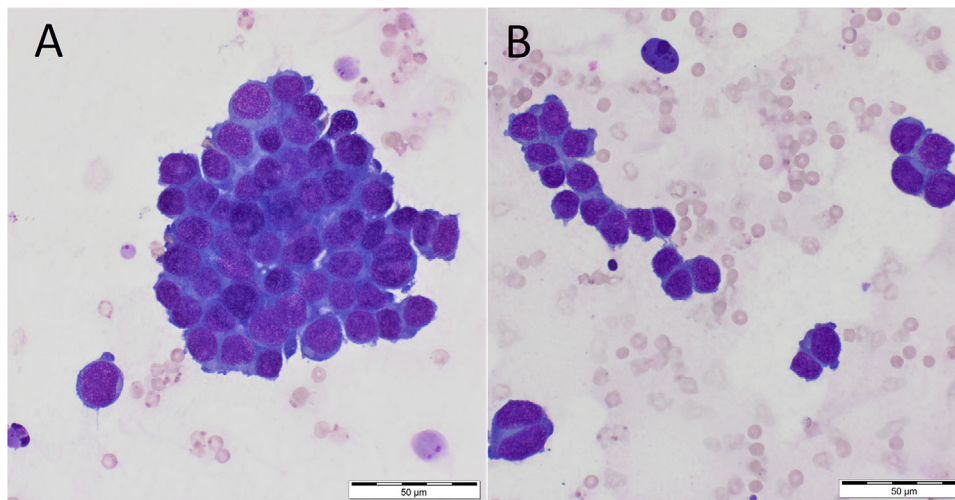
A 7-year-old male intact Holland Lop was presented to the UC Davis Companion Avian and Exotic Pet Medicine Service for pathologic castration. The patient had just recently finished radiation therapy for his thymoma, and also had a history of recently treated right sided congestive heart failure, with grade I-II/VI left sided systolic murmur and mild tricuspid regurgitation. Additional history included resolved exophthalmos, superficial corneal ulcer, and nasolacrimal disease. The third phalanx of the left hind limb had been amputated due to luxation suspected to be secondary to osteomyelitis.

Upon presentation, the patient was moderately under-conditioned (BCS 3/9) and the left testicle was enlarged (30 × 10 × 7 mm). A grade I/VI pododermatitis (Mancinelli et al., 2014) affecting the hind limbs was also noted. The owner reported polyuria and polydipsia as well as one episode of diarrhoea that resolved in 12 h. Mineralization of the aorta was noted on computerized tomography scan.

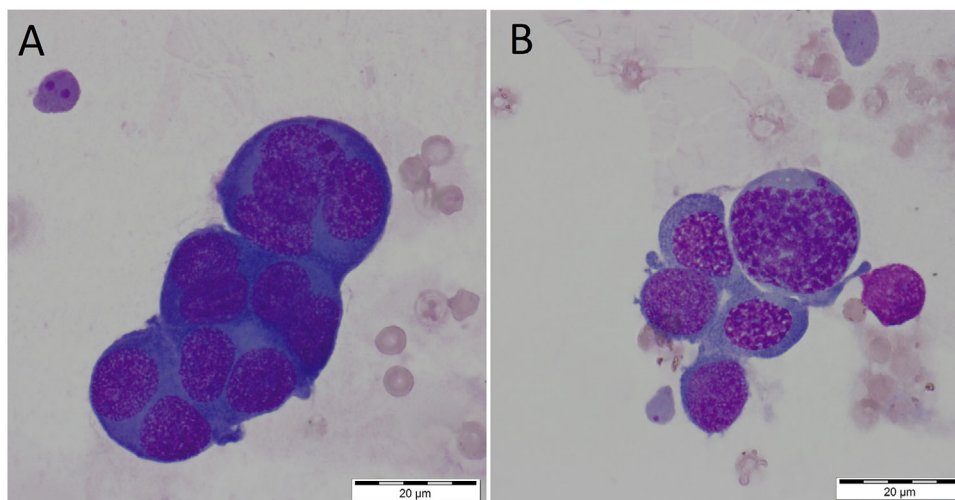
A completed blood count (CBC) was performed, which revealed no abnormalities. The chemistry panel revealed a mild hypoglycaemia (101 mg/dl, reference interval: 109–197), hyponatremia (131 mmol/L, reference interval: 140–148), hyperkalaemia (8.9 mmol/L,

