Equine idiopathic eosinophilic IBD: diagnosis and management

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VERONICA ROBERTS discusses the practical considerations when confronted with these conditions, as well as outlining the clinical signs and available treatments

EOSINOPHIL-DOMINATED inflammatory infiltration of the equine intestine may occur with a clear cause, such as severe endoparasitosis (Makinen et al, 2008). However, falling within the inflammatory bowel disease (IBD) complex in the horse are a number of idiopathic eosinophilic intestinal conditions of growing importance.

These intestinal conditions are characterised by active inflammation where eosinophils form a major component. They are usually accompanied by characteristics consistent with inflammation of greater than three days' duration, such as neovascularisation, fibrosis, lymphocyte and plasma cell infiltration (Makinen et al, 2008). The colon (colitis), small intestine (enteritis), or both (enterocolitis) may be affected. Inflammation may be diffuse through the intestine (diffuse eosinophilic enteritis/enterocolitis [DEE]; Figure 1), or form in single or multiple, focal, circumferential or plaque-like constrictions, usually in the small intestine – although segments of the large intestine may be affected (idiopathic focal eosinophilic enteritis [IFEE], or segmental eosinophilic colitis; Figure 2).

While the inflammation in DEE tends to be located in the mucosa and IFEE in the submucosa and muscularis externa, it appears the two conditions are not separate. Even in the grossly normal areas of intestine in an IFEE case, histology usually reveals inflammation consistent with DEE, suggesting IFEE to be a focally exacerbated inflammatory reaction in horses with DEE (Makinen et al, 2008).

Multisystemic eosinophilic epitheliotrophic disease (MEED) is possibly a related subset, where eosinophilic infiltration also affects other organs and tissues including the skin, oral cavity and lungs (Kalck, 2009).

Why do they happen?

The aetiology is unknown. A hypersensitivity or other immune-mediated reaction is considered likely and infectious agents, including endoparasites, have not been identified (Southwood et al, 2000). Changes in management, dietary factors and death of migrating parasites due to anthelmintic treatment are possible contributing factors (Southwood et al, 2000; Archer et al, 2006). No relationship between age, sex or breed has been detected (Southwood et al, 2000; Archer et al, 2006). It has been suggested gluten intolerance may play a part in some cases, with raised gluten-dependent antibodies and, in one case, a good clinical response to a gluten-free diet (van der Kolk et al, 2012).

In human eosinophilic-gastrointestinal diseases (EGIDs), food allergy is often implicated (Furuta et al, 2008).

Prevalence

There are no data on prevalence or incidence of these conditions. They may be considered emerging diseases (Archer et al, 2006), although it is unclear whether there is a true increase in the condition or an increase in its recognition.

In humans, a rapid rise in prevalence of some EGIDs has been documented in several populations (Furuta et al, 2008). This increasing prevalence mirrors the rise in allergic disease that has been occurring for the past four decades, which, in turn, parallels a declining incidence of infectious diseases, in particular with helminth parasites (Furuta et al, 2008). It is certainly tempting to draw a direct parallel from the human situation to the equine and would be very interesting to follow any changes in prevalence and incidence of equine eosinophilic IBD, which may follow a move towards targeted parasite control. However, to do this the incidence and prevalence of eosinophilic IBD among the general equine population must be determined.

Presenting signs

Clinical signs may be very variable between individuals. Chronic cases would usually present with clinical signs of malabsorption and maldigestion, so weight loss is seen in enteritis cases and diarrhoea in colitis cases. They may concurrently, or alone, suffer chronic or recurrent colic. Horses may also present with acute colic, which may be severe. These may have obstruction from a circumferential band of inflammation, although underlying these there is usually a more chronic diffuse inflammation. Those with chronic diffuse inflammation also seem able to suffer an acute

exacerbation, so the first presenting sign may be acute colic. Others may present as large intestinal displacements, possibly secondary to poor digestion of carbohydrates in the small intestine, resulting in excess production in the large intestine.

