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Pathology in Practice

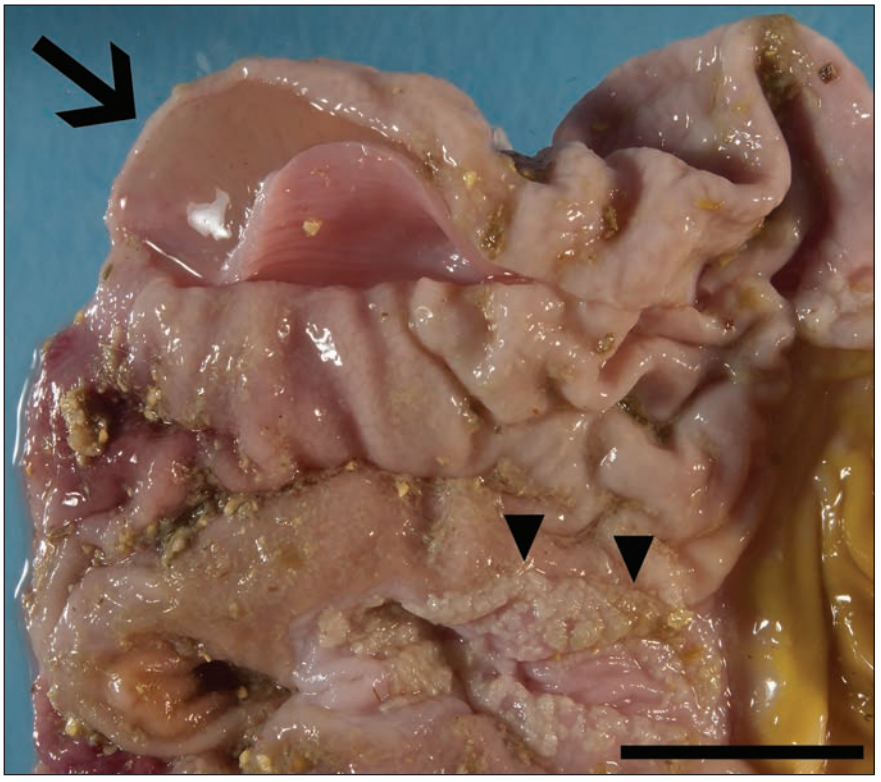

Figure 1—Photograph of the mucosal aspect of a portion of the stomach of a 7-week-old Yorkshire pig from a group of 30 Yorkshire pigs that had been weaned 4 weeks prior but had never thrived, with some pigs having developed diarrhea and coughing. Five pigs had died. The pig was submitted for euthanasia and necropsy. Notice the marked mural edema of the gastric fundus (arrow) and hyperkeratosis of the pars esophageal region (arrowheads). Bar = 2 cm.

History

A 7-week-old 9.6-kg (21.1-lb) female Yorkshire pig was submitted for euthanasia and necropsy to the Animal Disease Diagnostic Laboratory at Purdue University. The pig was from a group of 30 Yorkshire pigs that had been weaned 4 weeks prior but had never thrived, with some pigs having developed diarrhea and coughing. In the 2 days prior to submission of the pig, 5 other pigs in the group developed clinical signs including shivering, lethargy, dyspnea, and staggering that progressed to paddling and death within 12 to 14 hours. Some of the affected pigs had swollen eyelids. The antemortem clinical signs of the submitted pig were not reported. Twenty-nine of the pigs, including the pig submitted, had been treated with antimicrobials.

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Gross Findings

The pig was euthanized via alternating current electrocution in accordance with the 2007 AVMA Guidelines on Euthanasia and the Purdue University Animal Care and Use Committee recommendations. The pig was in adequate body condition and had multiple dermal abrasions on the right hind limb and left pinna. Bilaterally, the eyelids were mildly swollen. The gastric fundic mucosal rugae were flattened. On cut surface, the wall of the fundus was expanded by clear to red, wet, gelatinous tissue (**Figure 1**). Incidentally, the mucosa of the pars esophageal region of the stomach was thickened and its surface was rough. Mesenteric lymph nodes were mottled gray to dark red and enlarged. The inguinal lymph nodes were also enlarged.

Formulate differential diagnoses from the history, clinical findings, and Figure 1—then turn the page →

Histopathologic Findings

Specimens of major organs and tissues including the stomach were collected, fixed in neutral-buffered 10% formalin, routinely processed, embedded in paraffin, sectioned, stained with H&E stain, and examined by light microscopy. The most important histopathologic findings were detected in the gastric fundus. At this level, the gastric submucosa was severely expanded by edema and free erythrocytes (**Figure 2**). Multifocally, submucosal vessel walls were brightly eosinophilic and lacked cellular detail (fibrinoid necrosis; **Figure 3**). Surrounding the affected vessels were few neutrophils, lymphocytes, and erythrocytes. Some submucosal vessels contained fibrin thrombi, and a few vessel walls were infiltrated by moderate numbers of neutrophils and lymphocytes. The lamina propria contained free erythrocytes, lymphocytes, and eosinophils. The serosa was mildly expanded by edema.

