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CJON BOOK EXCERPT SERIES

Capillary Leak Syndrome

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This excerpt, chapter 27 from the book *Clinical Manual for the Oncology Advanced Practice Nurse* (2nd ed.), edited by Dawn Camp-Sorrell, MSN, FNP, AOCN[®], and Rebecca A. Hawkins, MSN, ANP, AOCN[®], is a part of a series of clinically relevant reprints that appear regularly in the *Clinical Journal of Oncology Nursing*.

- I. Definition: Shift of intravascular fluid and plasma into the extravascular space (Fardet et al., 2004)
- II. Physiology/Pathophysiology (Fishel, Are, & Barbul, 2003; Marx, 2003)
 - A. Normal: Small blood vessels carrying blood and forming the capillary system. Capillaries connect the smallest arteries (arterioles) with the smallest veins (venules).

B. Pathophysiology

- 1. Generalized capillary endothelial cell injury in multiple organs is responsible for the development of capillary leak syndrome (CLS).
- 2. Endothelial cell damage may occur because of endotoxin exposure, ischemia, vessel injury with platelet deposition, or mechanical injury.
- 3. Cytokines such as interleukin (IL)-2, tumor necrosis factor (TNF)-alpha, anti IL-1 B, and CD8-positive lymphocytes are present and may have a role in triggering CLS.
- 4. Platelet-activating factor and vascular endothelial growth factor increase vascular permeability.
- 5. Inflammatory reactions occur and cause microvascular permeability, capillary leak, loss of protein, tissue edema, and hypoalbuminemia.
- 6. A shift of fluid and albumin into body tissues occurs.
- 7. An associated decreased peripheral vascular resistance, hypotension, and intravascular volume compound the fluid shift.
- III. Clinical features (Cahill, Spitzer, & Mazumder, 1996; Nurnberger, Willers, Burdach, & Gobel, 1997)
 - A. Risk factors
 - 1. Blood and marrow stem cell transplant
 - a) During preparative regimen
 - b) During time of engraftment along with abnormalities in liver and renal function
 - c) During rapid steroid tapers
 - d) During infection or graft-versus-host disease
 - e) During infusion of donor white blood cells (WBCs)
 - f) During infusion of marrow/blood stem cells
 - g) Human leukocyte antigen mismatched bone marrow transplant recipient

- h) Oxygen toxicity
- 2. Kidney transplant
- 3. Liver transplant
- 4. Biotherapy (especially IL and TNF)
- 5. Chemotherapy
- B. History
 - 1. History of cancer and cancer treatment
 - 2. Current medications: Prescribed and over-thecounter
 - 3. History of presenting symptom(s): Precipitating factors, onset, location, and duration
 - 4. Changes in activities of daily living
- C. Signs and symptoms
 - 1. Ascites
 - 2. Weight gain
 - 3. Edema and/or anasarca (generalized total-body edema)
 - 4. Chest pain
 - 5. Shortness of breath
 - 6. Productive or nonproductive cough
 - 7. Tachypnea
 - 8. Decreased urine output
 - 9. Fever
 - 10. Lethargy, malaise, or obtundation
 - 11. Confusion and restlessness
 - 12. Cyanosis and pallor of skin, lips, and nail beds
- D. Physical exam
 - 1. Vital signs: Weight (signs of gain), blood pressure (hypotension), pulse (tachycardia)
 - 2. Pulmonary exam: Presence of rales and rhonchi on auscultation; dullness on percussion over consolidated areas
 - 3. Cardiac exam: Presence of \$3, \$4, murmur, or gallop; tachycardia; peripheral edema

