

# Common oncologic emergencies

Laura Regnier MSc MD CCFP Anna N. Wilkinson MSc MD CCFP FCFP

Family physicians must be able to recognize any oncologic emergencies that patients present with in their offices, on hospital wards, or in emergency departments (**Box 1**).<sup>1</sup> This article reviews the presentation and management of 3 common oncologic emergencies: malignant spinal cord compression (SCC), superior vena cava obstruction (SVCO), and febrile neutropenia.

## Malignant SCC

Spinal cord compression occurs when malignant cells within the vertebrae or epidural space compress the thecal sac, leading to venous congestion within the epidural vasculature and vasogenic edema. Spinal cord infarction and irreversible neurologic damage can occur if the compression is not alleviated promptly (**Figure 1**).<sup>2,3</sup> Spinal cord compression is most commonly seen with prostate, breast, and lung cancers,<sup>4</sup> although non-Hodgkin lymphoma, renal cell carcinoma, and multiple myeloma are also causative. All levels of the spine can be affected, but the most frequent site of cord compression is the thoracic spine.<sup>5</sup> Any complaint of worsening back pain in a patient with a history of malignancy should prompt providers to include SCC in their differential diagnosis.

Signs and symptoms of SCC (**Box 2**)<sup>2</sup> are similar to those seen with cauda equina syndrome. However, in contrast with cauda equina syndrome, the level of sensory disturbance in SCC corresponds to the vertebrae involved, and the central nature of SCC causes hyperreflexia as opposed to hyporeflexia.

Contrast-enhanced magnetic resonance imaging is the most sensitive imaging modality for the diagnosis of SCC (**Figure 1**).<sup>2,6,7</sup> If magnetic resonance imaging is unavailable or contraindicated, contrast-enhanced computed tomography can be used.

Initial management of SCC includes immediate administration of dexamethasone. An intravenous bolus

of 10 mg followed by 4 mg of dexamethasone every 6 hours will diminish pain, perilesional edema, and associated disability.<sup>8</sup> Urgent consultation with neurosurgery and radiation oncology should be sought. The best clinical outcomes are achieved with direct decompressive surgery followed by postoperative radiotherapy; however, not all patients are surgical candidates (**Box 3**).<sup>9-11</sup>

Radiation therapy is the mainstay of treatment for SCC as only 10% to 15% of patients qualify for surgical decompression.<sup>12</sup> External beam treatments are typically 20 Gy, administered in 5 fractions, although a single fraction of 8 Gy can be offered.<sup>13</sup> Stereotactic body radiation therapy is reserved for postoperative treatment or for radioresistant or recurrent spinal metastases given the time required for treatment planning.<sup>14-17</sup> Chemotherapy has little role in the treatment of SCC given its delayed onset of action. Physicians should also ensure patients receive pain control, management related to bowel and bladder function, and referral to rehabilitation services.<sup>18</sup> Venous thromboembolic prophylaxis should not be overlooked given elevated risk in these patients.<sup>19</sup> Treatment within 48 hours of neurologic deficits will help prevent loss of limb function and loss of bladder and bowel function and improve quality of life.<sup>20,21</sup> The most important factors in predicting ambulatory status posttreatment are pretreatment ambulatory status and time from development of motor deficits to radiotherapy or surgery.<sup>22-24</sup>

## Malignant SVCO

Superior vena cava obstruction occurs when there is extrinsic compression of the SVC or direct invasion by a tumour, impairing venous return to the heart. Lung cancers and non-Hodgkin lymphoma account for most cases of malignant SVCO.<sup>25</sup> Thrombus formation caused by indwelling venous devices can also put oncology patients at increased risk of SVCO.<sup>26</sup>