Reaching a diagnosis

Horses that present with acute colic will often meet criteria for exploratory laparotomy. The gross appearance of the gastrointestinal (GI) tract seems to vary a lot between individuals. In some, there will be part or the entire GI tract that appears abnormal, being discoloured and/or thickened. Others will appear grossly normal, but have abnormal histology. In those with circumferential mural bands, the remainder of the GI tract may appear normal, although it is likely to be diffusely inflamed. A circumferential mural band in the small intestine may cause a functional obstruction, with small intestine distended proximally. These bands may be confused with focal damage to the intestine from a transient entrapment.

In horses having an emergency exploratory laparotomy, where either no diagnosis is made or eosinophilic IBD is suspected, full thickness biopsies should be taken. These should be taken both in areas of the GI tract that appear unaffected and those that do. Biopsies can be very difficult to interpret, as normal horses may have a degree of eosinophilic mural infiltration, so a pathologist with experience of the condition should interpret the histopathology (Schumacher et al, 2000).

Biopsy is also the mainstay of diagnosis for horses with a chronic presentation. Exploratory laparotomy to investigate other possible causes and take multiple full-thickness biopsies is ideal diagnostically, but may not be the optimum course of action for many patients. Rectal biopsy is likely to be the first step, being simple and far less invasive. Care must be taken in using rectal histology to give information about possible pathology in the colon and even greater care with possible pathology of the small intestine. One study (Lindberg et al, 1996) found correlation between rectal biopsy and postmortem results in approximately 50 per cent of idiopathic eosinophilic cases. It is possible to obtain pinch mucosal biopsies from the duodenum via gastroscopy. These can be helpful for small intestinal disease, but a full-thickness biopsy may be required to detect eosinophilic infiltration. Should these be unrewarding, surgical biopsy should be considered. Biopsies can be taken from the small intestine via standing laparoscopy or laparoscopic- assisted laparotomy, but it is not always possible to sample the large intestine. Resection of an abnormal length of small intestine may be possible via standing laparoscopic-assisted laparotomy.

Haematology is likely to be unremarkable. Some cases will have anaemia of chronic disease. MEED cases may have a peripheral eosinophilia. Biochemistry may reveal hypoalbuminaemia and hyperfibrinogenaemia, but this would depend on severity and chronicity. On occasion, there may be signs of inflammation in a peritoneal fluid sample.

Abdominal ultrasonography may reveal thickening to the small or large intestinal walls, but is poorly

sensitive and specific. Oral glucose tolerance test (OGTT), if abnormal, would be consistent with poor absorption from the small intestine. However, the small intestine may be diseased and give a normal OGTT and the OGTT does not help differentiate between possible causes of small intestinal malabsorption.

Treatment

The mainstay of treatment is corticosteroids. There is little evidence as to dose and length of course required. Response to treatment varies between individuals, with some responding to one course of treatment, some needing repeated courses, some lifelong treatment and others not responding at all. There appears to be little correlation between histological and gross severity and clinical response to treatment. The author empirically may start with two to three days of 0.1mg/kg dexamethasone (IV), then 1mg/kg once a day prednisolone (PO) for one week, then every other day for two weeks, then halving the dose for four weeks. This is not evidence-based and subject to change dependent on the patient's response.

Surgical resection of affected areas of intestine may be bene_ cial where the disease is either localised or has a very severe local exacerbation. However, the disease is usually diffuse, even if the intestine appears grossly normal.

Dietary management is very important in people, who start an exclusion diet. We know little about this in horses, which effectively eat an exclusion diet anyway. There may be some benefit in increasing the short fibre proportion of the diet to decrease digestive workload. Adding *Saccharomyces cerevisiae* to feed may increase pH, which may be beneficial to an inflamed intestine. One horse appeared to respond to a gluten-free diet (van der Kolk et al, 2012).

What still needs to be discovered?

Further work on epidemiology and to _ nd a cause is required. It appears, in humans at least, to be a disease of the first world, so the effects on the immune system of deworming and exposure to gluten may be involved.

Case study

A 16-year-old warmblood mare presented with a threemonth history of mild, recurrent colic and, more recently, severe weight loss. On rectal palpation, the intestinal wall felt thickened. Abdominal ultrasonography revealed a distended, poorly motile loop of small intestine with a thickened, oedematous wall (Figure 3). Standing laparoscopy con_ rmed several metres of poorly motile, distended small intestine with petechiation (Figure 4). There was too much affected intestine to be able to perform a resection via standing laparoscopic-assisted laparotomy. At a standard laparotomy, 15 metres of grossly affected small intestine was resected. Histology showed severe eosinophilic enteritis with almost no absorptive surface remaining (Figures 5 and 6). The mare was

initially treated with intravenous dexamethasone and then oral prednisolone, decreasing the dose over a threemonth period. The mare is pictured (Figure 7) following three months of treatment, having gained 100kg in weight, but still needing to gain more and then at eight months (Figure 8). She required no further corticosteroids and was clinically normal at one year follow-up.

