Cranial Vena Cava Syndrome

Angell Memorial Animal Hospital
Boston, Massachusetts
Andrea Nicastro, DVM
Etienne Côté, DVM, DACVIM (Cardiology, Internal Medicine)

ABSTRACT: Cranial vena cava syndrome is an uncommon but easily recognized sequela to obstruction of the cranial vena cava. Clinical signs are characteristic—symmetric, nonpainful, pitting edema of the head, neck, and forelimbs. Causes include thrombosis of the vessel along with compression or invasion by tumors and granulomas. Evaluation typically includes thoracic imaging and tissue sampling of masses for cytologic or histologic diagnosis. Treatment is aimed at correcting the underlying process; however, endovascular therapies currently used in human medicine may apply to veterinary patients. The prognosis reflects the underlying etiology and is therefore generally guarded.

Venous return from the head, neck, and forelimbs drains into the cranial vena cava (CrVC) before entering the right atrium. When obstruction of the CrVC occurs, venous drainage is impaired (Figure 1). This disturbance can result in cranial vena cava syndrome (CrVCS), a condition in which the cranial half of the body becomes edematous. In canine and feline patients, CrVCS has traditionally been considered a life-threatening condition that occurs as a sequela to invasive mediastinal disease or thrombosis of the CrVC. Although widely recognized in human medicine, this syndrome is sparsely reported in the veterinary literature.

CrVCS, also known as caval syndrome, precaval syndrome, and superior vena cava syndrome, was first described in humans in 1757. At that time, infection was considered the most common cause. In 1934, thoracic tumors and aneurysms were implicated as the most common inciting causes. In recent years, small-cell bronchogenic carcinoma and lymphosarcoma have become the most frequently diagnosed causes of CrVCS in humans, accounting for approximately 95% of reported cases.

In 1961, one of the earliest veterinary cases of CrVCS was reported. Since then, few articles have described this uncommon but distinctive clinical syndrome in animals. Although heartworm caval syndrome shares a similar name with CrVCS, the two syndromes have an entirely different etiology, pathophysiology, and clinical presentation in veterinary patients. Heartworm caval syndrome is a severe form of heartworm disease involving retrograde movement of adult heartworms from the pulmonary arteries toward the right atrium and cavae.

PATHOGENESIS

CrVCS is a clinical manifestation of external compression, invasion, or intralu-
lipomas, mediastinal edema or hemorrhage, mediastinitis, metastatic neoplasia, teratomas, thymic branchial cysts, thymic hyperplasia, and tumors of neurogenic origin. However, to our knowledge, none of these diseases has been reported as a cause of CrVCS in dogs or cats.

In general, thrombus formation of the CrVC is another recognized cause of CrVCS. Thrombus formation is believed to occur as a result of blood stasis, turbulent blood flow, or disrupted vascular endothelium secondary to a hypercoagulable state. Certain systemic diseases may increase the likelihood of clot formation, including sepsis, immune-mediated hemolytic anemia, neoplasia, cardiac disease, corticosteroid excess, and protein-losing nephropathies. In addition, central venous catheterization has been implicated as a potential cause of CrVCS in both human and veterinary patients. Patients requiring central venous catheters are also more likely to be afflicted with serious underlying diseases that may induce a prothrombotic state, thus further increasing the risk for CrVCS. CrVCS is a well-recognized complication of transvenous pacemakers in humans and could conceivably occur in an animal with a transvenous pacemaker.

Infectious disease is a rare cause of CrVCS in both veterinary and human medicine. Two infectious causes, cryptococcosis and blastomycosis, have been described in the veterinary literature. Patients requiring central venous catheters are also more likely to be afflicted with serious underlying diseases that may induce a prothrombotic state, thus further increasing the risk for CrVCS. CrVCS is a well-recognized complication of transvenous pacemakers in humans and could conceivably occur in an animal with a transvenous pacemaker.

Infectious disease is a rare cause of CrVCS in both veterinary and human medicine. Two infectious causes, cryptococcosis and blastomycosis, have been described in the veterinary literature. In both cases, post-mortem examination revealed a fungal granuloma obstructing the CrVC.

We observed CrVCS in a 13-year-old castrated male golden retriever presented to our hospital for evaluation of collapse. On echocardiography, a large mass was obstructing flow from the CrVC into the right atrium (Figure 3).