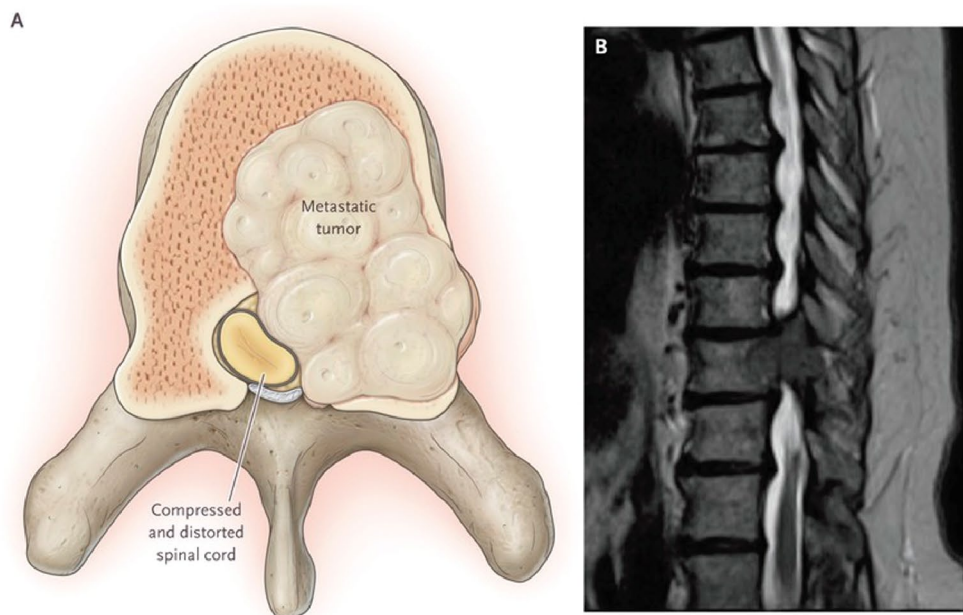
The most common presenting symptoms of malignant SVCO are secondary to venous congestion and include face or neck swelling (87%), cough (70%), upper extremity swelling (64%), dyspnea at rest (64%), and dilated neck and chest veins (38%) (**Figure 2**).<sup>27,28</sup> Collateral vessels develop with slowly growing tumours, causing a gradual onset of symptoms; while in an acute obstruction, symptoms present abruptly.<sup>28</sup> In severe SVCO, laryngeal edema with associated stridor and confusion secondary to raised intracranial pressure can occur. Symptoms typically worsen when the patient is supine, as flow through the residual SVC lumen may be further compromised.

Investigation should begin with a chest x-ray scan. Typical x-ray scan findings include superior mediastinal widening or a mass located in a position to cause SVCO,

### Box 1. Common oncologic emergencies

- Spinal cord compression
- Superior vena cava obstruction
- Febrile neutropenia
- Pericardial effusion
- Tumour lysis syndrome
- Hyperviscosity syndrome
- Hypercalcemia
- Syndrome of inappropriate antidiuretic hormone secretion
- Immunotherapy-related complications

Data from Higdon et al.<sup>1</sup>

**Figure 1. Acute spinal cord compression owing to metastatic involvement of vertebral body**

Reprinted with permission from the Massachusetts Medical Society.<sup>2</sup> Copyright © 2017.

### Box 2. Signs and symptoms of SCC

#### Signs

- Weakness
- Sensory level
- Hyperreflexia and clonus (variable)
- Loss of anal sphincter tone

#### Symptoms

- Back pain (exacerbated by Valsalva maneuvers)
- Numbness below the spinal level involved
- Paresthesia
- Weakness
- Urinary retention (often reported as incontinence owing to overflow)
- Bowel incontinence (often reported as diarrhea owing to loss of sphincter control)

SCC—spinal cord compression.  
Data from Ropper and Ropper.<sup>2</sup>

### Box 3. Factors favouring surgical decompression for SCC

- Undiagnosed malignancy requiring tissue for pathology or unknown primary cause where the cancer diagnosis is in doubt
- Pathological vertebral fracture with unstable spine
- Relatively radioresistant tumour
- Previous radiotherapy at the level of SCC
- Disease localized to a single vertebral level
- Good prognostic factors (age <65 y, life expectancy >6 mo, systemic treatment options)