Références

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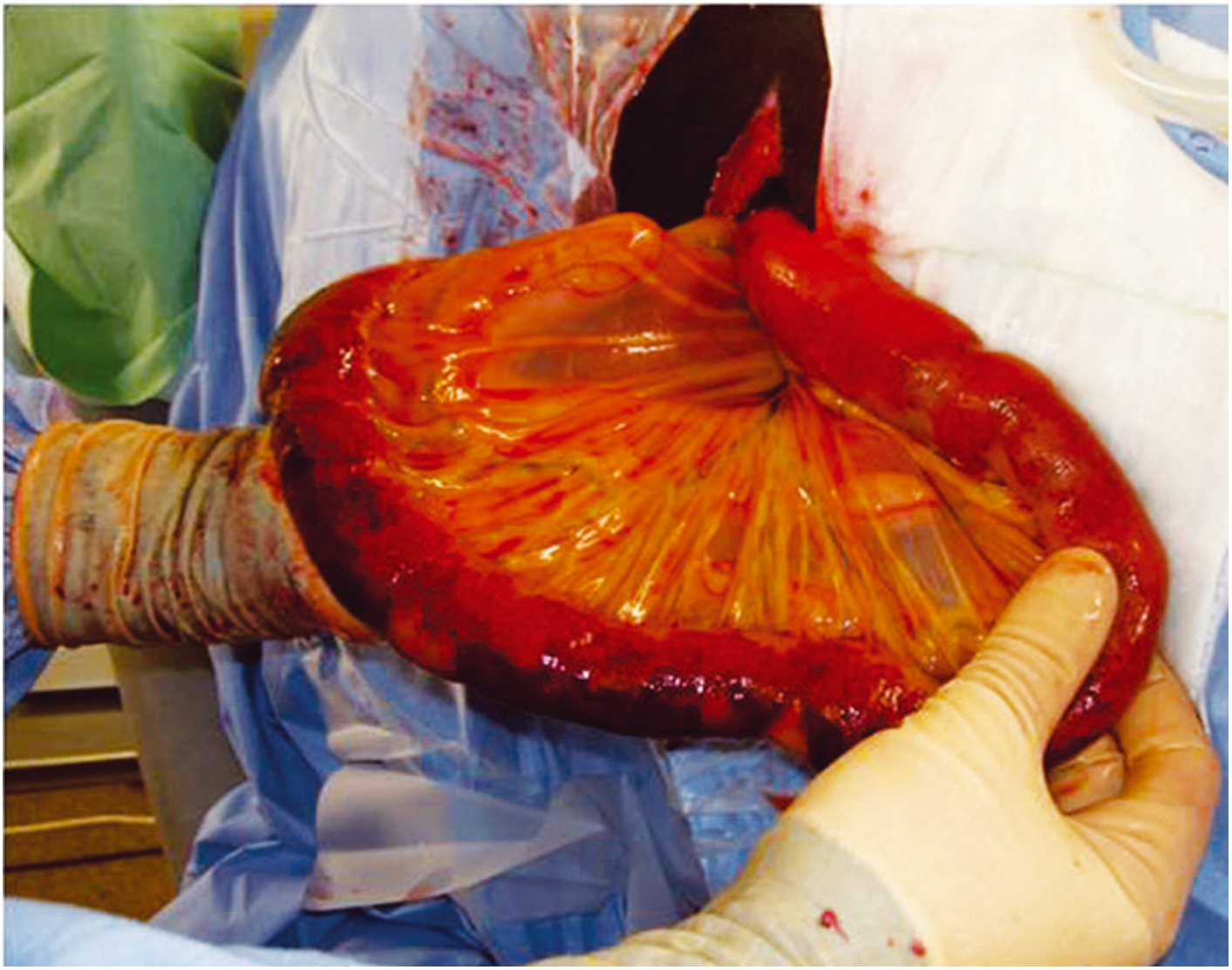

Figure 1. Thickened, haemorrhagic small intestine in a horse with eosinophilic enteritis. Presented with recurrent, low grade colic. Biopsies taken with laparoscopic assisted laparotomy. Excellent response to one course of corticosteroids.