Morphologic Diagnosis and Case Summary

Morphologic diagnosis: severe gastric submucosal edema, with vasculitis, fibrinoid degeneration, and mild eosinophilic and lymphocytic gastritis.

Case summary: edema disease in a pig.

Comments

For the pig of the present report, a diagnosis of edema disease was made on the basis of clinical signs, gross evidence of eyelid and gastric edema, and supporting histopathologic lesions. Edema disease is an enterotoxemia caused by Shiga toxin 2e–producing *Escherichia coli* (STEC), usually organisms of the O138, O139, and O141 serogroups.[1,2] The susceptibility of pigs to STEC F18 is genetic and dependent on a substitution of guanine for adenine at nucleotide 307 of the alpha(1,2)-fucosyltransferase (*FUT1*) gene on chromosome 6. Pigs with an *AA* genotype are resistant to STEC F18, and pigs with *GG* or *AG* genotype are susceptible to STEC F18.[3] Furthermore, a recent study[4] found that *FUT1* gene expression is age dependent; expression decreased from days 8 to 18 and then increased from days 30 to 35, with the highest expression at the time of weaning.

When STEC F18 binds to enterocytes within the small intestine, Shiga toxin 2e translocates through the enterocytes and enters the bloodstream via a yet unknown pathway. In target tissues, especially in the cerebellum and gastric and colonic submucosa, Shiga toxin 2e binds to endothelial cells of small arteries and arterioles and causes angiopathy, resulting in endothelial damage and necrosis, vascular leakage, and tissue edema.[1,5,6]

Tissue edema is the classic finding during both gross and microscopic examinations. Gross lesions are variable, and edema in the cardia and greater curvature of the stomach, mesocolon, and mesenteric lymph nodes is the most common feature. Other findings include edema of the eyelids, face, and ventral aspect of the abdomen; hydropericardium; and pulmonary edema.[1,2] Histopathologic lesions are also variable depending on the time course of the disease. With peracute death, histologic lesions may be minimal. In acute to subacute cases, the major histologic findings are edema in affected tissues, swelling of endothelial cells, fibrinoid degeneration, and myocyte necrosis in the tunica media of small arteries and arterioles. Hemorrhage and vasculitis are variably present. More chronic cases may have a proliferation of mesenchymal cells within the tunica media and tunica adventitia. In the CNS, the disease often results in cerebrospinal angiopathy with meningeal edema and distended Virchow-Robins spaces and, rarely, with ischemic necrosis in chronic cases. However, no CNS lesions were observed in the pig of the present report either because of the acute course of the disease or difficulty in distinguishing cerebral edema from preparation artifact.[1]

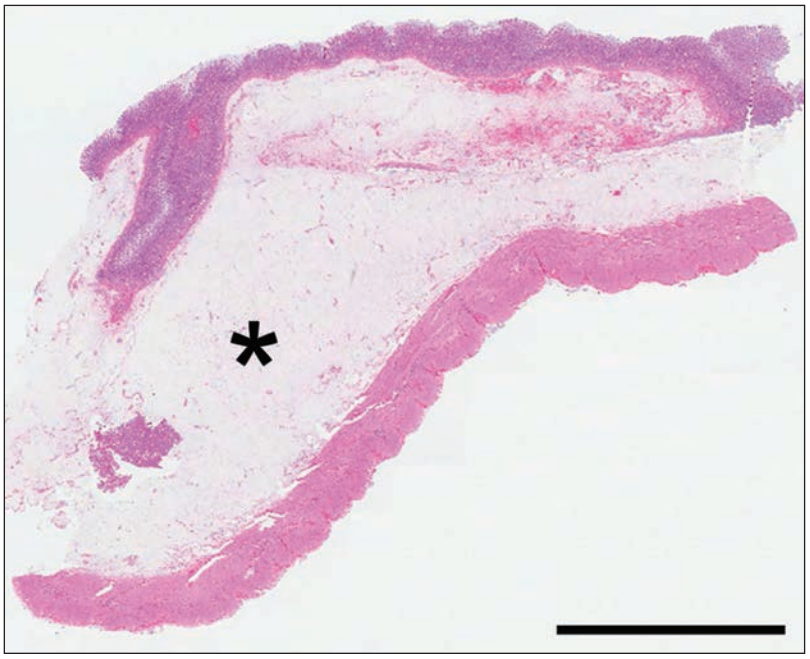
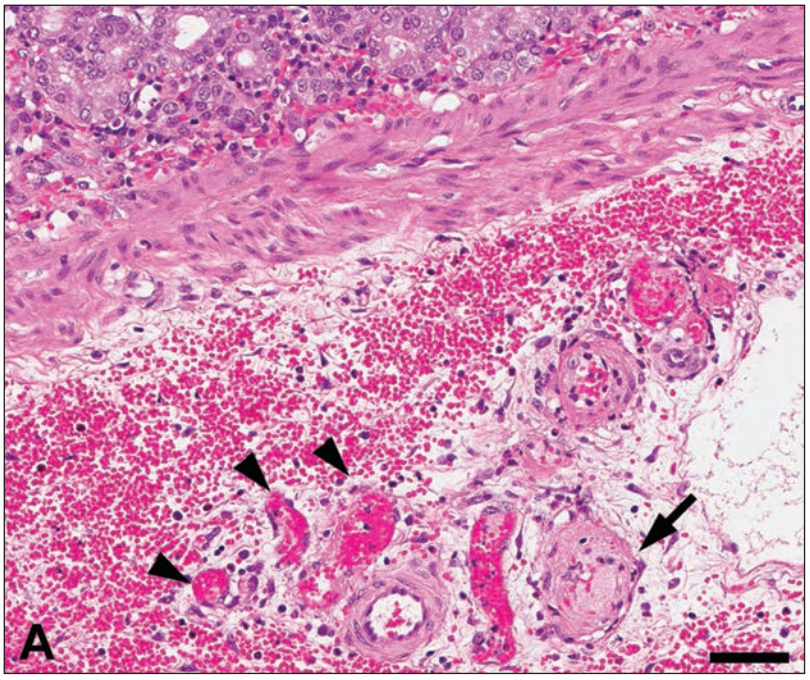