SCC—spinal cord compression.  
Data from Walji et al.<sup>9</sup>

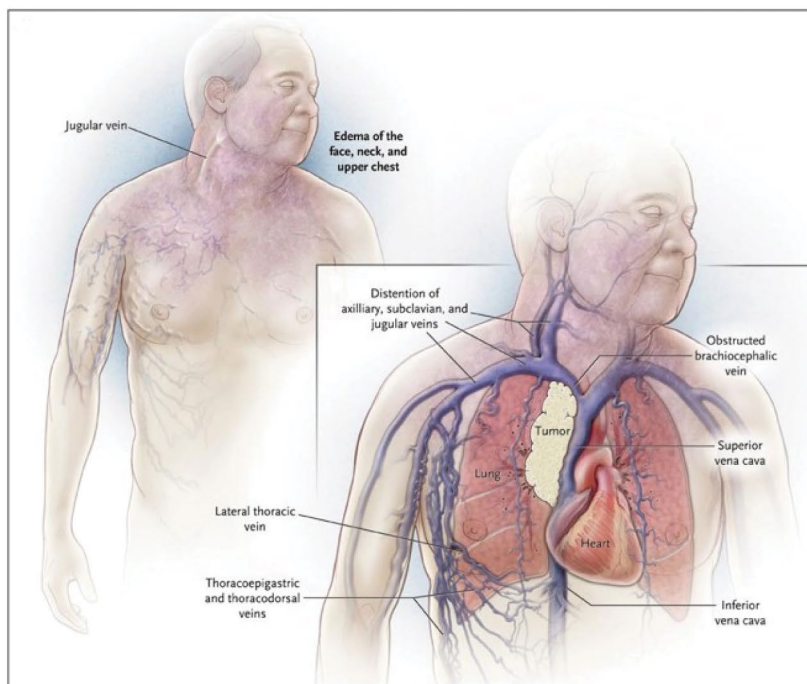
often with an associated pleural effusion (Figure 3).<sup>29</sup> Contrast-enhanced computed tomography can identify the precise location and extent of obstruction and detect the presence of a thrombus.<sup>30</sup> For some patients SVCO will be the initial presentation of malignancy, so a biopsy should be obtained.

Treatment options depend on symptom severity and tumour histologic findings. General measures include head elevation and use of glucocorticoids. Despite minimal evidence, steroids are given to help prevent edema in patients receiving urgent radiotherapy.<sup>31</sup> Insertion of an endovascular stent is the most effective and

immediate means of resolving symptoms in acute SVCO.<sup>32</sup> Anticoagulation treatment and thrombus removal should be considered for SVCO secondary to thrombus formation.<sup>33,34</sup> If symptoms are mild to moderate, radiotherapy can be first-line treatment. Chemotherapy can be considered for chemosensitive malignancies such as lymphoma or small cell lung cancer.<sup>31</sup>

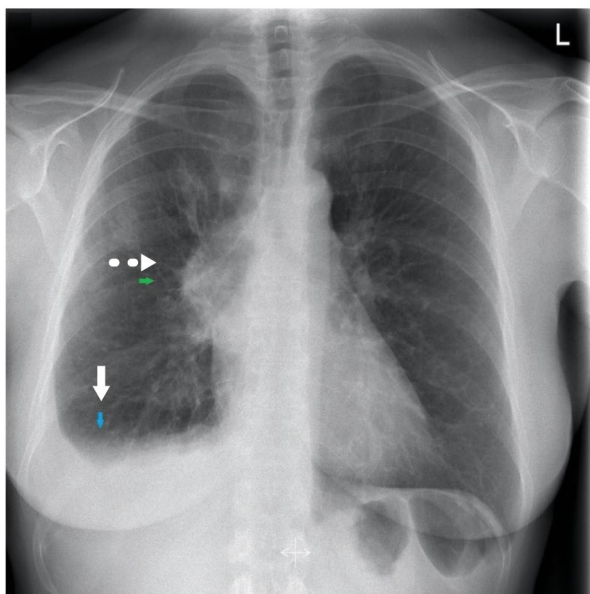
### Febrile neutropenia

Febrile neutropenia occurs when myelosuppression from chemotherapy, and occasionally targeted therapies, results in decreased neutrophil production that causes impaired immune response to bacterial infections.<sup>35</sup> Any patient with a fever receiving these treatments should be assessed thoroughly and providers should have a low threshold for initiating antibiotic therapy.

**Figure 2. Clinical findings and pathogenesis of SVCO**

SVCO—superior vena cava obstruction.

Reprinted with permission from the Massachusetts Medical Society.<sup>28</sup> Copyright © 2007.

**Figure 3. Chest x-ray scan depicting SVCO in a patient with small cell lung cancer: Broadened mediastinum is visible (dotted arrow) and pleural effusion (solid arrow).**

SVCO—superior vena cava obstruction.

