The thrombocytopenic patient

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Ashley qualified as an RVN in 2017. She began in first opinion before moving to the Internal Medicine department of the Royal Veterinary College. After delving into the world of veterinary medicine, she became interested in immune-mediated diseases. Ashley is passionate about conservation and would like to volunteer abroad.

ABSTRACT Immune-mediated thrombocytopenia (IMTP) is a life-threatening condition. Although it is not unheard of in felines, it is seen most commonly in canines (Donoghue, 2019). IMTP is a common disease in veterinary medicine and can affect any breed or age of dog but is most common in cocker spaniels, toy poodles, and middle-aged female dogs (Gorman, 2021).

Management of IMTP includes immunosuppressive and steroid treatment alongside a range of nursing care considerations. It is important that, as veterinary nurses, we understand the underlying physiology of the disease in order to best treat it. This article will provide an overview of IMTP and highlight key aspects of nursing care we can put to use in practice.

Keywords IMTP, immune-mediated thrombocytopenia, platelets, haemostasis

Introduction

Immune-mediated thrombocytopenia (IMTP) is a condition where the body's immune system starts to damage and destroy its own platelets, and is classed as either a primary or secondary condition. Primary IMTP has no known cause and is therefore referred to as being idiopathic.

Secondary IMTP occurs when there is a separate trigger or underlying cause. Large cells called megakaryocytes located within the bone marrow constantly produce platelets which are released into the bloodstream to support haemostasis. Haemostasis is the stoppage of bleeding and has three stages that occur within a short amount of time. Once haemostasis has happened, the repair of the tissue can start to take place (LaPelusa & Dave, 2020).

IMTP is one of the most common immune-mediated conditions seen in practice to date (Sellon, 2011). Platelets are vital for the formation of blood clots. They form together into a plug to help reduce and stop blood flow. The normal circulating platelet count at any one time can vary between 200,000 and 500,000 platelets per microlitre of blood. These platelets can last between 8 and 12 days and, once the old platelets are no longer of use, the spleen produces cells called phagocytes, which absorb the old cells and dispose of them, thereby creating space for a new batch (Brooks, 2003).

Phagocytosis is a naturally occurring process where phagocytes dispose of healthy platelet cells. This happens when immunoglobulins (antibodies produced by white blood cells) attach themselves to the outside of the platelet, thinking it is a foreign invader, and aids its destruction (Pullen, 2015). During IMTP, phagocytosis occurs 10 times faster than the normal rate. When the platelet count is reduced to between 20,000 and 50,000 platelets per microlitre of blood, spontaneous bleeding and bruising occurs (Brooks, 2003).

Presentation

On presentation, a patient can appear acutely unwell and, by this time, may already be severely thrombocytopenic as a result of platelet destruction. Presentation is varied due to the range in severity and clinical signs, but may include any of the following:

- Ecchymosis
- Petechiae
- Epistaxis
- Scleral haemorrhage
- Haematuria
- Mucosal bleeding
- Anaemia
- Hyphema
- Lethargy and weakness
- Anorexia
- Melaena
- Acute collapse

On examination, small pinpoint areas of bleeding called petechiae can be found on the skin and mucosal surfaces **(Figures 1 and 2)**. Larger areas of ecchymosis will accompany this and can often be found around the abdomen and groin areas. These clinical signs are the direct result of bleeding that has happened underneath the skin (BluePearl Specialists, 2021). Bleeding can also occur from the gastrointestinal tract and the patient will begin to pass melaena. Gastrointestinal bleeds are a prognostic indicator and linked to a more guarded prognosis due to likeliness of internal haemorrhaging (Gorman, 2021).

