A Retrospective, Multi-Case Study on the Effect of Vincristine Administration and Subsequent Platelet Recovery Time as Treatment for Immune-Mediated Thrombocytopenia in Canines at an Emergency Clinic

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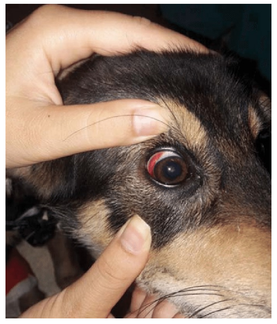
Abstract

Canine immune-mediated thrombocytopenia (ITP) results when a dog's immune system malfunctions and attacks the blood's platelets, which leads to clotting issues. Patients can present with bruising, bleeding, lethargy, and other symptoms. The immune system must be suppressed so the platelet count can return to normal, and vincristine is commonly introduced as a secondary treatment to steroids to accomplish this. This study analyzes data from 8 canines with ITP that had been treated with vincristine at an emergency clinic and compares their platelet recovery time and variation in treatment protocol.



Example of canine with scleral hemorrhage

Example of canine with petechiae on the abdomen

Introduction

ITP requires a diagnosis of exclusion to confirm that the dog's immune system is responsible for the platelet destruction. The diagnostic workup is complicated since other possible causes of the presenting symptoms must first be eliminated based on clinical grounds that lack objective proof. The presenting symptoms often include ecchymosis (bruising), anorexia (decreased appetite), lethargy (tiredness), oral hemorrhage (bleeding from the mouth or gums), melena (dark, tarry stool), petechiae (small dots caused by bleeding into skin), and more. Steroids are the primary treatment method, but due to the difficulty identifying the disease and few studies available, secondary medications are still being debated regarding which is the most effective at decreasing the amount of time needed for platelet recovery. The first major study of vincristine used to treat ITP was in 1982 (Greene et al.), but since then there has been a paucity of peer-reviewed studies on the effects of vincristine specifically and its effect on platelet recovery time to at least 30,000/µL. The studies that have been done often have small numbers of patients. Because of this lack of conclusive data, this study is pertinent to the field of veterinary science and can add to the discussion on the most effective treatment plan for this serious and life-threatening disease.

Vincristine is commonly used as a chemotherapy drug, but its physiological effects include triggering the release of premature platelets from the bone marrow, which increases platelet count, therefore making it a viable option for a secondary treatment for ITP. Other secondary options include azathioprine, cyclosporine, leflunomide, human intravenous immunoglobulin, and a splenectomy, which have been explored in other historical studies. The purpose of this study was to see how the patients reacted to the vincristine treatment and outline the treatment plan variations in each patient. A case study approach allows for a more accurate understanding on the variability of this disease between each case while also highlighting common patterns.

Methodology

Data from 8 patients diagnosed with ITP was collected from the clinic database at Veterinary Care and Specialty Group in Chattanooga, Tennessee. Bloodwork and diagnostic tests performed, time of vincristine administration, platelet recovery time, medications given, blood transfusions, symptoms, and additional unique patient data were analyzed. The data was then stratified and compared to historical studies to highlight patterns in the cases to analyze the efficacy of the primary vincristine treatment and if any of the additional treatments led to a different outcome.

Results

Fig. 1 Presenting Symptoms

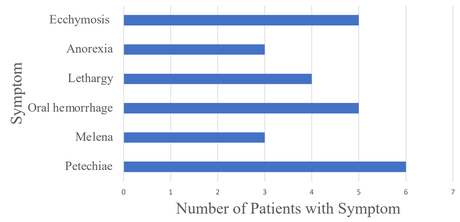


Fig. 2 Most Common Treatment Medications

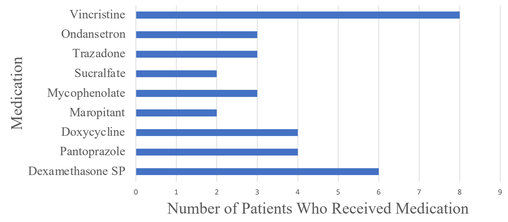
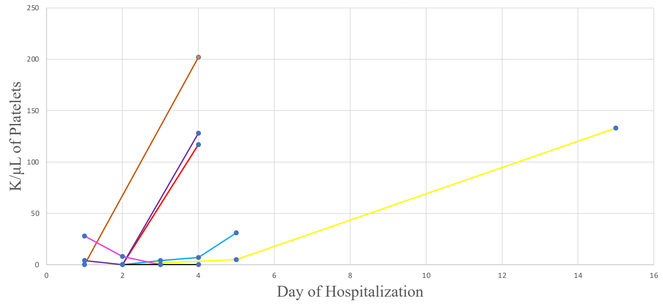


