

Case report

Superior vena cava syndrome associated with uterine serous carcinoma

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1. Introduction

Superior vena cava syndrome is caused by intrinsic or extrinsic compression of the superior vena cava (SVC), compromising return flow to the heart. Most commonly associated with lung malignancies and lymphomas, it is considered an oncologic emergency (Khan et al., 2017). In most instances, it is treated with steroids, radiation and possibly endovascular stenting. SVC syndrome associated with gynecologic malignancies is rare. In this report, we describe the events surrounding a patient with uterine serous carcinoma who experienced rapid demise with SVC syndrome despite aggressive therapy. This case highlights the importance of explicit goals of care conversation.

2. Case

A 62-year old African-American woman presented with 3 months of post-menopausal bleeding. Transvaginal ultrasound was significant for an 8.1 mm endometrial stripe and an enlarged uterus with multiple fibroids. Endometrial biopsy demonstrated uterine serous carcinoma diffusely positive for p53 and p16, focally positive for ER and negative for PR. The patient underwent a total abdominal hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymph node dissection, omentectomy and peritoneal biopsies. Surgical pathology confirmed the diagnosis of stage II uterine serous carcinoma with lymphovascular space invasion (LVSI). Adjuvant chemotherapy and radiotherapy were recommended, however, the patient refused.

Post-operatively, the patient was lost to follow up and re-presented sixteen months later. CT at this time demonstrated 2 solid nodules in

the right upper lobe of the lung measuring 1.7 × 1.9 cm and 1.5 × 2.2 cm with mediastinal and supraclavicular lymphadenopathy suspicious for metastatic disease. Fine needle aspiration (FNA) of a 5.7 cm right supraclavicular lymph node was recommended, however, due to personal scheduling conflicts, the patient was unable to undergo the procedure.

Two months later, the patient presented to the emergency department with anorexia, shortness of breath, sore throat, difficulty swallowing, and a productive cough. Physical exam demonstrated a 10 × 5 cm enlarged right supraclavicular lymph node with deviation of the trachea. Breath sounds were decreased at the bases bilaterally with wheezing on expiration. CT scan reported multiple pulmonary metastases and an increase in the size of the nodules in the right upper lobe, now measuring 3.3 × 3.0 cm and 2.9 × 2.7 cm. The right supraclavicular lymph node had also increased in size with invasion into the right aspect of the thyroid gland, displacing the trachea to the left. The adenopathy continued into the upper mediastinum where it encased but did not occlude the right subclavian and carotid artery. The right and left brachiocephalic veins and superior vena cava (SVC) were severely narrowed but patent (Fig. 1). An FNA demonstrated metastatic high-grade carcinoma consistent with her primary cancer. Radiation oncology was consulted to initiate palliative radiation. The patient developed worsening respiratory symptoms, facial and upper arm swelling, facial plethora, and voice hoarseness. Given symptoms that were consistent with acute superior vena cava syndrome, she was admitted to the hospital.

During admission, she underwent emergent stenting of the SVC and bilateral brachiocephalic veins and was started on therapeutic

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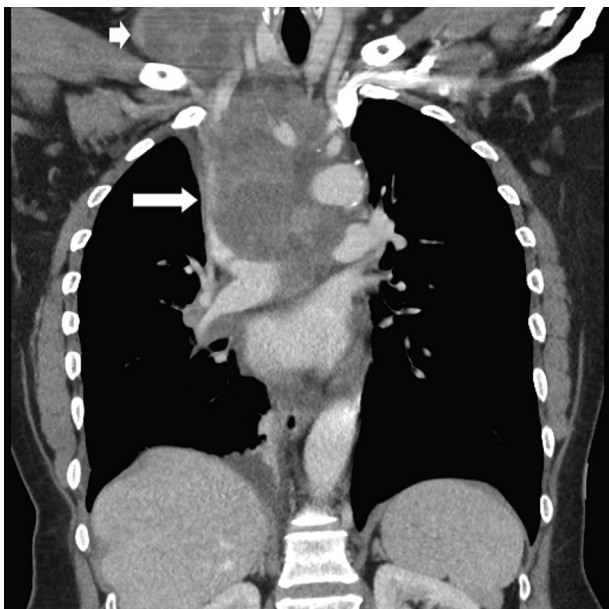


Fig. 1. Coronal CT of the chest demonstrating the enlarged right supraclavicular lymph node (short arrow), mediastinal adenopathy (long arrow), and compression of the right and left brachiocephalic vein and vena cava.

anticoagulation, steroids and palliative radiotherapy to the mediastinal lymph nodes and neck (Fig. 2).

