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Septic Peritonitis: Focus on rapid diagnosis and the essentials of initial management

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The reported mortality rate for septic peritonitis in veterinary patients remains high and varies between 20 – 68%. This contrasts with human studies where mortality ranges between 2 – 20%. These number can increase dramatically in the setting of severe sepsis or septic shock. Outcomes of septic peritonitis are related to achievement of an early diagnosis, aggressive optimization of physiology, early surgical source control, and continued aggressive post-operative critical care management. The focus of this session will be on obtaining a rapid diagnosis followed by highlights of the key components in the front-line management of canine and feline patients with septic peritonitis.

PATHOPHYSIOLOGY

A discussion on any disease process would be incomplete without an understanding of the deranged physiology resulting in the patient's clinical symptoms. Secondary septic peritonitis is a consequence of an underlying primary disease process and is the most common cause of septic peritonitis in dogs and cats. Further to that, the most common underlying primary disease process, is a loss of integrity of the gastrointestinal tract. Enteric bacteria are therefore, not surprisingly the most common organisms isolated (#1 bug = *Escherichia coli* followed by various others including *Bacteroides* spp., *Clostridium* spp., *Klebsiella* spp., *Enterococcus* spp.).

The outer membrane components of bacteria initiate the release of inflammatory cytokines, like TNF-α, IL-1, IL-6, into the abdominal cavity primarily through their binding and activation of peritoneal macrophages, neutrophils, and lymphocytes. The interactions of these peritoneal cells along with mast cells promote cytokine expression, chemoattraction, and phagocyte recruitment. Proinflammatory cytokines, in turn, produce toxic mediators including prostaglandins, leukotrienes, platelet-activating factor, and phospholipase A2 that act to damage the endothelial lining leading to increased capillary leakage and vasodilation. Fluid and albumin influx into the peritoneal cavity causes peritoneal effusion and hypovolemia.

Following abdominal injury, there are several intraperitoneal substances, such as gastric mucin, bile salts, hemoglobin, and blood that act as adjuvants to augment peritonitis. These adjuvants have affects that include destruction of peritoneal mesothelial cells, interference of phagocytic cell activity, and provision of a bacterial growth medium.

Septic peritonitis, in the early stages of the inflammatory process, should be considered a local/ peritoneal disease. Human studies have demonstrated high concentrations of several cytokines in

the peritoneal fluid of patients with secondary peritonitis. Additionally, these patients had a large gradient between the peritoneal fluid and plasma concentrations of cytokines with no correlation between them, suggesting plasma levels may increase only after saturation of tissues within the abdominal compartment.

An inability to interrupt this local inflammatory response will result in progression of the septic process. Neutrophils are a key component of the innate immune system and early in the immune response help to contain and clear infectious agents. However during sepsis, neutrophil reprogramming occurs resulting in accumulation of these cells not only in the target tissue but also in distant vital organs. Once activated, neutrophils release their cell contents causing vasodilation (clinically manifesting as hypotension and hypoperfusion) and endothelial injury. This endothelial injury in combination with the known disruption of coagulation during systemic inflammation results in diffuse thrombosis, development of tissue ischemia, and ultimately organ failure. The cytokines released during inflammation also circulate to cause distant organ dysfunction. A well-recognized example of this problem is cytokine induced myocardial depression. In this advanced stage of severe sepsis and/or septic shock it has now progressed to a systemic problem, and these patients are unstable exhibiting high mortality rates.

The role of inflammatory cytokines can also directly affect the success of surgery. TNF-α is known to decrease synthesis of collagen and transforming growth factor-β which are important aspects of wound healing. Collagen can also be destroyed by collagenases of neutrophil origin. The inability to control these inflammatory mediators may predispose patients to post-operative gastrointestinal dehiscence.

DIAGNOSIS

As septic patients are a time-sensitive emergency, early diagnostic markers are vital components to improve outcome. There are no pathognomonic symptoms of septic peritonitis and a high index of clinical suspicion is required during careful patient examination. Most patients may fulfill the criteria for systemic inflammatory response syndrome (SIRS). Table 1 summarizes the SIRS criteria for dogs and cats, where 3 of 4 conditions are required.

Table 1 – SIRS criteria for dogs and cats

	CANINE	FELINE
Body Temperature (°C)	< 37.2 or > 39.4	< 37.2 or > 39.4
Heart rate (bpm)	> 150	< 140 or > 220
Respiratory rate (bpm)	> 40	> 40
WBC count (X 10^9/L)	< 5 or > 19 ± > 5% bands	< 5 or > 20

Although the clinicopathologic abnormalities in cats with septic peritonitis are similar to those reported for dogs, cats have certain unique features including the occasional patient that presents with bradycardia and others with an apparent absence of abdominal pain.

Definitive diagnosis of septic peritonitis is usually made from positive identification of intracellular microorganisms on abdominal fluid cytology or from bacterial culture and sensitivity results. Fluid cytologic examination has been reported to be 57 – 87% accurate in the diagnosis of septic peritonitis. This variability likely reflects the influence of the administration of antibiotics prior to sample collection, presence of localized infection, staining techniques, and the experience of the cytologist. Bacterial isolation remains the gold standard for diagnosis, however results cannot be obtained in a timely manner and can still be influenced by the prior administration of antibiotics.