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- 4. Abdomen exam: Ascites, tenderness, distention, softness or firmness, hepatomegaly, splenomegaly, presence or absence of bowel sounds
- 5. Dermatologic: Presence of purpuric lesions, flesh-colored or erythematous lesions (Fardet et al., 2004)
- IV. Diagnostic tests
 - A. Laboratory
 - 1. Complete blood count with differential
 - a) Elevated WBC count may increase suspicion of infection.
 - b) Hemoconcentration may occur with an increased WBC count and hematocrit.
 - 2. Urinalysis
 - a) Presence of leukocytes may be caused by infection.
 - b) Presence of protein or casts may indicate renal failure or disease.
 - 3. Liver function tests, including total and direct bilirubin, to rule out hepatobiliary disease
 - 4. Renal function tests, including urea and creatinine, to evaluate renal function
 - 5. Serum albumin: May be decreased, leading to decreased oncotic pressure and edema
 - B. Radiology: Chest x-ray: To rule out noncardiogenic pulmonary edema, pleural effusion, pulmonary venous hypertension, interstitial infiltrates, and pericardial effusions
 - C. Other
 - 1. Bronchoscopy, with or without lung biopsy, can rule out infection, hemorrhage, or other causes of respiratory distress.
 - 2. Arterial blood gases may show hypoxia and CO2 retention.
 - 3. Pulmonary function tests reveal decreased pulmonary compliance.
 - Hemodynamic monitoring including pulmonary capillary wedge pressure (PCWP) and cardiac output to measure fluid status (normal PCWP = 6-12 mm Hg; normal cardiac output = 4-8 liters/ minute)
 - a) Decreased PCWP may indicate hypovolemia.
 - b) Increased PCWP may indicate left ventricular failure or cardiac insufficiency.
 - c) Cardiac output may be increased early in CLS, then decreased later in the syndrome.
 - 5. Skin biopsy: Mild perivascular, nonspecific dermal mononuclear infiltrates; mucinous deposits; mild lymphocytic infiltration (Fardet et al., 2004)
- V. Differential diagnosis (Fardet et al., 2004)
 - A. Paraproteinemias or diseases/conditions with low protein levels
 - B. Lymphoma
 - C. Psoriasis
 - D. Drug-induced, such as IV cyclosporine or amphotericin-B, biotherapy
 - E. Viral syndrome, such as cytomegalovirus
 - F. Pneumonitis
 - G. Sepsis (see Chapter 140)
 - H. Disseminated intravascular coagulation (see Chapter 118)
 - I. Cytokine reaction

- VI. Treatment: Supportive care until CLS resolves (Amoura et al., 1997; Fardet et al., 2004; Fishel et al., 2003; Marx, 2003)
 - A. Treat the underlying cause.
 - B. Administer glucocorticoids at high doses, then taper quickly as tolerated.
 - C. Provide IV fluid replacement.
 - 1. Infusion of colloids rather than crystalloids, such as blood or albumin
 - 2. Infusion of albumin
 - D. Administration of diuretics is controversial because intravascular hypovolemia is present and acute renal failure may develop.
 - E. Restrict oral fluids to 500–1,000 ml per day. Gradually increase fluids as condition improves.
 - F. Hemodialysis may be necessary if acute renal failure occurs.
 - G. Mechanical ventilation may be indicated if respiratory distress or failure occurs.
 - H. Prophylactic antibiotics may promote growth of organisms and are not recommended.
 - I. Administer vasopressors as needed for management of hypotension.
 - J. Provide nutritional support, such as enteral feedings or total parenteral nutrition, to maintain high caloric intake because of increased energy expenditure.
 - K. Clinical studies using antibodies to IL-1, IL-6, TNF-alpha, angiopoietin-1, and endothelin A receptor antagonist blocks or reduces capillary leak in animal models (Fishel et al., 2003).
- VII. Follow-up
 - A. Inpatient hospitalization is necessary to manage the signs, symptoms, and complications of CLS.
 - B. Perform daily monitoring of intake, output, weight, and renal and liver function.
 - C. Perform frequent chest radiographs to monitor pulmonary edema.
- VIII. Referrals
 - A. Nephrologist: To evaluate acute renal failure and recommend management
 - B. Pulmonologist: To evaluate lung function, perform bronchoscopy, and recommend management

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