Reproduced with permission from BMJ Publishing Group Ltd.<sup>29</sup> Copyright © 2018.

Febrile neutropenia is defined as a single oral temperature of 38.3°C or higher or a sustained temperature of 38°C or higher for at least 1 hour, and absolute neutrophil count (ANC) of  $1.0 \times 10^9/L$  or less; severe neutropenia is defined as ANC of  $0.5 \times 10^9/L$  or less.<sup>36</sup> Elderly or profoundly immunosuppressed patients may not be able to mount a fever and may be afebrile despite the presence of infection. In these patients, clinicians must be aware of alternative presentations for sepsis such as hypothermia, hypotension, or clinical deterioration.<sup>35</sup> Myelosuppression typically occurs 1 week after chemotherapy treatment.<sup>37</sup>

Patients receiving chemotherapy or select targeted therapies who present with fever require a complete history, physical examination, and investigations to establish ANC and determine possible infectious sources (**Box 4**).<sup>38</sup> Blood cultures should always be drawn and central venous access devices should be carefully assessed, as these are common portals for infection. The presence of mucositis identifies a breakdown of mucosal barriers, allowing for a translocation of enteric bacteria with potentially worse outcomes.<sup>37</sup> Rectal examinations should not be performed owing to increased risk of bacteremia. Chest x-ray scans may not show lung infiltrates in neutropenic patients due to their decreased ability to mount an inflammatory response.<sup>39</sup> Only 20% to 30% of patients with febrile neutropenia will have an identifiable infectious cause.<sup>40</sup>

Empiric broad-spectrum antibiotic therapy should be initiated once cultures are drawn, ideally within 1 hour

of triage.<sup>36</sup> The Multinational Association for Supportive Care in Cancer risk index is a validated online tool that can be used to determine who must be admitted to hospital and who can safely be treated as outpatients (Box 5).<sup>36,41,42</sup> Clinicians should have a low threshold for admission, and any patients who look systemically unwell or have unstable vital signs should be treated as inpatients. Patients with no measurable neutrophils are not candidates for outpatient therapy.

Suggested antibiotic treatments for low- and high-risk patients are presented in Box 6.<sup>35,36,38</sup> Low-risk outpatient treatment should be prescribed for at least 7 days. Patients should be reassessed if fever persists beyond 48 to 72 hours, if there is any clinical deterioration, or if there are positive blood culture results or microbiological tests not susceptible to the chosen antibiotic regimen.<sup>36</sup> Clinicians should consider patterns of antibiotic resistance in their setting when choosing therapies.

#### Box 4. Recommended workup for febrile neutropenia

- Complete blood cell count with differential leukocyte count
- Creatinine level
- Blood urea nitrogen level
- Electrolytes
- Hepatic transaminase enzymes
- Total bilirubin
- Blood cultures from central venous catheter, if present, and from peripheral vein site
- Culture specimens from any suspected site of infection (eg, urine, throat, skin)
- Consider viral culture
- Chest x-ray scan if respiratory signs or symptoms

Data from Freifeld et al.<sup>38</sup>

#### Box 5. Criteria for low-risk outpatient treatment for febrile neutropenia

- Outpatient with controlled malignancy
- MASCC risk index score  $\geq 21$
- No clinical evidence of any specific infection
- No signs or symptoms of systemic infection other than fever (eg, no hypotension, rigours, respiratory insufficiency)
- No clinically significant comorbid illness
- ANC  $>0.1 \times 10^9/L$ , recovery of neutrophils expected within 7 to 10 d
- Peak temperature  $<39^\circ C$ , no neurologic or mental status changes, respiratory rate  $<24$  breaths per minute
- No hepatic or renal insufficiency
- No nausea, vomiting, diarrhea, or severe mucositis
- No antibiotics in past 7 d
- No known allergies to penicillin or quinolones

ANC—absolute neutrophil count, MASCC—Multinational Association for Supportive Care in Cancer.  
Data from Crepsio et al.<sup>36</sup>

#### Box 6. Antibiotic treatments for febrile neutropenia in low- and high-risk patients

##### Low risk

- 750 mg of ciprofloxacin taken orally every 12 h, and 875 mg of amoxicillin and 125 mg of clavulanic acid taken orally twice daily
- If patient is allergic to  $\beta$ -lactams, consider oral ciprofloxacin and oral clindamycin