As haemostasis will be compromised in an IMTP patient, a presenting sign can be anaemia. Anaemia will result from an excessive amount of blood being lost, so added clinical signs to look out for would be:

- Pale mucous membranes
- Tachypnoea
- Tachycardia

Testing and diagnosis

On presentation, if the patient has not yet developed anaemia, it would still be important to monitor the patient's packed cell volume (PCV) and total protein (TP) closely. This is because, during hospitalisation, deterioration can occur quickly as the patient will be at a higher risk of spontaneous bleeding. Heart rate, and respiratory rate and effort, should be regularly monitored to ensure the patient is cardiovascularly stable. A spike in these could indicate the patient is becoming anaemic and may require a packed red blood cell (PRBC) transfusion. Fresh whole blood may be considered in emergencies, which may help the patient form enough platelets to stop

Figure 1. Gum petechiae.

Figure 2. Abdomen petechiae.

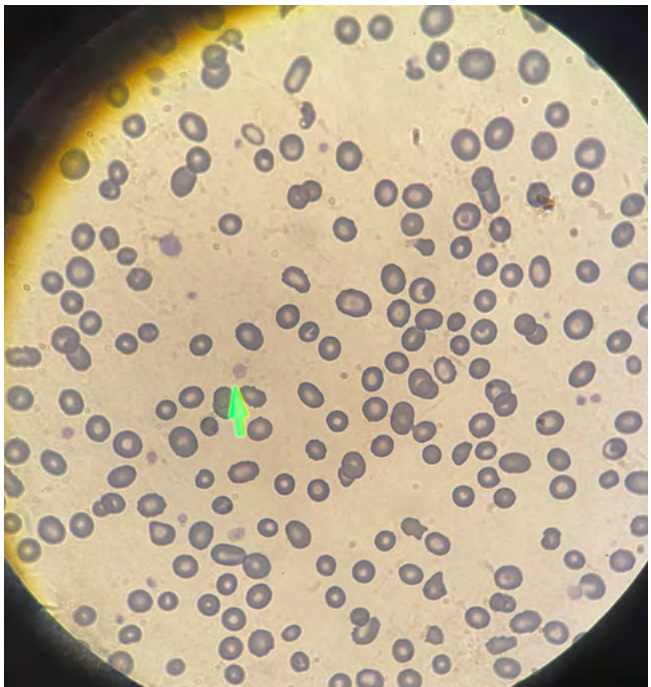

Figure 3. Blood smear identifying a platelet.

acute bleeding. However, it may not make a significant enough impact due to the declining platelet factor after initial collection (Walton & Tappin, 2021).

No single test can confirm a diagnosis of IMTP (Lo & Deane, 2014) but a thorough clinical examination alongside detailed history gathering is essential for a diagnosis of IMTP to be made. Initial blood samples should be taken for blood gas, to monitor urea and nitrogen, and for a complete blood count (CBC), biochemistry and coagulation panel. An assessment of the patient's blood smear **(Figure 3)** should be done in-house for a manual platelet count and also sent away to a laboratory. As the patient at this point would be thought to have IMTP, it is very important that the bloods obtained are taken from a peripheral vein. A pressure bandage should be applied to reduce the risk of haemorrhage and further severe bruising.

IMTP can be caused by several diseases and infections, so it is important to rule out the most likely causes and determine whether IMTP is primary or secondary. Further blood sampling can be obtained for 4DX and angiosnap. This should be taken to check whether the patient has any tick-borne or infectious diseases such as ehrlichiosis or babesiosis which could be causing the patient to be thrombocytopenic (Herrtage et al., 2020).

Once the patient is deemed stable, sedation for further imaging, such as abdominal ultrasound and computed tomography (CT), would be recommended to discover whether the patient has primary or secondary IMTP. Intramuscular sedation should be avoided in these patients and an intravenous catheter placed with care to reach a sedated effect. Carrying out imaging on IMTP patients is an important requirement as this condition can be frequently associated with neoplasia (secondary IMTP). This goes hand in hand with carrying out a CBC, biochemistry and coagulation panel and urinalysis, to help pinpoint any underlying causes. Automatic analysers can sometimes deliver spurious results so it is always imperative to create a manual smear when obtaining a blood sample. Once a diagnosis is confirmed, treatment plans can be decided, based on these findings. However, if the patient is diagnosed with secondary IMTP then treatment of the secondary cause would be vital, alongside treating the IMTP.