IMAGE: Dylan Gorvy.

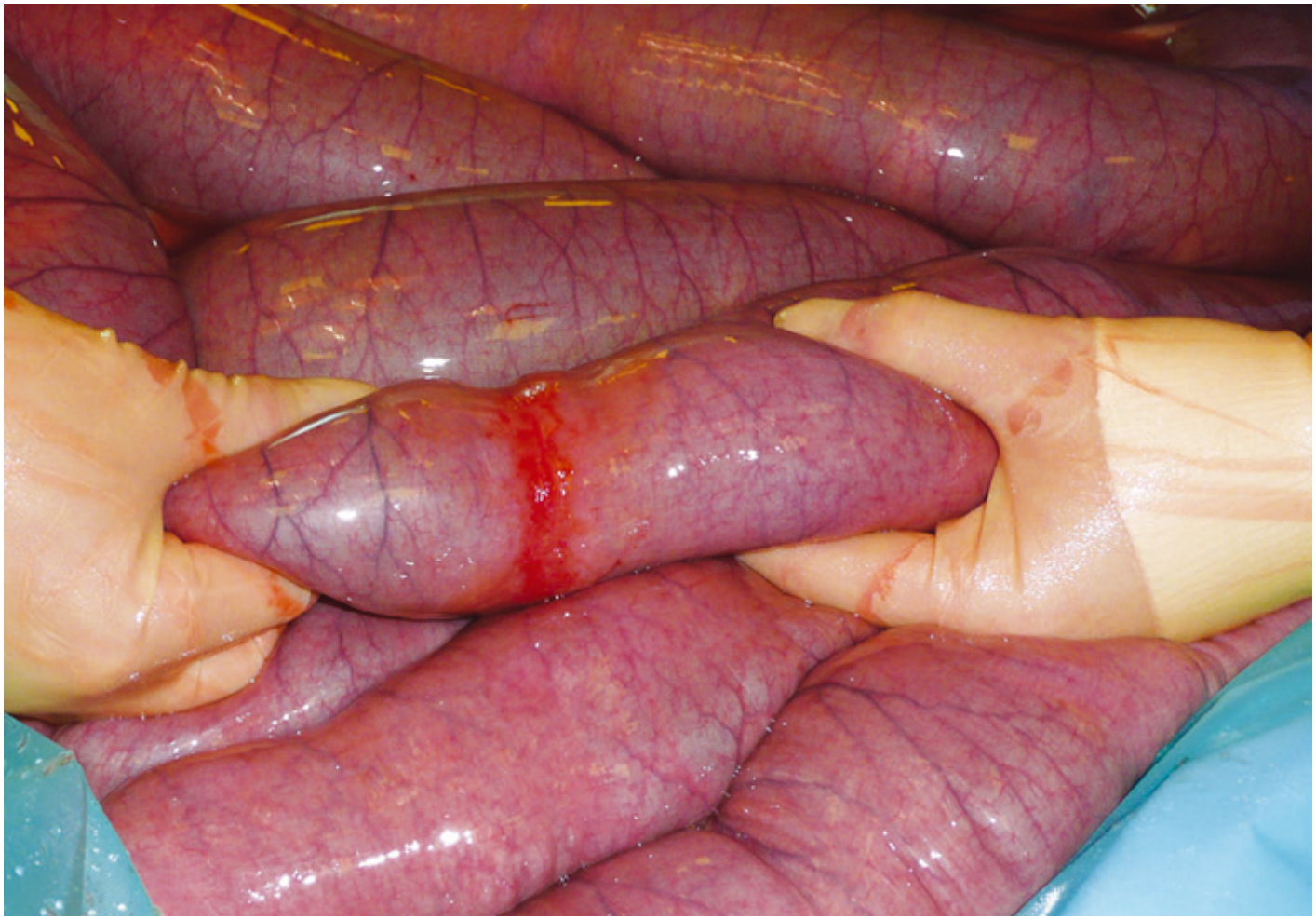

Figure 2. Circumferential mural band in the small intestine of a horse presented with acute colic, distended small intestine and gastric over-filling.

