Immunosuppressive Treatment for Autoimmune Diseases Hemolytic anemia (IMHA) and Thrombocytopenia (ITP)

While there are nuances in the treatment of autoimmune diseases, for many of them the cornerstone of treatment is to suppress the animal's immune system so that it stops making antibodies against its own cells or organs. Traditionally the first line of defense against these diseases is a glucocorticoid, usually prednisone or the synthetic prednisolone which is generally better tolerated by dogs. While effective, these drugs don't produce as rapid a response as is optimal when treating IMHA and/or ITP, so a second or sometimes even a third drug may be added to more rapidly stabilize a dog, especially one in crisis. When choosing that second drug speed of action may be critical, but other considerations also exist, safety and cost being paramount. Once the levels of red blood cells and/or platelets start to normalize drug doses should be reduced in a timely fashion. Multiple studies have shown that keeping the dog on a low dose (or in some cases a high one) of immunosuppressant indefinitely does not reduce the risk of relapse, and often makes the animal much sicker producing among other things iatrogenic Cushing's disease if steroid therapy is continued too long. This is marked by increased drinking, urination, and eating; panting; restlessness; muscle weakness and wasting; hair loss; gastrointestinal ulceration; thromboembolic disease (blood clots, which can be life-threatening); and protein in the urine. Steroids can also induce or worsen congestive heart disease. (Most dogs will develop iatrogenic Cushing's, but most symptoms will resolve as the dose is tapered.)

Most veterinarians have developed their own preferred protocol, and this must be modified for each patient as the diseases will not be identical from dog to dog. This is mine and it is a general guide, and not a recipe that must be followed to the letter.

Many dogs with IMHA and/or ITP may be presented in crisis, and blood products (whole blood, packed red cells, platelet rich plasma) may be needed to support the critical patient. Dogs may not be able to take oral medication on presentation. Vincristine in a single dose stimulates bone marrow to release platelets into the circulation and may be given to speed response in cases of ITP.

Glucocorticoids are the cornerstone of treatment. Dexamethosone may be given intravenously during stabilization. In dogs that can be started on oral drugs, prednisolone is given at a dose of 2mg/kg/24h for 2-4 weeks (this may be divided into twice daily dosing), and then the dose is reduced to 1 mg/kg/24h. When this happens depends upon patient response. Glucocorticoids are cheap and given the wide array of doses available it is easy to dose accurately, but as we have seen, the side effects are significant. They should always be given with a gastroprotectant (I prefer omeprazole) and a drug like clopidogrel to prevent blood clots.

When I first started treating autoimmune diseases, the most used secondary steroid-sparing drug used was azathioprine. This is started at a dose of 2mg/kg once a day for up to 14 days, then the dose should be dropped to 1mg/kg/day or 2mg/kg every other day. Azathioprine is inexpensive, but it is toxic to the liver, can cause pancreatitis and it also suppresses bone marrow cell production. Owners must wear gloves to handle it and the pills cannot be split so it must be specially compounded for many dogs.

Another secondary drug is cyclosporine; it is dosed at 2.5 -5 mg/kg/12h. Side effects include vomiting, diarrhea, anorexia, gum overgrowth and secondary infections especially fungal and bacterial urinary tract infections because it acts by suppressing lymphocytes. It is expensive.

My preferred drug is mycophenolate, because it can produce immunosuppression within hours of administration which is far faster than the other drugs. It has a relatively short half life and dosing three times a day, especially early in therapy is probably preferable, otherwise dose at 10-15 mg/kg/12h for 3-4 weeks and then drop to 10 mg/kg/q24h. Side effects include diarrhea or anorexia and very rarely gastrointestinal hemorrhage. It can also be given intravenously.

Leflunomide is another newer immunosuppressive drug. It is metabolized to its active form in the gastrointestinal tract. It is dosed at 2-4mg/kg/q24h. Side effects include anorexia, diarrhea and vomiting, but the most common side effect is an ulcerative skin eruption on the nose, face and/or footpads or less often the neck or trunk, this will disappear if the drug is discontinued. The drug is now available in a generic form which has made it far less expensive. It can be given with prednisolone and cyclosporine, but never with azathioprine.

Tapering Immunosuppressive Drugs

The sooner you can start to reduce the dose of immunosuppressive drugs the better. Once the patient is responding positively (hematocrit stable or rising, platelet count over 25,000 for 1-2 weeks) drug doses are tapered by 25-50% one drug at a time every 2-4 weeks. If the dog is on more than one drug start with the one causing the most side-effects – or if financial considerations are paramount start with the most expensive. PCV and/or platelet counts should be checked weekly once stable and out of the hospital and then 1-2 weeks after each drug reduction. Weaning should take about 3-6 months, and because the immune system is suppressed the patient must be closely monitored for signs of infection.

While IMHA and ITP can have no apparent cause, we are aware that both diseases can be secondary in nature. IMHA has been linked to recent vaccination particularly rabies vaccination. Sulfa-based antibiotics can trigger ITP within 5-7 days and any unexplained bruising or bleeding is likely ITP; penicillins and cephalosporins have also been implicated. Neoplasia – especially lymphoma – can cause ITP. Both IMHA and ITP have been linked to infectious diseases especially tickborne infections; Babesia, Ehrlichia, anaplasmosis, leischmania, leptospirosis, heartworm, Lyme disease and Rocky Mountain Spotted Fever have all been found in cases of IMHA and ITP. Removing the causative drugs or treating the underlying condition will be necessary for a successful therapeutic outcome.

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