Figure 4. Dexamethasone treatment.

Treatment

In IMTP patients, the immune system has become extremely overactive and is causing life-threatening platelet destruction at a fast rate. Therefore, one of the essential initial actions is to try to suppress this overactivity of the immune system. Corticosteroids are the mainstay of treatment and are gold standard practice. Given their known efficacy, not to use them may be considered unethical (Herrtage et al., 2020). During initial stabilisation of IMTP patients, dexamethasone, which is a glucocorticoid steroid, is used as an intravenous medication **(Figure 4)**. Once stabilised on this, the patient can be moved to an oral corticosteroid medication, also known as prednisolone, which has functional anti-inflammatory properties. See the table **(Table 1)** for other advantages of using corticosteroids in IMTP patients. The patient should also be monitored for any side effects outlined in the table.

The choice of which of the next two drugs are used will be clinician and case dependent. Two forms of immunosuppressive treatment can be used alongside prednisolone: cyclosporine and azathioprine. The

Table 1. Advantages and side effects of using corticosteroids.

Advantages of using corticosteroids	Side effects of using corticosteroids
Works directly on cells, interrupting phagocytosis	Polyuria and polydipsia (PUPD)
Inhibits destruction of antibody-sensitive platelets by macrophages	Increased appetite
Can impair auto-antibody production	Vomiting
Increases capillary resistance to haemorrhage which, in return, reduces severity of haemorrhage while waiting for the platelet count to increase	Skin infections, due to immunosuppression
May stimulate platelet production in some patients	Steroid-induced diabetes

advantage of using one of these drugs in conjunction with prednisolone is that it can lower the prednisolone dose administered, reducing severe side effects (Foale, 2015).

When a patient is on azathioprine, it can cause bone marrow suppression (Makielski et al., 2018). If this occurs, the patient will be open to further infections and it can lead to the patient becoming neutropenic. If neutropenia is indicated in an IMTP patient then help in reducing any potential acquired infections is important. Introducing antibiotics may help in the control of any developing infection. In addition to this, the patient may also experience vomiting, diarrhoea, inappetence and nausea, so may need adjuvant therapy on top of immunosuppressants to help reduce these side effects. Gastroprotectants and antiemetics such as omeprazole, ondansetron, maropitant and sucralfate will be beneficial in helping to control these side effects.

In most IMTP patients, platelet recovery can usually be seen 1–15 days after glucocorticoid treatment. However, if the patient is acutely unwell and at a risk of sudden death, another form of treatment that can be given is vincristine. Vincristine rapidly increases platelet numbers by stimulating platelet release from the bone marrow; it then stops phagocytosis of platelets and interferes with antibody formation. Vincristine also accelerates the breakdown of megakaryocytes and helps stimulate thrombopoiesis (Park et al., 2015). In addition, another form of treatment for consideration is human intravenous immunoglobulin (hIVIG). hIVIG treatment is when the required component immunoglobulin G (IgG) is derived from healthy humans. It can be given to refractory IMTP patients and acts as a strong anti-inflammatory. This works by blocking FC receptors on the phagocytic cells and helps stop platelet destruction (Olivares, 2021). However, hIVIG is rarely available as it is in high demand in human hospitals. A study has shown that, in refractory IMTP, vincristine should be the first choice for acute management due to its lower cost and ease of administration compared to hIVIG (Balog et al., 2013).

Figure 5. Jugular petechiae.

When considering the range of treatments available to IMTP patients, it is important to remember that treatment could potentially be lifelong and not withdrawn suddenly. Once the patient starts to improve, they are to be continuously monitored and medication doses tapered down accordingly to the lowest level achievable.

