International Journal of Livestock Research, Vol. 11 (5) May' 2021
http://www.ijlr.org
eISSN: 2277-1964

Case Report

# Surgico-Chemotherapeutic Management of Splenic Hemangiosarcoma Using VAC Protocol in German Shepherd Dog- a Case Report

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**How to cite this paper:** Mishra, M., & Akash (2021). Surgico-chemotherapeutic Management of Splenic Hemangiosarcoma using VAC Protocol in German Shepherd Dog- A Case Report. *International Journal of Livestock Research,* 11(5), 42-47. https://dx.doi.org/10.5455/ijlr.20210217045123

**Received** : Feb 19, 2021
**Accepted** : Apr 19, 2021
**Published** : May 31, 2021



## Abstract

*A 9yr uncastrated German Shepherd dog was presented to the Teaching Veterinary Clinical Complex with a history of Anorexia, weakness, weight loss, Lameness, intermittent sudden collapse and muscular incoordination. On further investigation it was found that dog was earlier having a history of seizures of unknown etiology. Initially the case was misdiagnosed as certain neurological conditions and the treatment led deterioration of the condition. Thus, whole body check-up was recommended the very next time. Thoracic radiograph revealed no abnormal findings while Abdominal Radiograph confirmed certain degree of splenomegaly. Ultrasonographic findings confirmed a highly echo dense structure at the cranial pole of spleen concluding it to be a splenic mass of about 4.93 cm. Animal was kept on vincristine doxorubicin and cyclophosphamide therapy (VAC Protocol) and continuous fluid maintenance therapy. Splenectomy was performed under General Anaesthesia through hilar ligation technique.*

**Keywords:** Echo Dense, Incoordination, Neurological, Seizure, Splenomegaly

## Introduction

Originating from the vascular endothelial cells, hemangiosarcoma is a malignant neoplasm which is characterized by widespread metastases with poor survival rates. Predilection site of hemangiosarcoma may be any site in the body, but the spleen is affected most commonly in dogs (Brown NO *et al*., 1985; Okansen A. 1978; Pulley LT and Stannard, A. A. 1990). Other primary sites include the right atrium and auricular appendage, liver, lungs, kidney, skin, and the subcutis (Pulley, L. T. and Stannard A. A. 1990). Older dogs are at greater risk, and German shepherd dog may have higher susceptibility than other breeds for developing the disease (Johnson KA *et al*., 1989). Dogs with hemangiosarcoma have a poor prognosis, and survival is short when treated with surgery alone (Brown NO *et al*., 1985; Prymak *et al*., 1985 and Johnson KA *et al*., 1989). Adjuvant chemotherapy using a protocol consisting of vincristine cyclophosphamide and methotrexate with mixed bacterial vaccine does not show any signs of improvement (Brown *et al*., 1985). Several reports using doxorubicin protocols in canine HSA show a trend towards improved survival rates (Rosenberg, S. A. 1985). Two similar chemotherapy protocols based on doxorubicin and cyclophosphamide, with and without the inclusion of vincristine, have been reported for the treatment of hemangiosarcoma in dogs (Hammer, A. S. *et al.*, 1991).

### History and Clinical Examination

A 9yr Old uncastrated Male German Shepherd dog weighing about 25 kg was presented to the Teaching Veterinary Clinical Complex with the history of sudden weight loss, anorexia, lethargy, lameness in hind limbs, muscular incoordination and sudden intermittent collapse. Animal was also treated earlier for seizures of unknown etiology. The case was misdiagnosed to be a case of Neurological importance and was treated accordingly and animal was called for follow-up after a period of 15 days. Follow up showed more deterioration of condition. A thorough whole-body check-up including physical examination, radiography, abdominal ultrasonography, echocardiography, electrocardiography and complete blood profiling was done to arrive at a confirmatory diagnosis.

On physical examination, animal was found tachycardiac with feeble femoral pulse and intermittent pulse deficits. Pale mucous membrane and CRT > 2 sec was indicating towards hypovolemic shock. Being in sternal recumbency animal was severely tachypneic, temperature was within limits. Mild abdominal distension was present. Thoracic and abdominal radiograph in both Lateral and Ventrodorsal were taken. Thoracic radiograph revealed no abnormal findings (Figure 1) while Abdominal Radiograph confirmed certain degree of splenomegaly but it was difficult to determine a distinct splenic mass (Figure 2 and 3). Ultrasonographic findings confirmed a highly echo dense or hyper echoic structure at the cranial pole of spleen concluding it to be a splenic mass of about 4.93 cm (Figure 4).