##### High risk


- Intravenous infusion of 4 g of piperacillin and 0.5 g of tazobactam every 6 h
- If patient is allergic to penicillin, prescribe fluoroquinolone and clindamycin
- Consider addition of vancomycin if patient is clinically unstable, is known to have MRSA, or has central venous catheter or skin infections
- Consider addition of antifungals or antivirals if there is clinical evidence of infection or if patient has persistent fever after 4 to 7 d of antibacterial regimen with no identified source of infection

MRSA—methicillin-resistant *Staphylococcus aureus*.

Data from Taplitz et al,<sup>35</sup> Crepsio et al,<sup>36</sup> and Freifeld et al.<sup>38</sup>

Patients admitted with febrile neutropenia can be stepped down from intravenous infusion to oral regimens if they remain afebrile, have evidence of ongoing neutrophil recovery, and have negative blood culture results.<sup>42</sup> Granulocyte colony-stimulating factors such as filgrastim promote neutrophil production in the bone marrow, and they are used prophylactically in patients receiving curative chemotherapy with a high risk of neutropenia but are not typically recommended in the treatment of febrile neutropenia.<sup>38</sup>

## Conclusion

This article summarizes important clinical aspects of SCC, SVCO, and febrile neutropenia. As SVCO and SCC can be the first presentation of cancer, family physicians must be able to recognize their presentations in primary care. A greater understanding of oncologic emergencies will assist family physicians in the care of patients with cancer, where timely intervention can preserve quality of life and reduce mortality. 

**Dr Laura Regnier** is Assistant Professor in the Department of Family Medicine at the University of Ottawa in Ontario, and a general practitioner in oncology in the Radiation Oncology Department at the Ottawa Hospital Cancer Centre. **Dr Anna N. Wilkinson** is Associate Professor in the Department of Family Medicine at the University of Ottawa, a family physician with the Ottawa Academic Family Health Team, a general practitioner oncologist at the Ottawa Hospital Cancer Centre, Program Director of PGY-3 FP-Oncology, and Regional Cancer Primary Care Lead for Champlain Region.

#### Competing interests

None declared

#### References

1. Higdon ML, Atkinson CJ, Lawrence KV. Oncologic emergencies: recognition and initial management. *Am Fam Physician* 2018;97(11):741-8.
2. Ropper AE, Ropper AH. Acute spinal cord compression. *N Engl J Med* 2017;376(14):1358-69.
3. Cole JS, Patchell RA. Metastatic epidural spinal cord compression. *Lancet Neurol* 2008;7(5):459-66.