**CLINICAL PRESENTATION**

Patients with CrVCS classically present with head, neck, and forelimb edema caused by impaired venous return from the cranial portion of the body, leading to interstitial fluid accumulation. In addition to edema formation, jugular venous distention and engorgement of conjunctival and scleral vessels may occur. Signs may be acute or gradual in onset. The onset and severity of
**Figure 2**—(A) A 12-year-old male miniature schnauzer with CrVCS. Note the symmetric pattern of swelling on the face, with swelling extending to both forelimbs. The dog was being treated for septic pancreatitis and receiving parenteral nutrition through an intravenous jugular catheter. However, a thrombus developed in the CrVC, resulting in CrVCS. (B) The same dog several weeks later. Signs of CrVCS regressed within days after the catheter was removed, and the dog made a complete recovery. (Photographs courtesy of Douglass K. Macintire, DVM, MS, Auburn University)

**Figure 3**—Right-sided, short-axis echocardiographic view at the level of the base of the heart and a corresponding diagram. In this golden retriever with CrVCS, the mass occupied virtually the entire right atrium and obstructed venous return from the CrVC. Note the distention of the vena cava. No pericardial effusion was observed, and radiographs showed no mediastinal abnormality. Color-flow Doppler demonstrated the very small amount of flow around the mass. (RV = right ventricle; LA = left atrium; Ao = aorta)
signs depend on the degree of development of collateral circulation. It is conceivable that the CrVC could be completely obstructed in a patient with minimal clinical signs if adequate collateral venous flow is present. Collateral circulation may develop within 1 week in patients with a completely obstructed CrVC.

Pleural effusion is frequently part of the clinical picture (at least 15 of 27 cases of CrVCS had pleural effusion) and tends to be chylous in nature. Chylothorax development has been reported clinically and shown experimentally. One study demonstrated that ligation of the CrVC impairs lymphatic flow into the venous system, resulting in lymphatic hypertension and subsequent lymphangiectasia and transmural insufficiency of the thoracic lymphatics (Figure 1). Thus chylous effusion may accumulate in the pleural space and, rarely, in the pericardial space.

**DIAGNOSIS**

A diagnosis of CrVCS can often be made in the examination room. The presence of head, neck, and forelimb edema should prompt the clinician to suspect CrVCS. However, other differentials with similar presenting signs must be excluded (Figure 4, Table 1); thus a thorough history and physical examination are necessary to make an accurate diagnosis. Once CrVCS is confirmed, an underlying cause must be sought to make appropriate therapeutic decisions (Figure 5).

Routine laboratory tests, including a complete blood count, serum biochemical profile, and urinalysis, should be conducted in all patients with possible CrVCS to help determine the underlying disease. In cats, feline leukemia and feline immunodeficiency virus tests may be helpful in evaluating for the presence of lymphoma. Additional laboratory tests may be needed to confirm possible underlying prothrombotic states or fungal disease.

Thoracic imaging is essential in pinpointing the cause of CrVCS. Chest radiographs can identify cranial mediastinal masses, pleural effusion, and potential pericardial effusion (enlarged cardiac silhouette). Thoracic ultrasonography is an important part of the diagnostic workup by allowing visualization of tumors causing compression or invasion of the vessel wall. In addition, ultrasonography, especially color-flow Doppler, can assess patency of the CrVC and is also useful for obtaining fine-needle aspirates or biopsies of thoracic tumors.

Nonselective angiography is a useful imaging modality if other results are inconclusive. This procedure can
Table 1. Differential Diagnosis of Head and Neck Swelling in Dogs and Cats