IMAGE: Debra Archer.

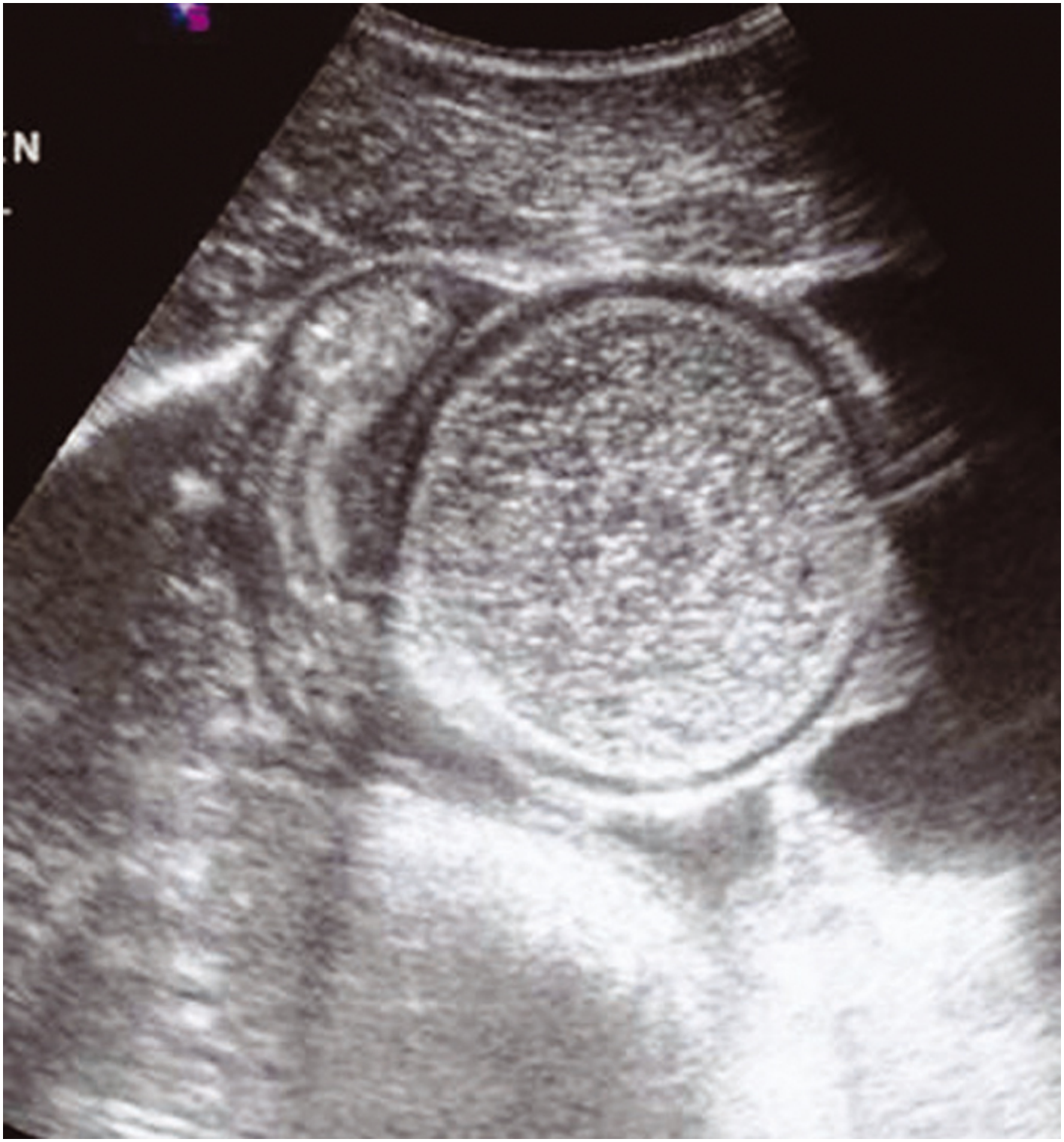

Figure 3. In the case study, abdominal ultrasonography revealed a distended, poorly motile loop of small intestine with a thickened, oedematous wall.

