Adjuvant Carboplatin for the Treatment of Intestinal Carcinoid in a Dog

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Abstract. A ten-year-old castrated male dog was presented due to a two-day history of constipation and tenesmus. At physical examination, the dog was depressed and unresponsive. Aggressive behavior was elicited by deep abdominal palpation and a mass was detected during the examination. Imaging studies evidenced a large jejunal mass. The lesion (6 cm in diameter) was surgically removed. The histopathology report gave a diagnosis of completely excised intestinal carcinoid. The patient recovered well from the procedure and was scheduled for adjuvant chemotherapy. The dog received four doses of carboplatin (300 mg/m²) every three weeks without showing signs of toxicity. The dog is still in remission after 18 months and is reassessed on a three-month schedule. This report represents the first description of long-term control of intestinal carcinoid in the dog and the first of adjuvant chemotherapy for this rare and aggressive neoplasm.

Case Report

A ten-year-old castrated male dog was presented with a 10-day history of weakness and ataxia. It had been experiencing constipation and tenesmus for the last two days. The dog was well muscled but evidenced pronounced weakness. The dog was depressed but still responsive to stimuli and had a normal rectal temperature.

Thoracic auscultation evidenced normal lung and heart sounds. The dog showed marked discomfort during abdominal palpation and the procedure elicited an aggressive behavior. An intestinal mass was evidenced during the physical examination. The dog had a complete blood cell count (CBC), a biochemical profile and urinalysis performed at the time of the first appointment. Abdominal ultrasonography confirmed the presence of a mass located in the jejunum (Figure 1). Thoracic radiographs were within normal limits. Since the hematological and biochemical examinations were within normal limits, the dog was scheduled for exploratory abdominal surgery, during which a 6 cm mass was removed from the jejunum. The dog was hospitalized for 24 hours and treated with injectable enrofloxacin at the dose of 5 mg/kg i.v. bid (Baitryl, Bayer Milan, Italy) and then discharged on oral enrofloxacin at the dose of 5 mg/kg p.o. bid for 6 days (Paraplatin, Bristol-Myers Squibb, Sermoneta, Italy). The patient’s recovery was uneventful and 10 days after the surgery, at the time of suture removal, the histopathology report gave a diagnosis of carcinoid (1). The tumor was formed by solid nests of small monotonous cells with occasional acinar or rosette formation. Neoplastic cells were separated by variable amounts of fibrovascular stroma and the neoplasm extended from the lamina propria to the serosal surface of the jejunum (Figure 2A and 2B). Immunohistochemistry demonstrated the expression of chromogranin A, neuron-specific enolase and synaptophysin in the neoplastic cells. Figure 2C and 2D depict examples of the immunostainings. Due to the metastatic potential (2-7) of this neoplasm, adjuvant chemotherapy was proposed. The dog received four doses of carboplatin (300 mg/m² i.v. every three weeks) and had his CBC checked one week after the platinum dose. The patient tolerated the therapy very well and the CBC did not show signs of toxicity. The dog has been reassessed on a monthly basis for three months and every three months thereafter. Follow-up appointments involve hematological and biochemical analysis, thoracic radiographs and abdominal ultrasonographic examination. The dog is still in complete remission 13 months from the end of chemotherapy and is monitored on a six-monthly basis.

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Discussion

Carcinoids are rare tumors of neuroendocrine origin that have been infrequently reported in dogs (2-7) and are characterized by a tendency to metastatize. In particular, in one study of canine intestinal neoplasms, it was shown that half of the metastases in the liver were from carcinoids, despite these tumors numbering only 4 out of a total of 35 (3). A similar aggressive pattern has been described in humans (8). Conventional chemotherapy has not shown significant activity in advanced carcinoids and neuroendocrine carcinomas in humans, with the exception of streptozotocin-based protocols for the treatment of pancreatic neoplasms (9-11). Other articles reported some antitumoral activity of platinum compounds in patients affected by carcinoids (12-14). The choice of carboplatin for the treatment of our patient was made based on the broad efficacy and low toxicity of the drug. The therapy has been well tolerated and the dog is disease-free after 18 months from the completion of the chemotherapy protocol. The long disease-free interval could be ascribed to the detection of the tumor prior to any regional or distant spread; however, the aggressiveness of this neoplasm in foregut and midgut locations in dogs leads us to believe that adjuvant chemotherapy played a role in this case. Moreover, several papers on humans describe better results with combined than with single modality therapy (15, 16). Additional studies are needed to evaluate the role of chemotherapy in the management of carcinoid tumors in companion animals, as well as the potential of growth inhibitors and apoptosis inducers such as octreotide (16, 17).

Figure 1. Ultrasonographic appearance of the intestinal mass. The sagittal image evidences a poorly marginated mass with mixed echogenicity.

Figure 2. A) Microscopic appearance of the tumor, showing the extension of the neoplastic mass from the lamina propria of the jejunum (hematoxylin/eosin, original magnification ×20). B) Higher magnification of the tumor, showing polygonal neoplastic cells with round hyperchromatic nuclei and a modest amount of eosinophilic cytoplasm, separated by fine fibrovascular stroma (hematoxylin/eosin, original magnification ×40). C) Most of the neoplastic cells react positively for chromogranin A (ABC methods with hematoxylin counterstain; original magnification ×40). D) Many neoplastic cells react positively for neuron-specific enolase (ABC methods with hematoxylin counterstain; original magnification ×40).
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