<table>
<thead>
<tr>
<th>Condition</th>
<th>Salient Features*</th>
<th>Differentiation from CrVCSb</th>
</tr>
</thead>
<tbody>
<tr>
<td>CrVCS</td>
<td>Pitting edema of the head, neck, and forelimbs</td>
<td>NA</td>
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<tr>
<td></td>
<td>Symmetric, cool, nonpainful swelling (Figure 2)</td>
<td></td>
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<tr>
<td></td>
<td>Pleural effusion possible</td>
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<tr>
<td>Angioedema</td>
<td>Exposure to antigen in previous 24 hr (e.g., from vaccine)</td>
<td>Usually improves/resolves in &lt;48 hr</td>
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<td></td>
<td>Pawing at face with/without signs of pain (e.g., resents pressure)</td>
<td>No mass in cranial chest (confirmed by physical examination or radiographs)</td>
</tr>
<tr>
<td>Rattlesnake bite</td>
<td>Outdoor dog/cat Region endemic for rattlesnakes Eyewitness to snakebite or dog/cat cried out while sniffing in bushes or under rocks</td>
<td>No thoracic mass; initial increase in swelling followed by a decrease (usually &lt;72 hr)</td>
</tr>
<tr>
<td></td>
<td>Asymmetric swelling of face, neck, or limb Puncture marks visible (rare)</td>
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<tr>
<td>Generalized peripheral edema</td>
<td></td>
<td></td>
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<tr>
<td>Hypoalbuminemia</td>
<td>Serum albumin level</td>
<td></td>
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<tr>
<td>Vasculitis</td>
<td>Edema not confined to head and neck Ascites also possible</td>
<td>Evidence of systemic inflammation (e.g., uveitis, fever, lameness/joint pain)</td>
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<tr>
<td>Right-sided CHF (edema seldom generalized)</td>
<td>Heart murmur, cardiomegaly possible Hepatic venous congestion, abnormal echocardiogram</td>
<td></td>
</tr>
<tr>
<td>Subcutaneous emphysema</td>
<td>Subcutaneous crepitus Whole-body involvement possible Recent history of trauma, jugular venipuncture, or intubation</td>
<td>Radiography (SC gas) Needle aspiration (SC air)</td>
</tr>
<tr>
<td>Acute blunt trauma and swelling</td>
<td>History of trauma Ecchymoses Lacerations Orthopedic lesions</td>
<td>Radiography</td>
</tr>
<tr>
<td>Lymphangiosarcoma of head and neck</td>
<td>Forelimbs may not be affected Firm nonpitting swelling (Figure 2)</td>
<td>Skin/SC biopsy</td>
</tr>
<tr>
<td>Myxedema</td>
<td>Firm thickening of facial skin Nonpitting</td>
<td>Serum thyroxine level/thyroid profile</td>
</tr>
<tr>
<td>Foreign body around the neck (e.g., elastic band)</td>
<td>Forelimbs not affected Presence of foreign body on physical examination or radiographs</td>
<td>Radiography</td>
</tr>
<tr>
<td>Salivary mucocele (cervical)</td>
<td>Flocculent, asymmetric swelling of the ventral neck</td>
<td>Fine-needle aspiration of saliva with/without sialography</td>
</tr>
<tr>
<td>Jugular thrombosis or mass</td>
<td>Forelimbs not affected</td>
<td>Neck ultrasonography, angiography, CT, MRI</td>
</tr>
<tr>
<td>Abscessation, cellulitis</td>
<td>Often asymmetric; inflammatory (warm, painful)</td>
<td>Fine-needle aspiration of pus Culture and sensitivity testing</td>
</tr>
</tbody>
</table>

* A mediastinal mass or venous thrombus could affect only certain tributaries leading to the CrVC, resulting in regional edema (e.g., forelimbs only or head and neck only). This variant of CrVCS could confuse the initial diagnosis but would likely progress to true CrVCS as the mass or thrombus enlarges.

b Differentiation in addition to patient history and physical examination.

CHF = congestive heart failure; CrVCS = cranial vena cava syndrome; CT = computed tomography; MRI = magnetic resonance imaging; NA = not applicable; SC = subcutaneous.
identify filling defects within the CrVC, localize the site of obstruction, and highlight collateral circulation. To perform angiography, iodinated contrast medium is injected into the jugular or cephalic vein(s) and thoracic radiographs are immediately taken. Until recently, angiography was the principal imaging modality used in human medicine. However, computed tomography and magnetic resonance imaging have now become the primary means of identifying lesions and pinpointing the site of obstruction in humans; venography is now used as a guide for obtaining biopsies, placing stents, and performing bypass surgery. Additional diagnostic tests may also be useful. Echocardiography can identify masses at the level of the terminal CrVC or right atrium as well as pericardial effusion. Cytologic examination of mediastinal masses or pleural/pericardial effusions may confirm infectious or neoplastic causes. Biopsy of thoracic masses may be necessary if fine-needle aspirates are nondiagnostic.