IMAGE: Debra Archer.

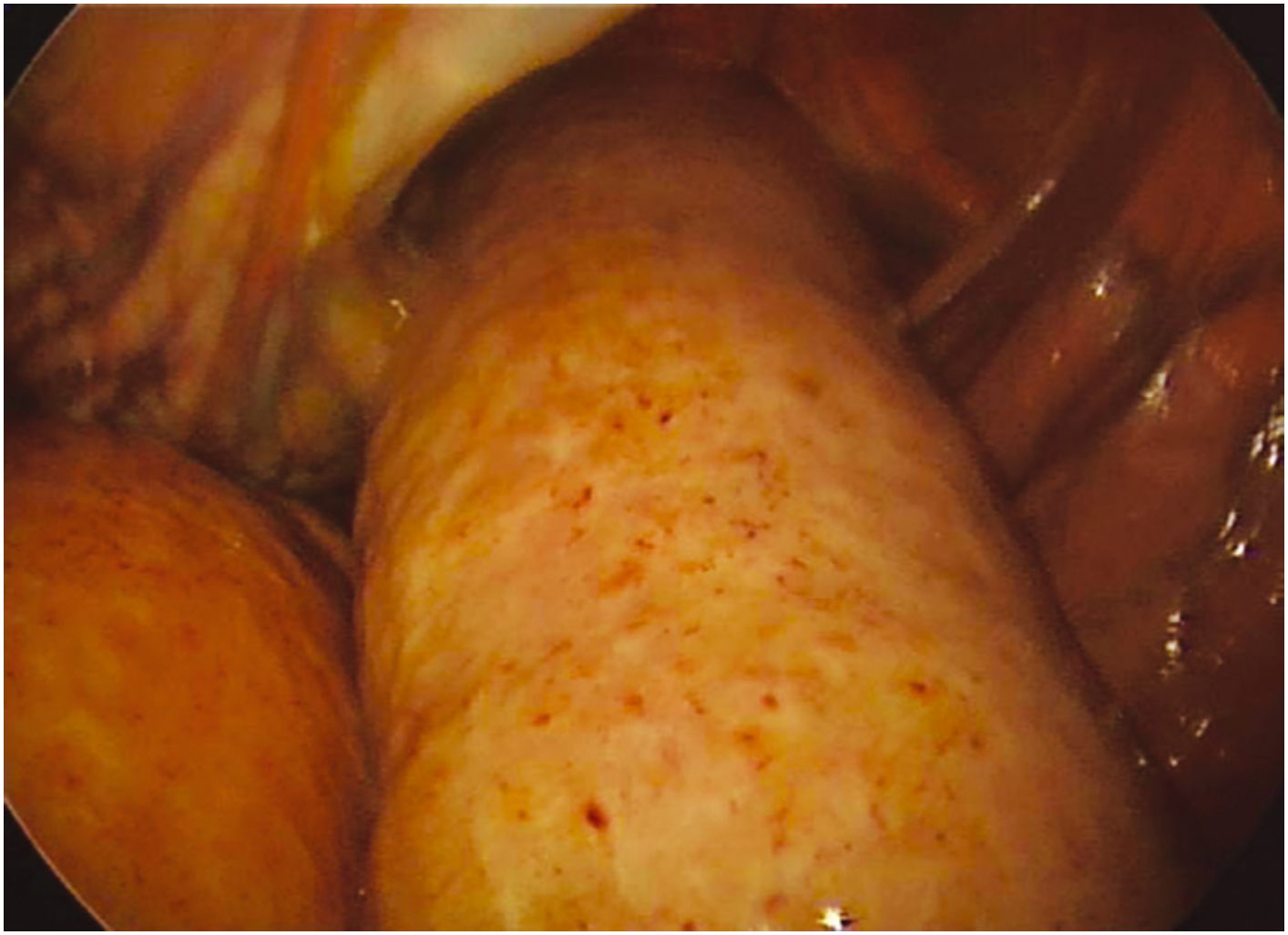

Figure 4. Standing laparoscopy confirmed several metres of poorly motile, distended small intestine with petechiation.

IMAGE: Dylan Gorvy.

