Multicentric B-cell lymphoma in a pygmy goat

Multicentrisch B-cellymfoom bij een dwerggeit

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ABSTRACT

A six-year-old, male pygmy goat was referred with a sudden onset of peripheral lymphadenopathy, which initially started as enlarged inguinal lymph nodes. Clinical examination showed swollen retropharyngeal, prescapular and inguinal lymph nodes. Serologic testing for bovine leukemia, caprine arthritis-encephalitis virus and caseous lymphadenitis was negative. Fine needle aspirates of the prescapular lymph nodes were taken and revealed multiple, large lymphoblastic cells on cytology. Because of the poor prognosis and clinical deterioration, the animal was euthanized. Full necropsy was performed and showed generalized lymphadenopathy. Further histological and immunohistochemical investigation of the lymph nodes characterized this neoplasia as a multicentric large B-cell lymphoma.

CASE DESCRIPTION

Case history and clinical examination

A routine consultation with preventive hoof care and deworming was performed, by the referring veterinarian, on two goats. The owner noticed that one of the goats showed signs of anemia and weight loss. On examination, the goat was found to be anemic and had a palpable inguinal lymph node. The owner also noticed that the goat was not eating and had lost weight. A complete blood count was performed, which showed a decrease in red blood cells and a decrease in white blood cells. A lymph node biopsy was performed and revealed a multicentric B-cell lymphoma. The goat was euthanized and a full necropsy was performed.

REFERENCES


Multicentric lymphoma is a sporadic disease in ruminants. It has been described in cattle (De Vliegher et al., 2000; Malatestinic, 2003; Schweizer et al., 2003; Braun et al., 2005; Duncan et al., 2005; Loh, 2007), sheep (Valenti and McDonough, 2003) and goats (Olson and Baumgartner, 1975; Olson et al., 1981a,b; Baker et al., 1982; Bakers and Sherman, 1982; Higges et al., 1984; de Silva et al., 1985; Craig et al., 1986; Smith and Sherman, 1996; Puette and Lalimer, 1997), but also in deer (Madson and Opriessnig, 2009; Klein schmidt et al., 2012; Reissig et al., 2013) and water buffalo (Vale-Echeto, 2009). In goats, as in other species, clinical presentation varies and depends on the localization of the tumor. Predilection sites are liver, spleen, lungs and peripheral lymph nodes (Rozear et al., 1998; Matthews, 1999). The most common associated clinical signs are anorexia, weight loss, depression, fever, dyspnea and peripheral lymphadenopathy (Higges et al., 1984; DiGrassie et al., 1997; Matthews, 1999). The involved cell type has only been reported in two goats, one T- and one B-cell (Rozear et al., 1998, Valentine et al., 2011). In this report, the clinical, pathologic and histologic examination of a six-year-old male goat with multicentric B-cell lymphoma is described.
the goats (male and six years old) seemed more dull recently and showed a stiff gait. A thorough clinical examination was performed, but no significant abnormalities were detected, apart from mild swelling of the left inguinal lymph node. Treatment with 10 mg doramectine (Dectomax©, Pfizer AH, Belgium) and 2 mg dexamethasone (Rapidexon©, Eurovet, Belgium) was started. On a control visit one month later, there was clinical deterioration and the animal demonstrated dysphagia. Clinical examination revealed swollen retropharyngeal, prescapular and inguinal lymph nodes (Figure 1). Complete bloodwork was performed and leukocyte differentiation on a blood smear (Hemacolor®, Merck KGaA, Germany) revealed 43% lymphocytes and 57% neutrophils. No abnormal cells were detected. Blood biochemistry revealed several mild abnormalities and a sharply increased creatine kinase, which was probably due to hemolysis. An abdominal and thoracic ultrasound was performed, but no internal mass or any other abnormality could be visualized. Ultrasound of peripheral lymph nodes showed sharp delineation of these lymph nodes with a homogenous echogenicity. Fine needle aspirates were taken (20G needle, 4 cm long) from the left and right prescapular lymph node for cytological evaluation and stained with Hemacolor® (Merck KGaA, Germany). Both aspirates revealed a monomorphic population of large round cells (20-35µm) with a large dark blue and round nucleus and a small amount of light blue cytoplasm (Figure 2). These cells were identified as lymphoblasts. Since these findings were indicative of lymphoma, it was decided to euthanize the animal.