TREATMENT

After CrVCS and its underlying cause have been confirmed, appropriate treatment can be instituted. Primary therapeutic goals include removing the obstructive lesion from the CrVC and treating the inciting cause. Depending on the histologic diagnosis, mediastinal masses can be treated with surgery, chemotherapy, or radiation, alone or in combination. Thymomas are typically treated surgically. After the thymoma is removed, compression of the CrVC should be alleviated. However, thymomas large enough to cause CrVCS are generally invasive and may infiltrate the vessel wall, rendering complete excision difficult. Therefore, radiation therapy may be instituted to noninvasively reduce tumor volume. Tumor removal from the lumen of the CrVC has been performed by temporary occlusion venous inflow, but this procedure may not be possible if tumor invasion is extensive. Mediastinal lymphoma, although seldom reported in the veterinary literature as a cause of CrVCS, can be treated with combination chemotherapy or possibly radiation therapy. Theoretically, tumor shrinkage should relieve CrVC obstruction. Treatment options for other neoplasms vary, depending on the tumor type.

Treatment of caval thrombosis should be aimed at managing the underlying cause. Specific therapy for systemic disease should be instituted as soon as possible, and jugular catheters, if present, should be removed promptly. Anticoagulant (heparin sodium) and thrombolytic (streptokinase) treatments were evaluated retrospectively in one study, but the value of such treatments remains unproven. Diuretics have also been administered to minimize edema formation, but their efficacy appears limited.

Human medicine offers some promising alternatives to the therapies currently available in veterinary medicine. In the past, radiation has been the standard therapy for palliation of human patients with CrVCS. Recently, however, endovascular therapy and surgical bypass have in many cases replaced radiotherapy in the treatment of patients with malignant CrVC obstruction. Endovascular therapy involves a combination of thrombolytic agents, angioplasty, and stent placement at the level of the obstruction. Occasionally, anticoagulants may be administered, but the need for anticoagulation with endovascular therapy is unproven. Thrombolysis is often part of the initial endovascular management because it can help uncover focal lesions, relieve signs, and allow optimal angioplasty and stent placement. Angioplasty, or balloon dilation, can be performed to widen the obstructed portion of the vessel. However, narrowing often recurs rapidly after angioplasty. Therefore, stents should be placed to maintain vessel patency. Success rates of 90% to 100% have been demonstrated with endovascular therapy. Complications occasionally occur with stent placement (e.g., recurrent stenosis, stent migration, stent occlusion, pulmonary thromboembolism, bleeding tendencies with thrombolytic and anticoagulation therapy) but are usually treatable with percutaneous procedures or, in cases of iatrogenic coagulopathy, with medical management. Given the risk of recurrent stenosis, stent placement
Do history and physical signs suggest CrVCS?

- **Yes**: Obtain thoracic radiographs
  - Mediastinal mass present?
    - **No**: Evaluate for other disorders (Table 1)
    - **Yes**: Ultrasound-guided fine-needle aspiration or biopsy
      - Based on results, consider:
        - Thoracotomy
        - Radiation therapy
        - Chemotherapy
        - Antifungal therapy
      - Also consider: Endovascular therapy

- **No**: Reevaluate for other disorders (Table 1)

Cranial thoracic ultrasound examination, including Doppler evaluation of the CrVC

- Thrombus seen?
  - **No**: Nonselective angiogram
  - **Yes**: Manage accordingly
    - Evaluate for prothrombotic diseases
    - Remove jugular catheters if present
    - Treat with anticoagulants with/without thrombolytics

Reevaluate for causes of head and neck swelling other than CrVCS (Table 1)

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**Figure 5**—Diagnostic algorithm for evaluating patients with swelling of the head, neck, and forelimbs.

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may be an appropriate and less-invasive alternative to relieve signs in patients with malignant disease and a short life expectancy.

In human patients with CrVCS, the gold standard for treatment is surgical bypass from a patent vein above the level of the obstruction to the right atrium. The conduit can be either an autogenous vein graft or polytetrafluoroethylene. This procedure is substantially more
invasive than endovascular techniques but is associated with excellent long-term patency and may be preferable in patients with benign causes of CrVCS and a long life expectancy.