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**FIGURE 1** Micrographs of a fine-needle-aspirate cytology sample of a seminoma in the testicle from a rabbit. (A and B) The sample is highly cellular. The background is pale blue and contains scattered erythrocytes. Large round cells are presented individually or in small cohesive clusters or rafts.

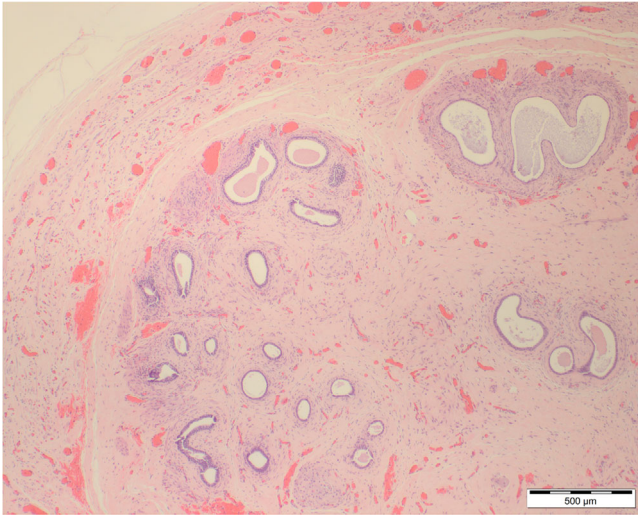


**FIGURE 2** Micrographs of a fine-needle-aspirate cytology sample of a seminoma in the testicle from a rabbit. (a and b) N/C ratios are high, and anisokaryosis and anisocytosis are marked with occasional karyomegalic and multinucleated cells noted. The cytoplasm is scarce and deep blue. Aberrant mitotic and pyknotic figures are also noted.

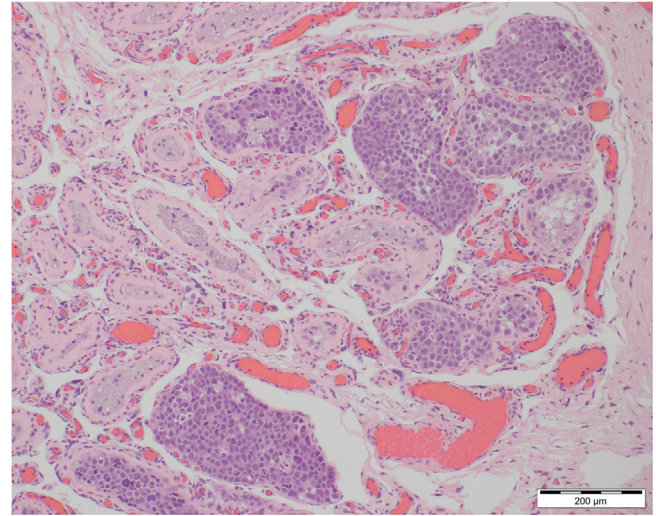
reference interval: 3.6–5.7), mildly and moderately elevated activities of aspartate aminotransferase (AST, 109 IU/L, reference interval: 10–52) and creatine kinase (3278 IU/L, reference interval: 23–950), respectively.

Aspirates of the left testicle were done and submitted for cytological analysis. The sample was highly cellular. The background was pale blue and contained scattered erythrocytes. A low number of large round cells were present individually or in small cohesive clusters or rafts (Figure 1). Nuclei were round to oval to rarely polygonal with rosy to finely stippled chromatin and multiple prominent, and variably sized and shaped nucleoli. N/C ratios were high, and anisokaryosis and anisocytosis were marked with occasional karyomegalic and multinucleated cells noted. Cytoplasm was scarce and deep blue. Aberrant mitotic and pyknotic figures were frequently noted (Figure 2). The sample was interpreted as malignant neoplasia.