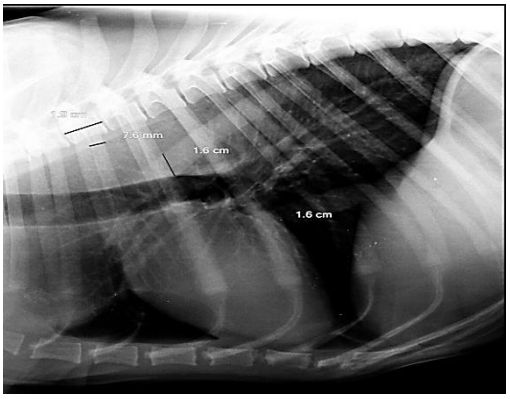


**Figure 1:** Right lateral Thoracic Radiograph showing normal pulmonary area, cardiac inclination angle along with well-defined cardiac vasculature

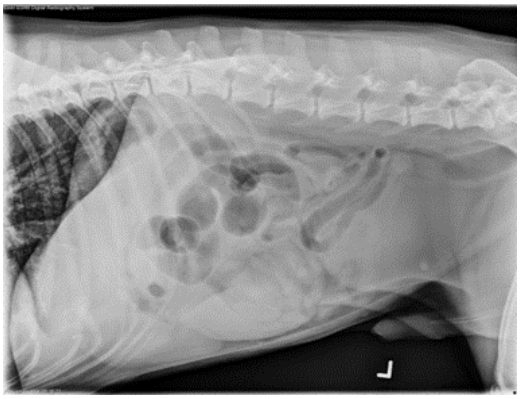

**Figure 2:** Right Lateral abdominal radiograph showing splenomegaly

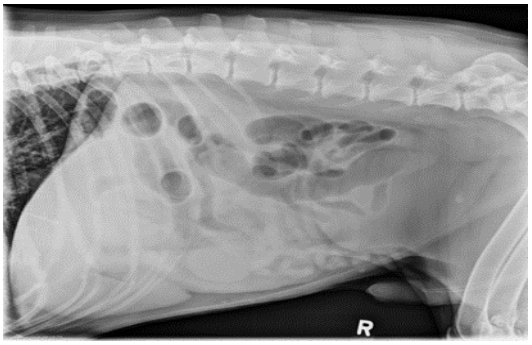

**Figure 3:** Left lateral abdominal radiograph showing splenomegaly, but does not confirm the presence of any splenic mass.

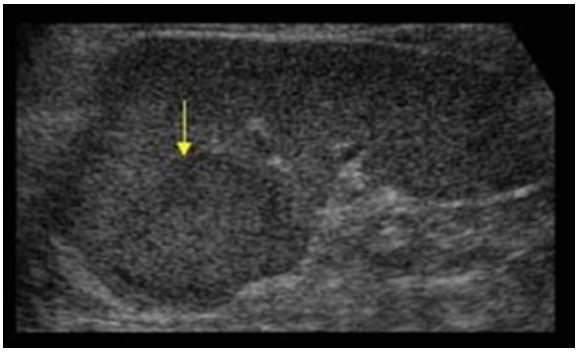

**Figure 4:** Ultrasonogram of spleen with yellow arrow pointing towards well defined demarcated highly echo dense splenic mass.

Electrocardiogram showed abnormality in sinus rhythm, QRS morphology (low voltage QRS complexes) causing slow ventricular depolarization which may be due to dysfunction in conduction system (Figure 5), while echocardiogram showed ejection fraction of 63% (Reference range: 50 to 70%) (Figure 6). Mitral pulse showed mild degree of regurgitation while aortic, pulmonary and Tricuspid flow velocities were mildly compromised (Figure 7). These abnormalities may be because of the disease condition and can also be associated to the age factor.