**PROGNOSIS**

The prognosis for veterinary patients with CrVCS is often considered guarded to poor. In 27 cases of CrVCS, the exact outcome was described in 10. Three dogs survived more than 6 months of age (two with thrombosis\(^1\) and one with thymoma\(^3\)). Two cats with CrVCS died, one within 24 hours after a diagnosis of lymphoma\(^9\) and one 10 days after a diagnosis of cryptococcosis.\(^{20}\) Five dogs were euthanized approximately 1 week after diagnosis: one dog with thyroid carcinoma,\(^5\) one dog with a mass at the right atrio caval vena caval junction,\(^28\) two dogs with thymoma,\(^10,12\) and one dog with carcinoma.\(^20\) The remaining 17 dogs reportedly died or were euthanized, but a time frame was not described for these patients.

Recent studies have demonstrated that physical obstruction of the CrVC is not always life threatening, even when signs of CrVCS occur. In seven dogs, experimental ligation of the CrVC produced signs of CrVCS, but the signs abated within 1 week and all dogs survived.\(^29\) Therefore, even with complete CrVC obstruction, collateral circulation can develop quickly and adequate venous drainage of the cranial half of the body can be restored. In human medicine, CrVCS does not confer a worse prognosis than the underlying disease, and patients have survived with unresolved CrVCS for decades.\(^4\) In a review of 1986 human cases of CrVCS, only one fatality was directly related to an obstructed CrVC.\(^31\) Thus the poor prognosis associated with this syndrome is apparently related to the severity of the inciting cause rather than the syndrome itself. Further studies are needed to reach this conclusion in veterinary patients.

**SUMMARY**

CrVCS is a distinctive clinical entity that is easily recognized in the examination room. It is usually associated with a serious underlying disease. The adoption of human techniques to alleviate clinical signs of this syndrome should be considered in veterinary patients.

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**REFERENCES**


**ARTICLE #4 CE TEST**

The article you have read qualifies for 1.5 contact hours of Continuing Education Credit from the Auburn University College of Veterinary Medicine. *Choose the best answer* to each of the following questions; then mark your answers on the postage-paid envelope inserted in *Compendium*.

1. Which of the following clinical signs is not consistent with CrVCS?
   a. forelimb edema  c. hindlimb edema
   b. dyspnea  d. head and neck edema

2. Heartworm caval syndrome and CrVCS
   a. have similar causes and treatments.
   b. are similar in name but not in clinical management.
   c. share similar causes but differ in terms of therapy.
   d. have essentially identical clinical signs.

3. Treatment of CrVCS may include any of the following except
   a. heartworm adulticide.
   b. surgical removal of thymoma.
   c. thrombolytic agents.
   d. angioplasty.

4. CrVCS cannot occur as a result of
   a. extraluminal compression of the CrVC.
   b. thrombosis of the CrVC.
   c. vasospasm of the CrVC.
   d. invasion of the CrVC wall.

5. In patients with CrVCS, pleural effusion
   a. is rarely chylous.
   b. can result in decreased lymphatic pressure caused by transmural insufficiency and lymphangiectasia of thoracic lymphatics.
   c. is not associated with dyspnea.
   d. is usually purulent.

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6. Which of the following statements regarding nonselective angiography is false?
   a. Iodinated contrast is injected into the right coronary vein.
   b. The degree of CrVC obstruction can be identified.
   c. The extent of collateral circulation may be demonstrated.
   d. The procedure can be used to guide stent placement.

7. Which of the following is not a recognized underlying cause of CrVCS?
   a. histoplasmosis  
   b. thymoma  
   c. mediastinal lymphoma  
   d. cryptococcosis

8. When comparing patients with the same underlying disease with or without concomitant CrVCS, the prognosis
   a. is worse in patients with concomitant CrVCS.
   b. is fair to good in patients with concomitant CrVCS, with approximately 75% survival 6 months after diagnosis.
   c. appears to be more favorable in human patients with concomitant CrVCS than in small animals.
   d. is independent of the underlying disease.

9. In patients with CrVCS, diagnostic imaging techniques do not include
   a. thoracic ultrasonography.
   b. magnetic resonance imaging.
   c. thoracic radiography.
   d. reverse-phase fluoroscopy.

10. Treatment of thrombosis causing CrVCS does not include
    a. thrombolytic agents.
    b. epsilon aminocaproic acid.
    c. heparin.
    d. removal of a jugular catheter.