4. Van den Brande R, Cornips EM, Peeters M, Ost P, Billiet C, Van de Kelft E. Epidemiology of spinal metastases, metastatic epidural spinal cord compression and pathologic vertebral compression fractures in patients with solid tumors: a systematic review. *J Bone Oncol* 2022;35:100446.
5. Hamamoto Y, Kataoka M, Senba T, Uwatsu K, Sugawara Y, Inoue T, et al. Vertebral metastases with high risk of symptomatic malignant spinal cord compression. *Jpn J Clin Oncol* 2009;39(7):431-4. Epub 2009 May 9.
6. Li KC, Poon PY. Sensitivity and specificity of MRI in detecting malignant spinal cord compression and in distinguishing malignant from benign compression fractures of vertebrae. *Magn Reson Imaging* 1998;6(5):547-56.
7. Husband DJ, Grant KA, Romaniuk CS. MRI in the diagnosis and treatment of suspected malignant spinal cord compression. *Br J Radiol* 2001;74(877):15-23.
8. Kumar A, Weber MH, Gokaslan Z, Wolinsky JP, Schmidt M, Rhines L, et al. Metastatic spinal cord compression and steroid treatment: a systematic review. *Clin Spine Surg* 2017;30(4):156-63.
9. Walji N, Chan AK, Peake DR. Common acute oncological emergencies: diagnosis, investigation and management. *Postgrad Med J* 2008;84(994):418-27.
10. George R, Jeba J, Ramkumar G, Chacko AG, Tharyan P. Interventions for the treatment of metastatic extradural spinal cord compression in adults. *Cochrane Database Syst Rev* 2015;(9):CD006716.
11. Patchell RA, Tibbs PA, Regine WF, Payne R, Saris S, Kryscio RJ, et al. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. *Lancet* 2005;366(9486):643-8.
12. Rades D, Abrahm JL. The role of radiotherapy for metastatic epidural spinal cord compression. *Nat Rev Clin Oncol* 2010;7(10):590-8. Epub 2010 Aug 31.
13. Hoskin P, Misra V, Hopkins K, Holt T, Brown G, Arnott S, et al. SCORAD III: randomized noninferiority phase III trial of single-dose radiotherapy (RT) compared to multifraction RT in patients (pts) with metastatic spinal canal compression (SCC). *J Clin Oncol* 2017;35(18\_suppl). Epub 2017 Jun 13.
14. Dunne EM, Liu MC, Lo SS, Sahgal A. The changing landscape for the treatment of painful spinal metastases: is stereotactic body radiation therapy the new standard of care? *Clin Oncol (R Coll Radiol)* 2022;34(5):325-31. Epub 2022 Mar 3.
15. Lee JH, Lee SH. Selecting the appropriate radiation therapy technique for malignant spinal cord compression syndrome. *Front Oncol* 2019;9:65.
16. Ghia AJ, Guha-Thakurta N, Hess K, Yang JN, Settle SH, Sharpe HJ, et al. Phase 1 study of spinal cord constraint relaxation with single session spine stereotactic radiosurgery in the primary management of patients with inoperable, previously unirradiated metastatic epidural spinal cord compression. *Int J Radiat Oncol Biol Phys* 2018;102(5):1481-8. Epub 2018 Aug 9.
17. Redmond KJ, Lo SS, Fisher C, Sahgal A. Postoperative stereotactic body radiation therapy (SBRT) for spine metastases: a critical review to guide practice. *Int J Radiat Oncol Biol Phys* 2016;95(5):1414-28. Epub 2016 Mar 26.
18. Christensen J, Biering-Sørensen F, Morgen SS, la Cour K. Survival, discharge destination, and referral for rehabilitation after metastatic spinal cord compression surgery. *Spinal Cord Ser Cases* 2021;7(1):63.
19. Zacharia BE, Kahn S, Bander ED, Cederquist GY, Cope WP, McLaughlin L, et al. Incidence and risk factors for preoperative deep venous thrombosis in 314 consecutive patients undergoing surgery for spinal metastasis. *J Neurosurg Spine* 2017;27(2):189-97. Epub 2017 Jun 2.
20. Chaichana KL, Woodworth GF, Sciubba DM, McGirt MJ, Witham TJ, Bydon A, et al. Predictors of ambulatory function after decompressive surgery for metastatic epidural spinal cord compression. *Neurosurgery* 2008;62(3):683-92.
21. Lak AM, Rahimi A, Abunimer AM, Tafel I, Devi S, Premkumar A, et al. Quantifying the impact of surgical decompression on quality of life and identification of factors associated with outcomes in patients with symptomatic metastatic spinal cord compression. *J Neurosurg Spine* 2020;33(2):237-44.
22. Douglas S, Huttenlocher S, Bajrovic A, Rudat V, Schild SE, Rades D. Prognostic factors for different outcomes in patients with metastatic spinal cord compression from cancer of unknown primary. *BMC Cancer* 2012;12:261.