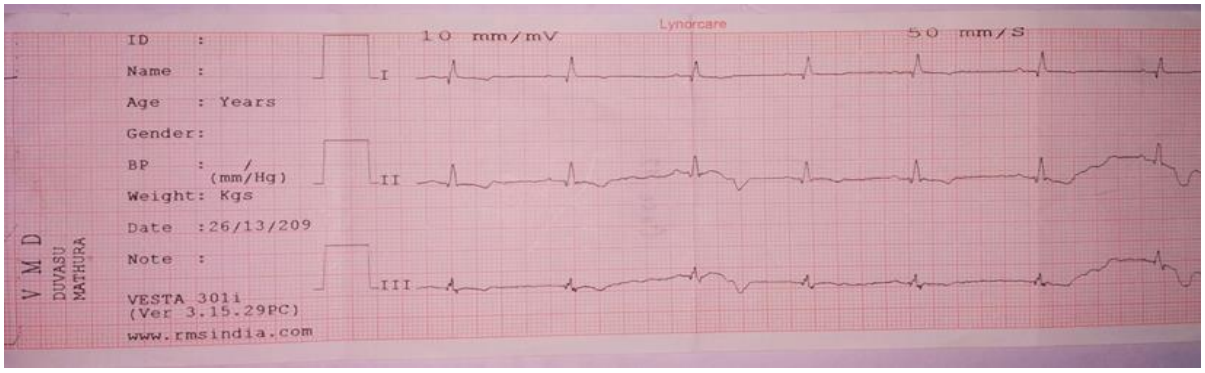


**Figure 5:** Electrocardiogram showing abnormal cardiac rhythm and electrical conductivity with low voltage QRS complex

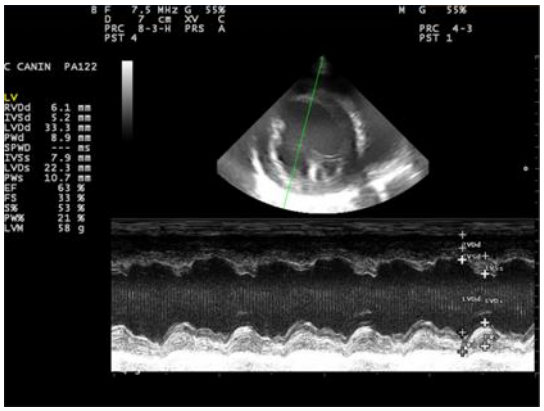

**Figure 6:** M-mode echocardiographic finding showing normal ejection fraction (EF)

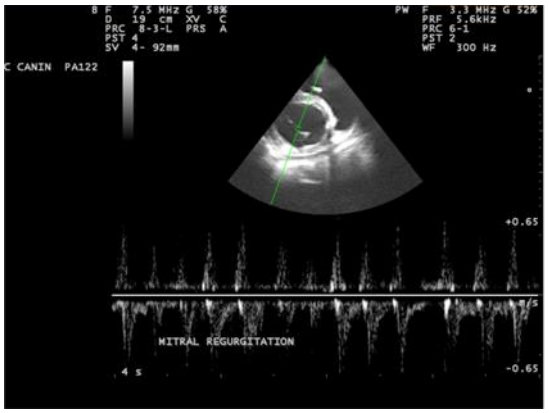


**Figure 7:** Mitral pulse finding indicates mild mitral regurgitation

Quick assessment tests were performed to evaluate certain parameters like packed cell volume/Total solid (PCV/TS) and Blood glucose along with complete blood count. Result showed 39.5% PCV and 62 g/L TS (Reference range: 37 to 55%, 52 to 82% respectively), values of both the parameters were in between low to normal. There were marked Hyperglycemia at 17.37 mmol/L (RR: 3.98 to 7.95 mmol/L) and mild neutrophilia of 13.33 x $10^9$/L (RR: 2 to 12 x $10^9$) along with mildly elevated creatinine at 163 micromol/L (RR: 44 to 150 micromol/L). Platelets were in low to normal range that lead to the suspicion of disseminated intravascular coagulopathy. These findings were indicating towards a stress leukogram and stress hyperglycemia. Hypovolumia, prolonged anorexia, azotemia and

decreased renal perfusion were supposed to be the reason behind elevated creatinine level.

**Surgical and Chemotherapeutic Management**

Initially the animal was stabilized and maintained with Dextrose Normal Saline solution (5%), prophylactic administration of ceftriaxone (50 mg/kg b.wt.) I/V, dexamethasone (1mg/kg b.wt.) and meloxicam (0.4mg/kg b.wt.) I/M. The dog was premedicated with Atropine sulphate (0.02 mg/kg b.wt.) I/M, Xylazine (1 mg/kg b.wt.) I/M. Anaesthesia was induced with Ketamine (5mg/kg b.wt.) I/M and maintained on Isoflurane.

