History

A 7-year-old 12-kg sexually intact male mixed-breed dog was presented with a 3-month history of a rapidly growing, nonulcerated cervical nodule (Figure 1). The clinical signs were lethargy and anorexia.

Clinical and Gross Findings

On physical examination, the dog had abdominal distension, and signs of pain were elicited on abdominal palpation. There was enlargement of the right mandibular lymph node. The lymph node was multilobulated, firm, and measured 9.8 X 7.6 X 5 cm. The rest of the findings on physical examination were clinically normal.

A CBC, serum biochemical analyses, and a urinalysis were performed and revealed mildly low alanine aminotransferase activity (16.8 U/L; reference range, 21 to 102 U/L). Abdominal ultrasonography revealed an enlarged, hypoechoic spleen with an irregular capsule. The splenic parenchyma was heterogeneous with mixed echogenicity resulting from the presence of a mass in the mesogastric region. The mass measured 28 X 20 cm and had poorly defined borders, irregular margins, and a heterogeneous echotexture with cystic areas. The dilated vascular pattern was suggestive of a splenic tumor. No other abnormalities were found on any other test or thoracic radiography. Fine-needle aspirate samples of the cervical nodule were submitted for cytology.

Formulate differential diagnoses, then continue reading.

Cytologic Findings

Cytologic examination of the aspirate sample of the cervical nodule, presumed to have been a mandibular lymph node, revealed a hypercellular sample with round cells, some of which formed cell clusters; cells had a large volume of cytoplasm and multiple cytoplasmic vacuoles (Figure 2). The nuclei were round and, in some cells, eccentric with a moderate nucleus-to-cytoplasm ratio and intense anisokaryosis. Atypical mitotic figures were present (0 or 1 mitotic figure/10 hpf [400X magnification]), and the evaluated area was 2.37 mm². Leukocytes were present and were mostly intact, with occasional plasma cells and erythrocytes present.

Histopathologic Findings

Splenectomy was performed; however, the owner elected for euthanasia because of complications during surgery. Necropsy revealed that the enlarged right mandibular lymph node and spleen were infiltrated by nonencapsulated and nonulcerated masses. In the lymph node, the mass replaced 90% of the parenchyma. The masses were composed of round polyhedral cells arranged in sheets and sometimes clusters, supported by a moderate fibrovascular stroma. The cytoplasm was scant, eosinophilic, and well defined. The nuclei were large with condensed chromatin. The cells had low adhesion. Pleomorphism was moderate, characterized by anisokaryosis and occasional giant nuclei. Atypical mitoses were frequent (1 to 3 mitotic figures/hpf [400X magnification]). In the spleen, multifocal to coalescent areas of intense hemorrhage were found at the margins of the tumor (Figure 3). The spleen was approximately 30 X 20.5 X 17.8 cm and weighed 2.4 kg.
Morphologic Diagnosis and Case Summary

Morphological diagnosis: canine transmissible venereal tumor (CTVT) in the right mandibular lymph node and spleen in a dog.

Comments

Canine transmissible venereal tumor is a contagious, malignant tumor. Initially, transmissible venereal tumor emerged from the somatic cells of a canid precursor that lived thousands of years ago. The neoplastic cells were transferred by direct contact from the original host to new hosts and, by this method, CTVT was disseminated across several continents. Another form of malignancy that spreads by cell implantation is the Tasmanian Devil facial tumor, in which the mortality rate reaches almost 100% of affected animals. In this tumor, the contagious tumor cells are transmitted through bites during social interactions.

There is an important difference between the somatic cells of the dogs and the cells of the CTVT. The number of chromosomes in the somatic cells is 78; of these, 76 are acrocentric and 2 are metacentric. The chromosomal count in the CTVT cells is 58 to 59, whereas 13 to 17 are classified as metacentric and 42 as acrocentric. This rearrangement has not been identified in any normal dog tissue and can be used to diagnose CTVT.

CTVT is considered a malignant neoplasm of round cells with a mesenchymal origin and is transmitted by implantation (direct contact in the mucosa of the external genitalia of dogs during coitus). However, the neoplastic cells can be implanted in extra-genital sites through licking or direct contact with the tumor. CTVT has a low metastatic potential; however, metastases to the skin, lungs, abdominal organs, and CNS have occurred. The lesions can be single or multiple, with dimensions ranging from a few millimeters to 10 cm or more. The masses are often ulcerated and have substantial inflammatory reactions.

After the implantation of CTVT cells in the host, the initial phase (progressive) is characterized by rapid growth, a large number of mitotic figures, and few infiltrated lymphocytes. The second phase (stationary) has a slower tumor growth, a lower number of mitotic figures than in the progressive phase, and a larger number of lymphocytes. Last, CTVT goes through the regressive phase, in which there is an abundance of lymphocytes that infiltrate tumor cells, promoting tumor regression. Although spontaneous and natural regression of CTVT is described, it does not occur in all cases, and the immunologic mechanisms that lead to this regression are still poorly characterized.