With the increasing availability of bed-side ultrasound, the presence of even small volumes of peritoneal fluid can be detected. Ultrasound guidance allows retrieval of fluid that may be localized and likely increases the success for a positive diagnostic abdominocentesis when compared to a blind approach. When there is a high index of suspicion for septic peritonitis based on clinical examination or gross characteristics of the abdominal effusion, assessment of the fluid's glucose and lactate concentrations compared with those of the peripheral blood may allow for the most rapid diagnosis.

Glucose concentrations in septic abdominal effusions are expected to be lower than peripheral blood due to glucose utilization by microorganisms and phagocytic cells and because of glycolysis in the peritoneal fluid. A blood-to-fluid glucose (BFG) concentration difference of > 1.1 mmol/L has been found to be fairly accurate for the diagnosis septic peritonitis in dogs and cats.

Conversely, lactate concentrations in septic abdominal effusions are expected to be higher than peripheral blood due to the presence of an anaerobic microenvironment, production of lactate by neutrophilic glycolysis, and from the presence of bacterial metabolites. An abdominal fluid lactate concentration > 2.5 mmol/L and a blood-to-fluid lactate (BFL) concentration difference of < -2 mmol/L have been found to be accurate objective tests for the diagnosis of septic peritoneal effusion in dogs. Although using these cut-off values have been examined in cats, this assay was found to be much less accurate in its ability of detect a septic process.

The studies examining the ability of BFG and BFL to diagnose septic peritonitis excluded patients with hemoabdomen therefore, it is currently difficult to interpret these results from grossly hemorrhagic effusions.

PRE-SURGICAL MANAGEMENT

Fluid Therapy

Hemodynamic stabilization through fluid resuscitation remains the cornerstone of initial management of septic patients. A balanced crystalloid solution is recommended with volumes required to achieve various resuscitation goals to include:

- mean arterial pressure (MAP) ≥ 65 mmHg,
- central venous pressure (CVP) 8 – 12 mmHg
- urine output of 0.5 – 1 mL/kg/h
- central venous oxygen saturation ($ScvO_2$) > 70%
- improved mentation
- evidence of lactate clearance

Echocardiography can also be used as a non-invasive tool to accurately predict a patient's fluid responsiveness and hemodynamic status. The use of hydroxyethyl starch, of any molecular weight, is no longer recommended due to the absence of any clear benefits and its association with an increased incidence of renal injury. Several studies have demonstrated the adverse effects of overhydration necessitating controlled fluid resuscitation. Specific to the management of septic peritonitis, fluid overload can aggravate gastrointestinal edema and cause an increase in intra-abdominal pressure. Gut edema leads to bacterial translocation and release of inflammatory cytokines exacerbating the sepsis cascade. Increasing intra-abdominal pressure causes progressive hypoperfusion to all abdominal organs, respiratory dysfunction, reduced venous return and cardiac output, and increased intracranial pressure.

Vasopressor Therapy

Norepinephrine is considered the first line vasopressor agent for treating septic patients. Following initial fluid resuscitation to correct hypovolemia, early administration of norepinephrine will help restore organ perfusion. Additionally, vasopressors may prevent excessive fluid resuscitation and overhydration. Human studies have found dopamine to be associated with an increased risk of developing tachyarrhythmias.

Antibiotic Therapy

Once a septic patient has been recognized, the administration of broad-spectrum antimicrobials is recommended as soon as possible. Obtaining appropriate diagnostic samples are still encouraged prior to initiating antibiotics, however this procedure should not significantly delay antibiotic administration. Inadequate antimicrobial therapy has been demonstrated to be strongly associated with a poor outcome in septic patients and thus empiric broad-spectrum coverage with subsequent de-escalation once culture results are available is the most appropriate strategy to the management of septic peritonitis. In treating abdominal sepsis, an awareness to the effects of an enlarged volume of distribution on commonly used hydrophilic antibiotics, such as β-lactams, are required. A "dilution effect" occurs lowering plasma antimicrobial concentrations. Recommendations are to administer initial doses at the higher end of the spectrum when using β-lactams, aminoglycoside, or glycopeptides to ensure optimal drug delivery to the affected

tissues. This "dilution effect" does not occur with lipophilic antibiotics such as fluoroquinolones. Reasonable antibiotic regimens to consider for treatment of septic peritonitis include cefoxitin, cefotaxime, ampicillin/sulbactam + enrofloxacin, and the addition of metronidazole when anaerobic presence is suspected.

Pain Control

The abdomen contains a large number of sympathetic efferent pain fibers and most patients with septic peritonitis present with moderate to severe abdominal pain. Analgesia with a pure mu-opioid agonist is recommended for both dogs and cats in conjunction with the supportive measures discussed above.

SURGICAL MANAGEMENT

It is not the intention of this session to discuss the surgical approach to septic peritonitis. Nonetheless, this section deserves mention as early surgical source control has been found to be the most important determinant for survival. Studies have found mortality rates to increase with increasing time between hollow organ perforation and surgery. Additionally, inadequate source control at the time of initial surgery will result in an increased mortality in patients with septic peritonitis. These factors clearly classify septic peritonitis as a true surgical emergency.

REFERENCES AVAILABLE UPON REQUEST.