**Necropsy, histology and immunohistochemistry**

Full necropsy was performed and confirmed the generalized peripheral lymphadenopathy primarily of the prescapular, mandibular, inguinal and popliteal lymph nodes (Figure 3). On closer inspection, enlargement of the deep cervical (lnn. cervicalis profundum, cranialis and caudalis), retropharyngeal (lnn. retropharyngealis) and thoracic lymph nodes (lnn. thoracicum dorsalis and ventralis) was noted. The abdominal lymph nodes of the rumen (lnn. ruminalis), mesenterium (lnn. mesentericum cranialis and ventralis) and aortic lymph nodes (lnn. hemales) were also enlarged. The liver was pale and showed a marked zonal pattern. Gross lesions were not detected in other organs. Within the hour after euthanasia, a bone marrow cytologic sample was taken, using a 18G needle, for a cytologic smear and stained (Hemacolor®, Merck KGaA, Germany). The number of lymphocytes was increased, but no abnormal cells were observed.

Samples of the prescapular lymph node, spleen, lung and liver were fixed in a 4% neutral-buffered formalin, routinely processed and embedded in paraffin. Five-µm-thick sections were mounted and stained with hematoxylin and eosin for histological examination. There were no significant histological abnormalities present in the spleen, lung and liver. The lymph nodes however, had completely lost their normal architecture due to massive infiltration of a monomorphic population of large (12-15µm) neoplastic lymphoblasts. There were mild anisokaryosis and anisocytosis. Mitotic numbers were less than one per ten high power field. The neoplastic population infiltrated the capsule multifocally. Immunolabelling for CD3 (T-cells) and
CD20 (B-cells) was performed as previously described (Vangeel et al., 2012). More than 95% of the cells demonstrated a membranous labeling for CD20, while only a small population of cells were positive for CD3 (Figure 4). Based on these results, this neoplasia was characterized as a multicentric large B-cell lymphoma.

DISCUSSION

Pygmy goats are increasingly popular as companion animals, which increases their lifetime and the amount of veterinary attention demanded by their owners. Lymphoma is the most common tumor in goats, followed by cutaneous squamous cell carcinoma and thymoma (Löhr, 2012). Multicentric lymphoma is the most common type of caprine lymphoma (De Silva et al., 1985; Craig et al., 1986 and DiGrassie, 1997 and Löhr, 2012). Age ranges from one to nine years and no breed or gender predilection has been detected so far (Löhr, 2012). The most common clinical sign is loss of normal body condition (Higgins et al., 1984; Craig et al., 1986 and DiGrassie et al., 1997). General peripheral lymphadenopathy, as described in the present case, is not a consistent clinical finding, but has been described in other cases (Baker and Sherman, 1982; Higgins et al., 1984; De Silva et al., 1985; Craig et al., 1986; Di-Grassie et al., 1997; Guedes et al., 1998). Other clinical signs are variable and related to the localization of the tumor. Involvement of the head with mandibular and maxillary bone swelling as well as conjunctival swelling or exophthalmos have been described (Baker and Sherman, 1982; De Silva et al., 1985; Craig et al., 1986; Guedes et al., 1998; Valentine et al., 2011). Paraparesis has been reported in a case of lymphoma with involvement of the spinal cord (Gygi et al., 2004).

In this case report, fine needle aspirates of two enlarged peripheral lymph nodes were taken for cytologic evaluation and proved to be accurate for the diagnosis of lymphoma. Since fine needle aspiration is minimally invasive, does not require patient sedation, is rapidly performed and inexpensive, it is commonly used in humans and dogs for the diagnosis of non-Hodgkin’s lymphoma/leukemia (Caniatti et al., 1996; Young et al., 1998; Culmse et al., 2001; Dong et al., 2001; Zeppa et al., 2003; Bangerter et al. 2007). In cattle, it was demonstrated that fine needle aspiration of enlarged peripheral lymph nodes is more specific than core needle biopsy of enlarged peripheral lymph nodes for the ante mortem diagnosis of enzootic bovine lymphosarcoma (Washburn et al., 2007). In goats, this technique has seldom been reported (Baker et al., 1982; de Silva, 1985), but it is a useful tool for practitioners. Furthermore, it is the experience of the authors that unstained cytological specimens can be used for immunophenotyping.