Sometimes, CTVT has a cauliflower shape when located in the external genitalia. In this case, the

Figure 2—Photomicrograph of a fine-needle aspirate sample of the enlarged right mandibular lymph node of the dog in Figure 1. There are individual and clustered round cells with basophilic cytoplasm and multiple cytoplasmic vacuoles; large, oval nuclei with a condensed chromatin pattern; and moderate anisocytosis and anisokaryosis. Panoptic stain; bar = 20 µm.

Figure 3—Postmortem gross (A) and photomicrographic (B) images of the spleen from the dog described in Figure 1. A—There is replacement and compression of the splenic parenchyma by irregular white masses with black-red areas. B—Note the round cells arranged in sheets and occasional clusters, supported by a sparse fibrovascular stroma. Cellular cytoplasm is scant, eosinophilic, and well defined. The nuclei are large with condensed chromatin, sometimes finely speckled, and prominent nucleoli. Moderate pleomorphism is present. H&E stain; bar = 20 µm.
lesions of the CTVT were seen in anomalous sites (spleen and right mandibular lymph node) and did not show this presentation.Macroscopically, necropsy revealed there were no changes in the entire reproductive tract of the dog. In addition, skin lesions were not identified, and the oral and nasal cavities were clinically normal. Although CTVT has a low metastatic potential, in this case, metastasis occurred to 2 distant organs, although the primary site was not detected. We hypothesized that the CTVT cells reached the mandibular lymph node from an oral location, thus suggesting an oral primary mass with dissemination to the spleen.

Although extragenital CTVT is less common than masses located in the genitalia, there is a considerable number of reports in the veterinary literature describing this type of CTVT. These include reports of nasal CTVT, a retrospective study with 21 cases of intraocular CTVT, and oral and nasal CTVT, and ocular and subcutaneous CTVT with cerebral metastasis. The diagnosis was suspected through anamnesis and clinical signs, and the definitive diagnosis was based on cytologic and histopathologic findings. In some cases, when the tumors are poorly differentiated, immunohistochemistry (IHC) or PCR assay may be needed to achieve a definitive diagnosis.

In this case, CTVT was diagnosed by cytology, the histopathologic examination was confirmatory, and IHC and PCR assay were not necessary because the tumor cells were well differentiated. The diagnosis of CTVT is complemented by a subclassification according to the predominant cell morphology divided into 3 groups (plasmacytoid, lymphocytic, or mixed). In the lymphoid type, morphologically round cells predominate, the cytoplasm is scant and finely granular, and vacuoles and round nuclei are present with coarse chromatin, along with the presence of 1 or 2 prominent nucleoli. Plasmacytoid tumors have greater cellularity with ovoid morphology, a lower nucleus-to-cytoplasm ratio, and eccentrically located nuclei. The mixed type exhibits mixed lymphoid and plasmacytoid cellularity. The plasmacytoid type is associated with greater tumor invasiveness, resistance to chemotherapy, and more frequent extragenital location.

Among splenic malignancies, hemangiosarcoma is the most common, representing 25% of all cases. The prevalence of splenic CTVT in dogs is unclear. Because it is a round-cell tumor, differentiation from other round-cell tumors, such as mast cell tumor, histiocytoma, lymphoma, amelanotic melanoma, and poorly differentiated carcinomas, is necessary. Immunohistochemical studies with a diverse panel of antibodies can rule out some differential diagnoses.

The histological characteristics of CTVT are uniform cells that are round to ovoid with large, round nuclei and a single central nucleus surrounded by chromatin. The cytoplasm is eosinophilic, and the mitotic index can be high. Lymphocytes, plasma cells, and macrophages can infiltrate the tumor. These characteristics concur with the histopathologic findings for the dog presented to us.

In some cases, even when immunohistochemical analysis with different tumor markers has been performed, the origin and immunophenotype of CTVT can remain uncertain. CTVT cells are negative for keratins, α1 smooth muscle actin, desmin, cluster of differentiation 3, immunoglobulins G and M, λ, light chains, and κ light chains. Thus, epithelial tumors, smooth muscle tumors, and T or B lymphomas can be excluded in the absence of these markers. In some cases, because CTVT has the same origin as histiocytic tumors, immunohistochemical analysis cannot give a confirmatory diagnosis of CTVT.

PCR assay for a CTVT-specific rearrangement of the c-Myc gene can be an effective method of diagnosis. The rearrangement is not present in normal somatic cells, gametes, or other tumor cells. Therefore, PCR to detect insertion of long, interspersed nuclear elements in the c-Myc gene is used as a tool to obtain a definitive diagnosis of CTVT.

References