Figure 2—Photomicrograph of a section of the stomach in the pig in Figure 1. Notice the marked submucosal edema (asterisk) and scattered hemorrhages. H&E stain; bar = 5 mm.

In disease outbreaks among pigs, morbidity rate is low (< 15%) but mortality rate can be between 50% and 90%.[1,2,7] Edema disease can occur sporadically or in larger outbreaks, and often, the most valuable animals in the group are affected. Clinical signs include anorexia, neurologic signs, and sudden death.[1,2] The disease typically affects 4- to 12-week-old pigs, usually 2 weeks after weaning, which correlates with *FUT1* gene expression. There is no treatment for edema disease in pigs after the onset of clinical signs. There is no commercially available toxoid vaccine, although vaccination with Shiga toxin 2e toxoid has been proven to be efficacious in preventing clinical signs and subclinical disease.[8] A high-fiber diet and good sanitation and management practices are



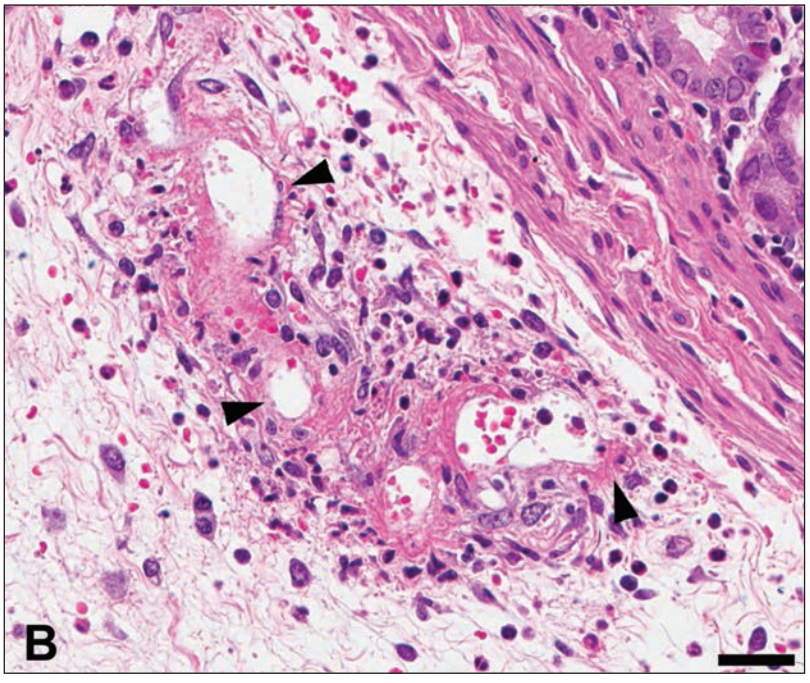


Figure 3—Higher magnification views of the section of stomach seen in Figure 2. A—Notice the fibrinoid degeneration of submucosal vessels (arrowheads). There is a vessel partially occluded by a fibrin thrombus (arrow). The submucosa is expanded by edema and free erythrocytes (hemorrhage). The lamina propria is infiltrated by lymphocytes and eosinophils. H&E stain; bar = 50 µm. B—In this area of fibrinoid degeneration of submucosal vessels (arrowheads) in the stomach tissue, notice the perivascular infiltrate of neutrophils and lymphocytes. H&E stain; bar = 25 µm.

important in preventing disease development among pigs.

No substantial bacterial growth was identified in cultures of any tissue samples from the pig of this report. However, the pig had a history of antimicrobial treatment, which could have precluded bacterial isolation. Although serologic identification of common STEC serotypes and PCR amplification of the genes for Shiga toxin 2e and F18 fimbriae can provide a rapid and definitive diagnosis, the diagnosis of edema disease can be made on the basis of clinical signs, gross findings, and histopathologic lesions; additional testing is not required and negative results of bacterial culture do not rule out infection with STEC.[2] Edema disease is reported less commonly in the United States today but remains an important disease. The remaining pigs in the original group appeared to respond to antimicrobial treatment, and no additional deaths occurred.

References

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