Table 1. Hematology and biochemistry results in a 6 year old male pygmy goat with multicentric large B-cell lymphoma.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Result 28/08</th>
<th>Result 12/09</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematology</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hematocrit</td>
<td>152 ml/l</td>
<td>220 ml/l</td>
<td>300-400 ml/l</td>
</tr>
<tr>
<td>Leukocytes</td>
<td>26,9 x 10^9/l</td>
<td>14,0 x 10^9/l</td>
<td>4-13 x 10^9/l</td>
</tr>
<tr>
<td>Neutrophils</td>
<td>0,2 x 10^9/l</td>
<td>1,3 x 10^9/l</td>
<td>0,6-4 x 10^9/l</td>
</tr>
<tr>
<td>Lymphocytes</td>
<td>2,3 x 10^9/l</td>
<td>2,2 x 10^9/l</td>
<td>2,5-7,5 x 10^9/l</td>
</tr>
<tr>
<td>Monocytes</td>
<td>0,39 x 10^9/l</td>
<td>/</td>
<td>0,025-0,84 x 10^9/l</td>
</tr>
<tr>
<td>Eosinophils</td>
<td>0 x 10^9/l</td>
<td>/</td>
<td>0-2,4 x 10^9/l</td>
</tr>
<tr>
<td>Basophils</td>
<td>0,001 x 10^9/l</td>
<td>/</td>
<td>0-0,2 x 10^9/l%</td>
</tr>
<tr>
<td>Biochemistry</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total serum protein</td>
<td>64 g/l</td>
<td>51 g/l</td>
<td>64-70 g/l</td>
</tr>
<tr>
<td>Albumin</td>
<td>65,3%</td>
<td>/</td>
<td>25-49%</td>
</tr>
<tr>
<td>Alpha globulins</td>
<td>19,7%</td>
<td>/</td>
<td>8,18 ± 3%</td>
</tr>
<tr>
<td>Beta-globulins</td>
<td>7,9%</td>
<td>/</td>
<td>5,6 ± 1%</td>
</tr>
<tr>
<td>Gamma-globulins</td>
<td>7,1%</td>
<td>/</td>
<td>20,4 ± 5%</td>
</tr>
<tr>
<td>Total bilirubin</td>
<td>0,1 mg/dl</td>
<td>/</td>
<td>0-0,1 mg/dl</td>
</tr>
<tr>
<td>Urea</td>
<td>/</td>
<td>14,1 mmol/l</td>
<td>2,16-10,5 mmol/l</td>
</tr>
<tr>
<td>GPT</td>
<td>/</td>
<td>14,1 U/L</td>
<td>50-130 U/L</td>
</tr>
<tr>
<td>AST</td>
<td>/</td>
<td>2500 U/L</td>
<td>46-161 U/L</td>
</tr>
<tr>
<td>LDH</td>
<td>/</td>
<td>8400 U/L</td>
<td>123-392 U/L</td>
</tr>
<tr>
<td>CPK</td>
<td>/</td>
<td>22500 U/L</td>
<td>104-219 U/L</td>
</tr>
<tr>
<td>AF</td>
<td>/</td>
<td>50 U/L</td>
<td>27-210 U/L</td>
</tr>
<tr>
<td>y-GT</td>
<td>/</td>
<td>71 U/L</td>
<td>34-65 U/L</td>
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</table>
The cell origin of caprine lymphoma has been poorly studied and in only two cases of caprine lymphoma, immunophenotyping has been reported. In one case, a diagnosis of T-cell lymphoma was made (Rozaer et al., 1998), whereas the second case was a multicentric B-cell lymphoma (Valentine et al., 2011). Since in the present case, a B-cell origin was also demonstrated in the multicentric form, it would be interesting to immunophenotype further cases. Improved knowledge of phenotype could be useful to evaluate therapies and/or to predict prognosis.

Treatment of lymphoma in goats is not routinely performed, but since more and more pygmy goats are kept as companion animals, it is likely that owners will demand it in the future. Currently, there are no reports of effective treatment. Only administration of glucocorticoids might cause transient improvement because of lympholysis (Radostits, 2007). Treatment has been extensively studied in small companion animals and the treatment options vary from inexpensive single-agent prednisolone to aggressive chemotherapy, radiation therapy and even bone marrow transplantation. In dogs and cats, the backbone of the current therapy for B and T-cell lymphoma is systemic multi-agent chemotherapy, using drugs, such as vincristine, cyclophosphamide and doxorubicin, with or without L-asparaginase (Chun, 2009; Marconato, 2010).

The prognosis for dogs with multicentric lymphoma is influenced by the clinical stage and substage of disease according to WHO classification at the time of diagnosis. Immunophenotyping is also clinically relevant, because T-cell immunophenotype is a significantly adverse prognostic factor (Teske et al., 1994; Ruslander et al., 1997). For both B- and T-cell lymphoma’s, an important factor influencing survival time is the presence or absence of complete remission during chemotherapy (Jagielsky et al., 2002). In goats, this disease has a very rapid course, with most animals dying within one to two months after clinical diagnosis (Jubb and Kennedy, 2007).

In conclusion, clinicians should keep caprine lymphoma as a differential diagnosis in mind in many rather vague clinical presentations. Careful inspection and palpation of the peripheral lymph nodes during clinical examination are crucial. In this case report, cytolologic evaluation of fine needle aspirates proved to be a simple and useful method to confirm the diagnosis in vivo. Immunophenotyping could be useful to predict prognosis.

REFERENCES


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