23. Liu YH, Hu YC, Yang XG, Lun DX, Wang F, Yang L, et al. Prognostic factors of ambulatory status for patients with metastatic spinal cord compression: a systematic review and meta-analysis. *World Neurosurg* 2018;116:e278-90. Epub 2018 May 4.
24. Rades D, Rudat V, Veninga T, Stalpers IJA, Basic H, Karstens JH, et al. A score predicting posttreatment ambulatory status in patients irradiated for metastatic spinal cord compression. *Int J Radiat Oncol Biol Phys* 2008;72(3):905-8. Epub 2008 Apr 23.
25. Friedman T, Quencer KB, Kishore SA, Winokur RS, Madoff DC. Malignant venous obstruction: superior vena cava syndrome and beyond. *Semin Intervent Radiol* 2017;34(4):398-408. Epub 2017 Dec 14.
26. Ponti A, Saltiel S, Rotzinger DC, Qanadli SD. Insights into endovascular management of superior vena cava obstructions. *Front Cardiovasc Med* 2021;8:765798.
27. Rice TW, Rodriguez RM, Light RW. The superior vena cava syndrome: clinical characteristics and evolving etiology. *Medicine (Baltimore)* 2006;85(1):37-42.
28. Wilson LD, Detterbeck FC, Yahalom J. Superior vena cava syndrome with malignant causes. *N Engl J Med* 2007;356(18):1862-9. Erratum in: *N Engl J Med* 2008;358(10):1083.
29. Nguyen AL, Belderbos H, van Harten JG, Wijne L. Superior vena cava syndrome presenting as position-dependent periorbital oedema. *BMJ Case Rep* 2018;2018:bcr2018225220.
30. Sonavane SK, Milner DM, Singh SP, Abdel Aal AK, Shahir KS, Chaturvedi A. Comprehensive imaging review of the superior vena cava. *Radiographics* 2015;35(7):1873-92. Epub 2015 Oct 9.
31. Rowell NP, Gleeson FV. Steroids, radiotherapy, chemotherapy and stents for superior vena caval obstruction in carcinoma of the bronchus: a systematic review. *Clin Oncol (R Coll Radiol)* 2002;14(5):338-51.
32. Léon D, Rao S, Huang S, Sheth R, Yevich S, Ahrar K, et al. Literature review of percutaneous stenting for palliative treatment of malignant superior vena cava syndrome (SVCS). *Acad Radiol* 2022;29(Suppl 4):S110-20. Epub 2021 Oct 1.
33. Xiao L, Tong JJ, Shen J. Endoluminal treatment for venous vascular complications of malignant tumors. *Exper Ther Med* 2012;4(2):323-8. Epub 2012 May 24.
34. Maleux G, Marchal P, Palmers M, Heye S, Verhamme P, Vaninbrouckx J, et al. Catheter-directed thrombolytic therapy for thoracic deep vein thrombosis is safe and effective in selected patients with and without cancer. *Eur Radiol* 2010;20(9):2293-300. Epub 2010 Mar 28.
35. Taplitz RA, Kennedy EB, Bow EJ, Crews J, Gleason C, Hawley DK, et al. Outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology and Infectious Diseases Society of America clinical practice guideline update. *J Clin Oncol* 2018;36(14):1443-53. Epub 2018 Feb 20.
36. Crepsa A, Forbes L, Vu K, Gallo-Hershberg D, Enright K, Abdallah M, et al. *Prevention and outpatient management of febrile neutropenia in adult cancer patients: clinical practice guideline*. Toronto, ON: Cancer Care Ontario; 2022. Available from: <https://www.cancercareontario.ca/en/guidelines-advice/types-of-cancer/38561>. Accessed 2022 Sep 13.
37. Zimmer AJ, Freifeld AG. Optimal management of neutropenic fever in patients with cancer. *J Oncol Pract* 2019;15(1):19-24.
38. Freifeld AG, Bow EJ, Sepkowitz KA, Boeckh MJ, Ito JI, Mullen CA, et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2011;52(4):e56-93.
39. Gerritsen MG, Willemsink MJ, Pompe E, van der Bruggen T, van Rhenen A, Lammers JWW, et al. Improving early diagnosis of pulmonary infections in patients with febrile neutropenia using low-dose chest computed tomography. *PLoS One* 2017;12(2):e0172256.
40. Long B, Koyfman A. Oncologic emergencies: the fever with too few neutrophils. *J Emerg Med* 2019;57(5):689-700. Epub 2019 Oct 18.
41. Klastersky J, Paesmans M, Rubenstein EB, Boyer M, Elting L, Feld R, et al. The Multinational Association for Supportive Care in Cancer risk index: a multinational scoring system for identifying low-risk febrile neutropenic cancer patients. *J Clin Oncol* 2000;18(16):3038-51.
42. De Naurois J, Novitzky-Basso I, Gill MJ, Marti FM, Cullen MH, Roila F, et al. Management of febrile neutropenia: ESMO clinical practice guidelines. *Ann Oncol* 2010;21(Suppl 5):v252-6.

Can Fam Physician 2023;69:28-32. DOI: 10.46747/cfp.690128