The animal was taken in dorsal recumbency, and the abdomen was prepared with standard aseptic technique. Animal was draped from xiphoid to pubis, a ventral midline abdominal incision from xiphoid to 2 to 3 cm caudal to umbilicus was made. Spleen was gently manipulated out of the body onto moistened laparotomy sponges (Figure 8). The hilar splenic vessels were visualized as they enter splenic parenchyma (Figure 9). Left gastroepiploic artery and short gastric vessels were preserved to maintain adequate perfusion to stomach. Using haemostatic forceps, the vessels were isolated and circumferential double ligature of hilar pedicle was done with 3-0 absorbable sutures (Figure 10). Before transection haemostatic forceps were kept close to the pedicle to avoid splenic bleeding. All the vessels of splenic hilus were double ligated, gastrosplenic ligament was detached and finally spleen was removed (Figure 11). Being a deep chested breed of dog prophylactic gastropexy was done to avoid future complications of gastric dilatation volvulus.

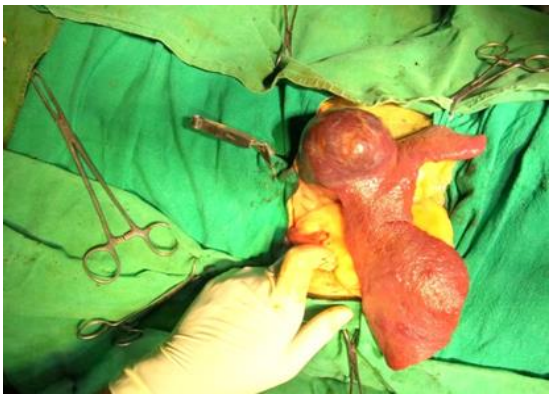

**Figure 8:** Gentle manipulation of spleen out of the body onto moistened laparotomy sponges

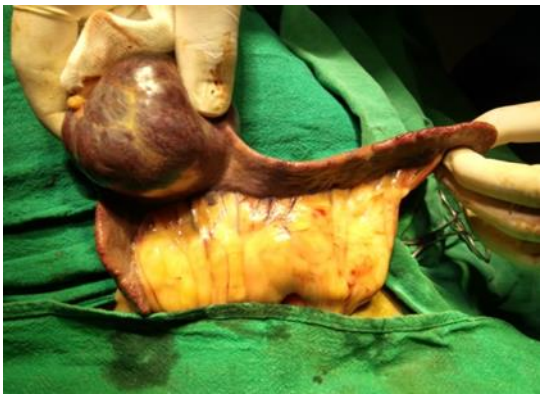

**Figure 9:** Splenic peduncle and hilus with splenic vasculature

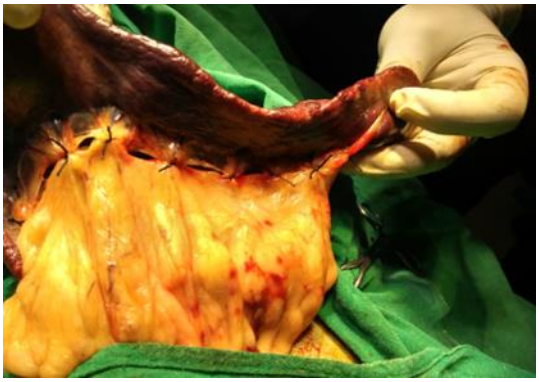

**Figure 10:** Ligation of splenic vessels through hilus ligation technique, circumferential double ligature of splenic vessels using 3-0 absorbable suture.