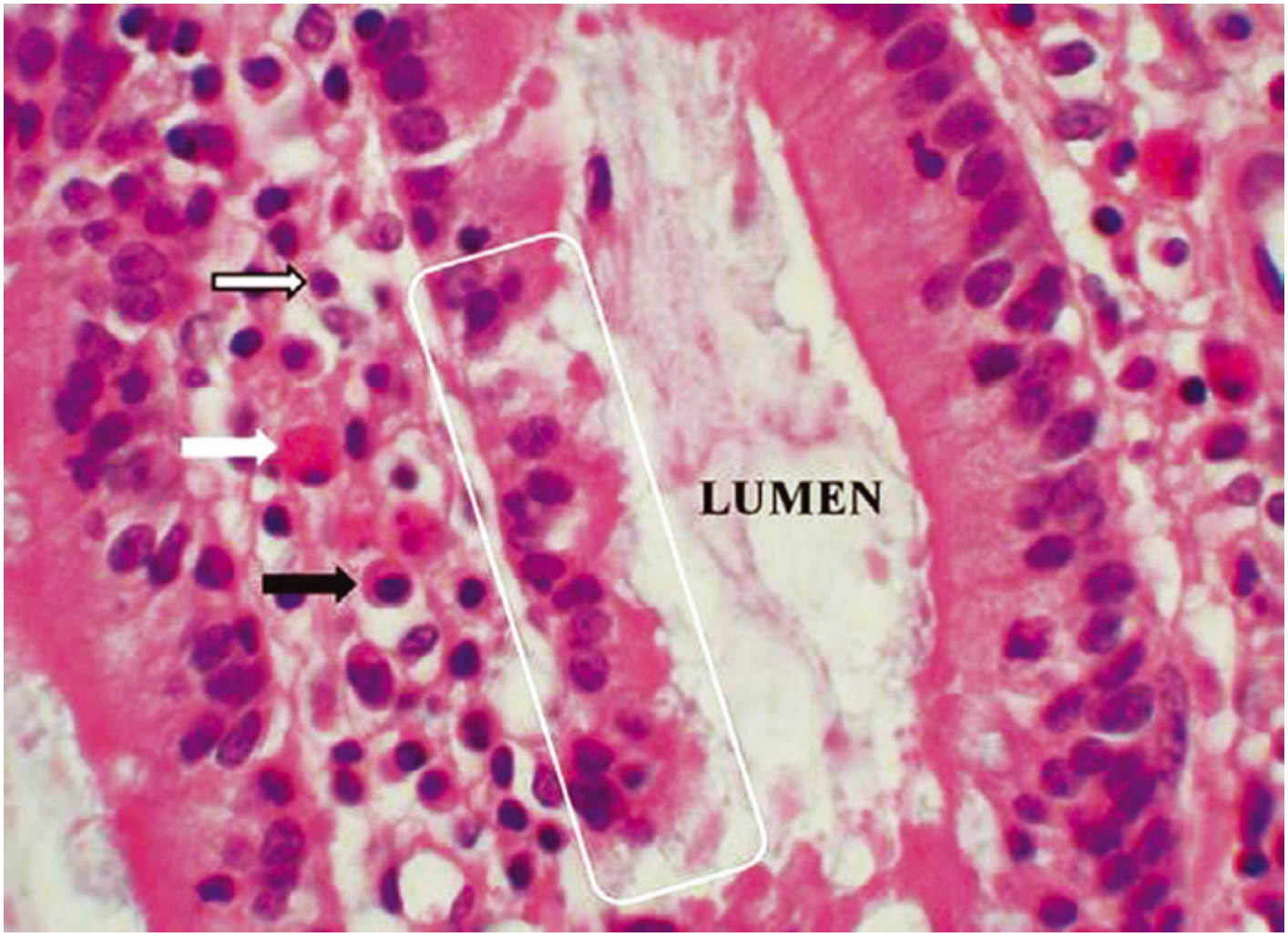

Figure 5 arrows, top to bottom: small lymphocyte, eosinophil, and plasma cell.**Figure 5** and **Figure 6.** Histology showed severe eosinophilic enteritis with almost no absorptive surface remaining.