After cytological diagnosis, the testicle was surgically excised and submitted for histopathological analysis. Sheets of densely packed neoplastic cells expanded the few remaining scattered seminiferous tubules that were widely separated by sclerotic collagen bundles. These sheets rarely extended beyond the borders of the pre-existing tubules (Figures 3 and 4). Neoplastic cells were round with distinct cell borders, scant to moderate amounts of pale basophilic to amphophilic vacuolated cytoplasm, and a large, round, central nucleus with finely stippled chromatin and 0–3, small magenta nucleoli. Fourteen mitotic figures were seen in five 400x fields; many of which were bizarre. Anisocytosis was moderate, and anisokaryosis was marked with occasional karyomegalic cells. Binucleate neoplastic cells were occasionally observed. Rare scattered apoptotic neoplastic cells were present (Figure 5). The neoplastic process was greater than 5 mm from the closest apparent margin. No recognizable normal seminiferous tubules were



**FIGURE 3** Histopathology micrograph of a seminoma in the testicle from a rabbit. Epididymal ducts are regionally and widely separated by dense bundles of collagen, that represents fibrosis and parenchymal loss associated with the lesion.



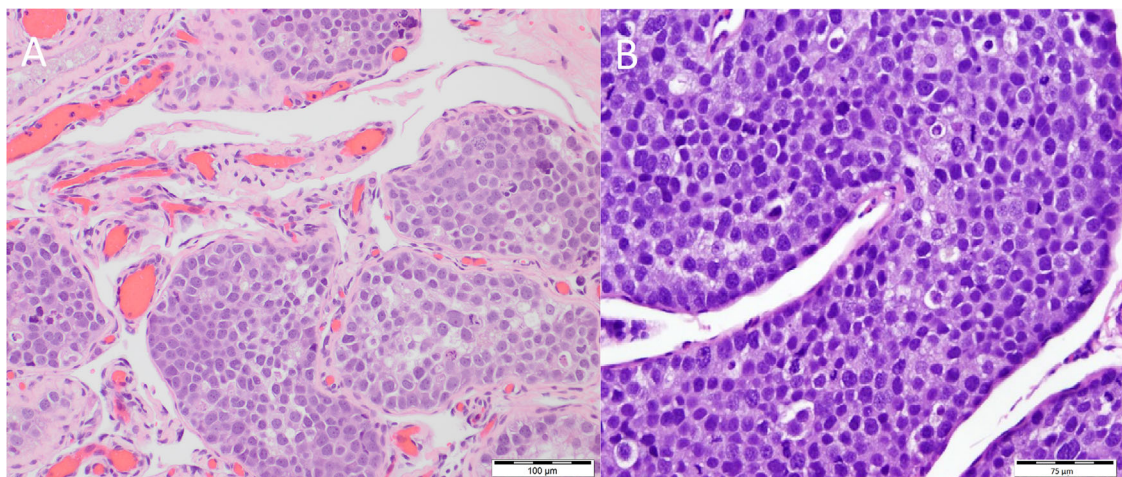
**FIGURE 4** Histopathology micrograph of a seminoma in the testicle from a rabbit. Seminiferous tubules are variably distended with sheets of neoplastic cells or collapsed and filled with pigment laden macrophages.

present, epididymal ducts were empty, and no active spermatogenesis was apparent (Figure 6). Rare veins were dilated webs of fibrillar eosinophilic material (fibrin thrombi). The diagnostic conclusion was a seminoma, of intratubular and diffuse form, fully excised with marked regional parenchymal loss, fibrosis, vascular thrombi, and aspermatogenesis (presumed secondary to torsion).