Nursing the patient

Nurses play a fundamental role in helping stabilise and manage IMTP patients. This can be a very challenging task as IMTP patients usually stay in for extended periods of time. It is important to consider the patient's accommodation, which will need to be padded (e.g. a patient mattress with a thick comfortable bed) due to the risk of localised bruising or bleeding from simple knocks to the body. It is also important the patient is only walked on a harness and not a slip/neck-lead as this could put excess pressure on the neck and cause further bruising and spontaneous bleeds if too much pressure is applied.

IMTP patients have their bloods taken regularly during their stay and it is vital that no jugular samples are obtained, as this is a major vessel. Complications arising from a jugular sample being taken **(Figure 5)** could be highly detrimental to the patient, due to the inability to safely apply post-sampling pressure to the jugular sufficiently and for long enough. This can lead to haematoma formation and occlusion of breathing. Ideal sampling areas would be from a cephalic or saphenous vein, followed by a pressure bandage. It is imperative that the pressure bandage is not left on for an extended period of time, as this can lead to further bruising and damage.

Intramuscular and subcutaneous injections should also be avoided where possible and medications should be given intravenously or orally. It is essential to note that when giving oral medication to an IMTP patient, it can potentially cause trauma to the mouth, especially in tricky patients. To minimise the trauma caused, medication can be hidden in food or can be continued intravenously, but it is helpful to ensure the patient is eating prior to transitioning to oral medications. This is to ensure that the medication has definitely been ingested, and that it has not led to food aversion. Food aversion should be avoided in an IMTP patient as even everyday tasks could cause their condition to deteriorate. For example, even if usually fed dry food at home, when these patients are in hospital soft food should be offered first, as dry food could damage their gums by causing mucosal bleeding. As the patient already has a low platelet count, this could lead to oral lesions that continue to actively bleed.

Figure 6. Haematuria.

Feeding tubes in IMTP patients are usually avoided as existing trials have not evaluated the feasibility of either nasogastric or oesophageal tubes being placed – due to the contraindication of bleeding complications (Patel et al., 2016).

As a whole, it is important to handle IMTP patients very gently in all aspects of treatment and care, due to their risk of haemorrhage following the slightest bump or knock, which could cause them to have a spontaneous bleed. The patient's vitals, such as heart rate and respiratory rate, should be monitored frequently. Documenting and monitoring the areas of localised bruising and petechiae on the patient should also be carried out, in order to monitor deterioration. This can be achieved either by carefully clipping the areas of bruising and marking with a pen, or by taking daily pictures. As the patient will be on a high dose of steroids, it is important to ensure they have free access to water and are able to reach this themselves. If not, offering them water frequently should be added to their hospital sheet. As the patient will be drinking more, they will need to toilet frequently so regular walks are necessary, along with absorbent bedding to reduce the risk of urine scalding. When walking, it is important to check their urine and note any abnormalities that may be present, such as haematuria **(Figure 6)** or pigmenturia. A urine sample for laboratory testing and monitoring may also need to be collected. Another nursing consideration would be wearing appropriate personal protective equipment (PPE) when handling the patient, such as gloves and an apron, because they are likely to be on immunosuppressant treatment and will need reverse barrier nursing for their own protection. If the patient has received cytotoxic treatment then a full-length apron and purple nitrile gloves will be sufficient.

Conclusion

Overall, it is found that dogs diagnosed with IMTP can have a good recovery rate of around 75–85% if caught early and treated accordingly. However, studies have shown that when the patient develops and starts to produce melaena, the chances of survival reduce to 60% (Gorman, 2011). IMTP patients can be one of the most challenging but also rewarding cases to nurse. There is a lot that veterinary nurses can do to help keep the patient comfortable while reducing their injury risks in hospital. It is imperative to alert other staff members to what can and cannot be done with the patient during their stay, so their injury risk is reduced and they have more chance of recovering from this life-threatening condition.

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