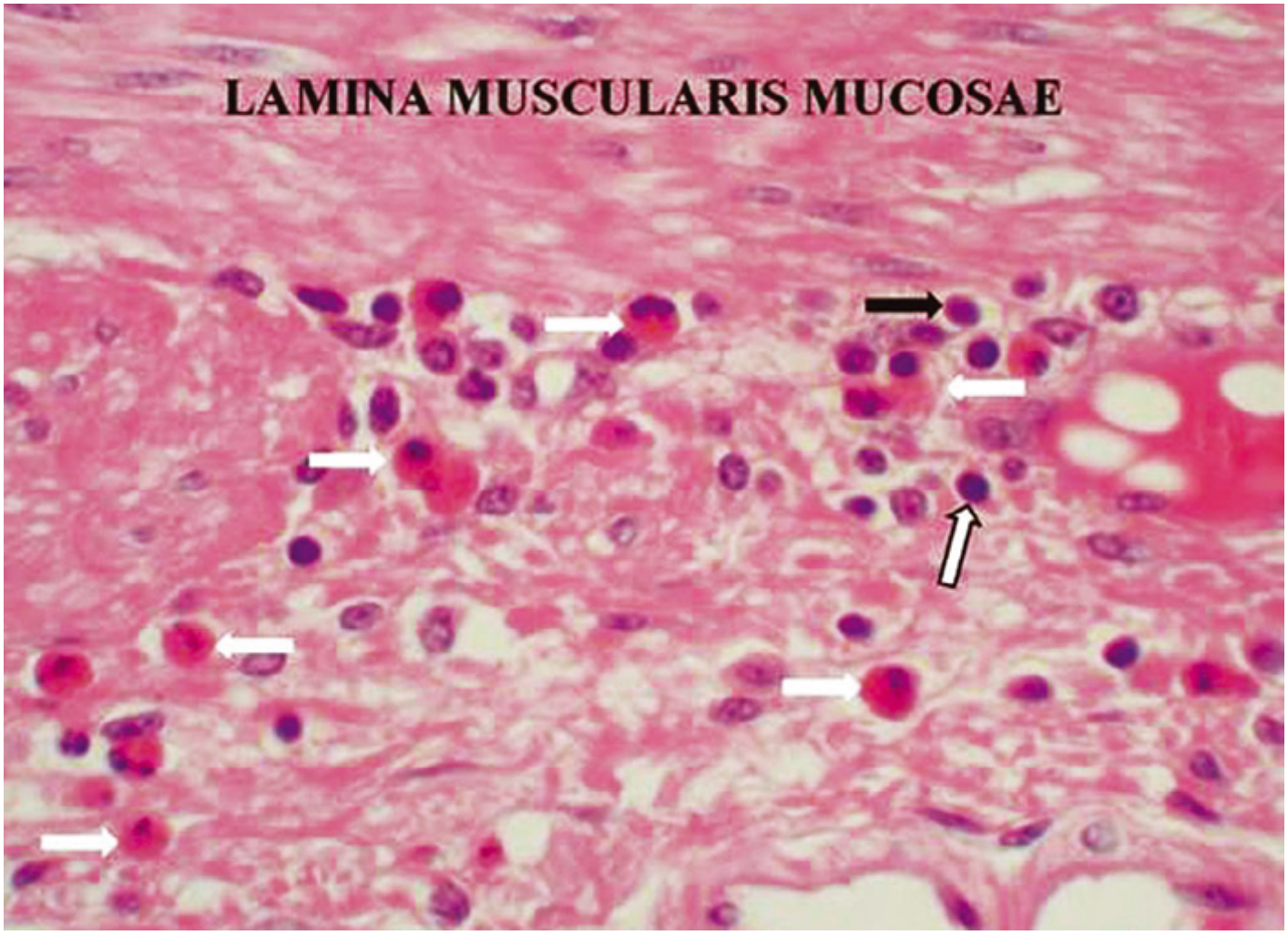

Figure 6 arrows: white arrows – eosinophils; yellow arrow – lymphocyte; black arrow – macrophage.**Figure 5** and **Figure 6.** Histology showed severe eosinophilic enteritis with almost no absorptive surface remaining.

IMAGES: Dylan Gorvy and Harold Tvedten.

Figure 7. The mare following three months of treatment.

IMAGE: Dylan Gorvy.

Figure 8. Eight months after surgery.

IMAGE: Dylan Gorvy.