Fig. 3 Platelet Recovery Time Starting with Day of Vincristine Administration for the 8 Patients in the Study



During the duration of their stay at the emergency clinic, 6/8 patients had petechiae, 3/8 had melena, 5/8 had ecchymosis, 4/8 had lethargy, and 5/8 had oral or gum bleeding. (Fig. 1) In addition, 6/8 patients had a high white blood cell count in the hospital, 6/8 had a low red blood cell count, and 6/8 had a low hematocrit.

Five of the patients reached an adequate platelet count for survival and were discharged, while 3/8 of the patients presented with melena and all were euthanized due to inadequate response to treatment, resulting in a 62.5% survival to discharge. The average time of hospitalization was 3 days, but the patients entered treatment in various stages of the disease. Half the patients were hospitalized for 3 days, and the remaining 4/8 were hospitalized for 1-5 days. One patient was able to achieve platelet recovery in the hospital (exceeding 30,000 /µL), but the remaining 4/8 patients were released since they were stable overall and reached platelet recovery at their regular veterinarian clinic. (Fig. 3)

Additional supportive medications were needed along with vincristine for maximum patient comfort and overall recovery. Maropitant is used to stop or prevent acute nausea and vomiting, which mycophenolate and other medications have been associated with, by inhibiting neurotransmitter Substance P. Ondansetron is a 5-HT3 receptor antagonist that blocks the effects of serotonin at the receptor site and works as an antiemetic. Trazadone relieves anxiety or stress for animals who may not be coping well with the hospital environment or treatment requirements by selectively blocking serotonin uptake, which leads to sedation. Pantoprazole is a proton pump inhibitor that reduces stomach acid and works as a GI protectant. Sucralfate binds to proteins at ulcer sites to help form a barrier of protection and can bind bile acids and reduce pepsin activity. In O'Marra et. al (2011), 85% of dogs take a gastrointestinal protectant, but the results did not show a correlation to an increased survival time. Mycophenolate is an immune suppressant via the inhibition of T and B lymphocytes, which can reduce the antibodies that lead to platelet destruction. Doxycycline is an antibiotic that is prescribed if secondary ITP from a tick-borne disease is predicted in a patient. Dexamethasone sodium phosphate is an injectable corticosteroid that decreases the immune response. The combination of medications used in each patient varied based on the severity of the disease and the different patients' reactions to the course of the disease. (Fig 2).

Discussion

O'Marra et al. (2011) reported a survival to discharge of around 73-84% for ITP patients with varying treatment methods and higher numbers of patients included in the study. Scuderi (2016) found there was no difference in surviving to discharge based on the different treatment protocols. In contrast, Bianco et al. (2009) determined that vincristine and prednisone used in combination had a more rapid increase in platelet count and shorter hospitalization when compared with treatment using human intravenous immunoglobulin

87.5% of the patients in this study had either petechiae or ecchymosis, which is greater than the 66% of patients who had at least one of these symptoms in Scuderi (2016). Scuderi (2016) also showed that 49% of patients had leukocytosis, while in this study 75% of the patients had leukocytosis.

The results of this study show that vincristine is an adequate secondary medication to steroids to improve the chances of patient recovery and is related to increasing platelet count. Further studies are needed to confirm the efficacy of vincristine, but this data illustrates the complexity of disease diagnosis and the variation in treatment methods and reactivity of patients. Ideally, more frequent and consistent bloodwork to better track the course of platelet recovery would be desired, but this is usually beyond the scope of retrospective studies since treatment outcomes are also influenced by personal decisions of the owners or the discretion of various doctors. In addition, a larger sample size would be beneficial for creating statistically significant results.

The goals for this project were achieved since additional data was able to be collected about a treating ITP with vincristine.

Example of canine with ecchymosis on the abdomen

Example of canine with oral hemorrhage

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