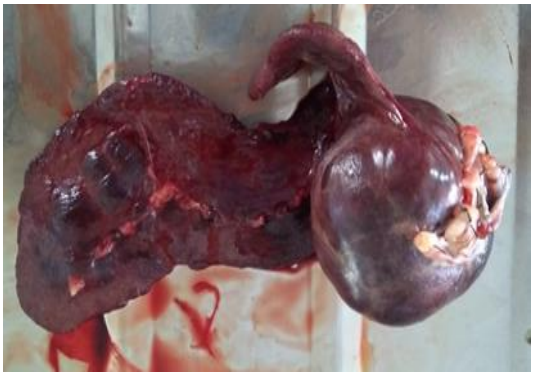

**Figure 11:** Detachment of gastrosplenic ligament, transection of all the hilus vessels and removal of spleen.

Post operatively animal was kept on intravenous fluids to match the patient's need. For initial 24-48 hrs IV analgesics were given which were switched to oral analgesics on 3rd day. Antibiotics were prescribed for a period of 7 days. Continuous postoperative assessment required. Alternate wound dressing was recommended at every alternate days for 2 weeks. Animal was kept on loose diet for a period of 15 days. Animal was given adjuvant chemotherapeutic treatment with doxorubicin and cyclophosphamide on day 1 at the dose rate of 30mg/m$^2$and

100mg/$m^2$ Intravenous respectively. Vincristine was given @ 0.75 mg/$m^2$ Intravenous on Day 8 and 15.5 successive cycles were repeated at 3 weeks apart. Animal was continuously monitored for chemotherapy induced neutrophilia and myelosuppression. Animal was followed for treatment up to a period of 6 months. Animal recovered without any signs of major toxicity.

## Discussion

Canine HSA is an aggressive tumour that requires a multimodality treatment. Soft tissue sarcomas commonly expand via intracavitary seeding, and invade along various tissue planes, thereby compressing surrounding structures and hampering tissue growth and supply, and may form a pseudo capsule around the tumour (Rosenberg SA *et al*., 1985). Surgical excision is often not curative because of local residual disease as well as early haematogenous metastasis. Primary internal (visceral) tumours are generally diagnosed later in the course of the disease when compared to external (subcutaneous) tumours. Subcutaneous HSAs are more easily detected and diagnosed before systemic illness becomes evident, whereas dogs with visceral involvement often have severe complications referable to their tumour. Such complications included acute collapse, shock, internal haemorrhage, cardiac tamponade, arrhythmias, and disseminated intravascular coagulation.

The biological behaviour of HSA is well known and dictates early, aggressive, and radical surgical approaches followed by adjuvant chemotherapy. Neoadjuvant chemotherapy, i.e., chemotherapy prior to surgical resection, may be another rational approach to improve surgical result. Van Vechten M *et al*., 1990 Reported that Canine HSA is more sensitive to doxorubicin containing chemotherapy protocols like VAC protocols. Prymak *et al*.,1988 reported a mean survival of 19 days in 59 dogs with HSA treated by surgery alone. There are several reports of adjuvant treatment of HAS (deMadron *et al*.,1987). Hammer *et a1*.,1991reported prolonged survival, when compared to historic controls, using vincristine, doxorubicin, and cyclophosphamide (VAC) in dogs with HSA that had undergone excisional or incisional biopsies. The overall median survival time in 15 dogs was 172 days, and 145 days in dogs with splenic HSA. The result appears comparable to the animal in this study.

Most toxicoses associated with the VAC chemotherapy are not life threatening. Neutropenia may be the most common complication. In the present study marginal decreases in the packed cell volume over time postoperatively (39-35.6%) was seen but no significant thrombocytopenia was observed. Palliation of clinical signs is a potential benefit from adjuvant chemotherapy of solid tumours. In people with soft tissue sarcomas, overall survival times may not be significantly prolonged, but adjuvant chemotherapy can prolong disease-free intervals and improve in quality of life (Rosenberg *et al*., 1985). This may also be an indication for chemotherapy in dogs with advanced nonresectable tumours. Both splenic disease and GDV are more prevalent in larger breed, deep chested dogs (DeHoff WD and Greene RW.,1973; Spangler WL and Culbertson MR.,1992). Further, one study evaluating relationship between gastric dilatation volvulus and splenectomy found that dogs with previous splenectomy are 5.3 times more susceptible for developing gastric dilatation volvulus than dogs without splenectomy (Sartor AJ *et al*., 2013).

Splenic hemangiosarcoma is a disease with a grave prognosis. No prognostic factors for survival following splenectomy are reported. Complications (i.e., DIC or ventricular arrhythmias) do not appear to affect the course of the disease after the immediate postoperative period. Various chemotherapeutic drugs and immune-response modifiers may improve survival times significantly in dogs with hemangiosarcoma.

## Conflict of Interests

There is no conflict of interest.

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