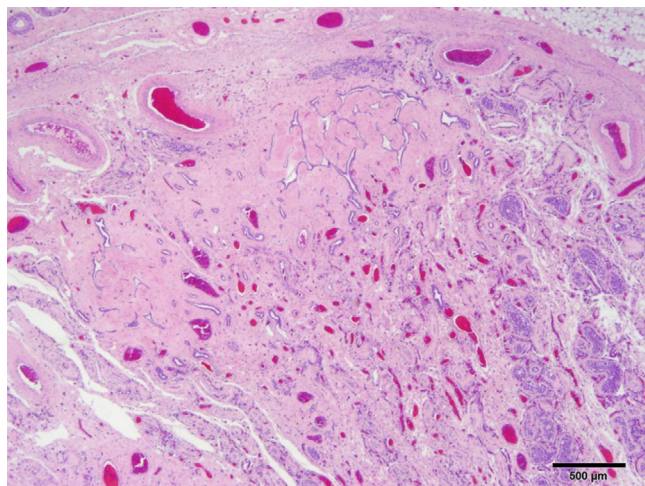
After castration, the patient was discharged with anti-inflammatories (Meloxicam 0.5 mg/kg PO q 12 h) and started on antibiotics (sulfadiazine/trimethoprim 30 mg/kg PO q 12 h) to prevent infection. The owners were recommended to follow up with routine checks, including abdominal ultrasonography and chest radiographs to screen for metastasis.

### 3 | DISCUSSION

On histopathology, seminomas are generally categorized as intratubular or diffuse. Our case exhibited elements of both. Cells can present as sheets of very large and polyhedral cells with sharp borders. Lymphocytic or granulomatous infiltrates may or may not be concurrent. Cells often demonstrate a characteristic diversity in size (small, intermediate, and large), vesicular nuclei and prominent nucleoli, 'blastic' appearance, and scant of dense basophilic or amphophilic cytoplasm. Mitotic figures are numerous and frequently bizarre, occasionally appearing as 'spiremes' or mats of filamentous chromatin (Agnew & MacLachlan, 2016). Carcinoma in-situ can be occasionally recognized (Bush et al.,



**FIGURE 5** Histopathology micrographs of a seminoma in the testicle from a rabbit. (a) Neoplastic cells are round to polygonal with distinct cell borders. They have scant to moderate amounts of pale basophilic to amphophilic vacuolated cytoplasm, and a large, round, central nucleus with finely stippled chromatin and 0-3, small magenta nucleoli. (b) Apoptotic cells are scattered creating a starry sky appearance, and mitotic figures are frequent and occasionally appear as spiremes. Binucleate cells are frequent.



**FIGURE 6** Histopathology micrograph of a seminoma in the testicle from a rabbit. The testicular parenchyma is widely replaced by sclerotic collagen bundles and interspersed with congested blood vessels. Scant remaining seminiferous tubules are expanded by sheets of neoplastic cells and do not show any evidence of spermatogenesis.

2011). On cytology, a distinct smooth and dispersed chromatin pattern is usually noted, along with prominent nucleoli and a significant increase in the mitotic rate.

Thus far, little documentation about the cytomorphology of seminomas among lagomorph is available. The presentation of this current case with cohesive cells is considered atypical when taken into account what is expected for other species, such as the dog (Agnew & MacLachlan, 2016). Because of that, other cytologic differentials ended up being included, such as gonadoblastoma and embryonal carcinoma. The available options for immuno/histochemical labelling that have promising diagnostic utility for seminomas include placental alkaline phosphatase and Periodic acid–Schiff stain.

Orchiectomy with scrotal ablation is usually described as curative when no metastasis is identified. However, other options of therapy including radiation and chemotherapy have also been described in animal patients (Dhaliwal et al., 1999; McDonald et al., 1988).

## PEER REVIEW

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## ORCID

Flavio H. Alonso  <https://orcid.org/0000-0002-0063-3583>

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