A goals of care conversation ensued and the patient expressed a desire to undergo therapies that might improve her respiratory status and discomfort. Despite these interventions, her respiratory status deteriorated. Imaging on hospital day #8 demonstrated acute pulmonary emboli in the pulmonary arteries and occlusion of the stents (Fig. 3). She was switched to a continuous heparin drip. On hospital day #16, her facial swelling had improved and an attempt was made to initiate TPA for the occluded stents. However, she experienced respiratory distress during the procedure and was intubated. A bedside bronchoscopy with a 5 mm scope demonstrated a narrowed distal trachea but successful passage into the 6th generation airways. Placement of a tracheal stent in the operating room was attempted but unsuccessful. An extensive goals of care discussion ensued with the patient’s family who decided that they wished to complete the palliative radiation to achieve maximal effect but consider extubation thereafter. On hospital day #23, she completed 33 Gy of a planned 45 Gy palliative radiation. Radiation was truncated due to deteriorating clinical condition, however, it was believed that the patient had received the majority of effect from the radiation already delivered. A rigid bronchoscopy on hospital



Fig. 3. Superior vena cavaogram demonstrating the stenting of the right (arrow) and left brachiocephalic vein.

day #27 showed improvement in tracheal compression and edema but 50% airway lumen occlusion. The patient passed a spontaneous breathing trial on hospital day #28 and per the family’s wishes, was extubated with plans for hospice care and no plans to reintubate for respiratory distress. Following extubation, she continued to have worsening hypoxia and production of secretions despite increases in oxygen supplementation and passed away a day later.

3. Discussion and conclusions

Superior vena cava syndrome is characterized by a constellation of symptoms that results from external or internal obstruction. The SVC is a thin-walled vessel that provides drainage from the head, neck, upper extremities and chest. Because of its location in the right mediastinum, the SVC is subject to compression from structural abnormalities arising from the trachea, right bronchus, aorta, pulmonary artery, perihilar or mediastinal lymph nodes. Obstruction of the SVC can occur above or below the insertion of the azygous vein, which can allow for collateralization of vessels (Yu et al., 2008). Signs and symptoms including cyanosis, plethora, and edema of the arms, head and neck, need to be quickly recognized. These signs may be less recognizable to the

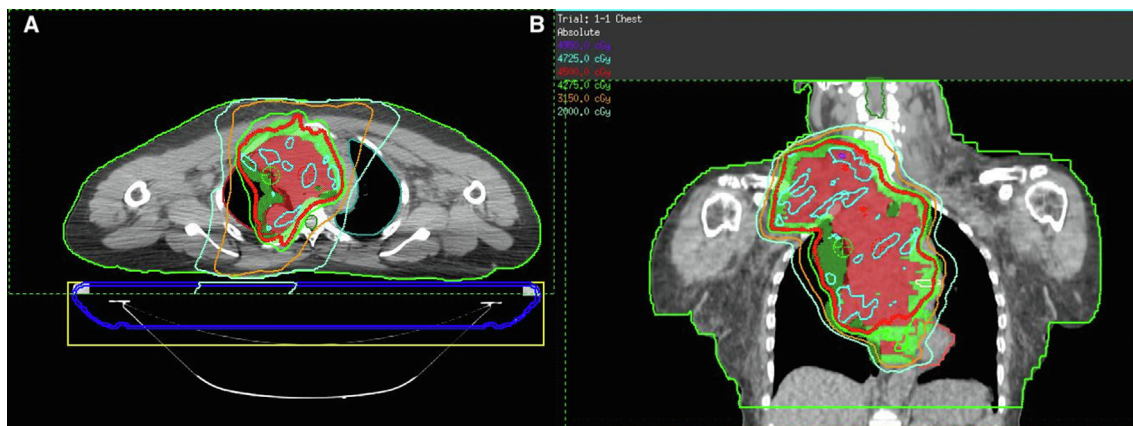


Fig. 2. Representative axial (A) and coronal (B) CT images with isodose lines depicting tumor coverage.

practitioner who does not readily follow the patient but are likely to be easily recognizable to the patient and her family. The severity of the syndrome is directly correlated to the rapidity, acuity and degree of the obstruction. More facial and/or neck congestion may occur with supra-azygous obstruction. With a slower trajectory of obstruction, collateral vessels can form above or below the azygous vein leading to the presence of dilated vessels on the chest and back or anterior/posterior abdominal wall. Late sequelae include airway compromise and cerebral edema which occurs in approximately 15% of SVC syndrome cases (Yu et al., 2008). Though 90% of SVC cases are associated with malignancy, the remainder are caused by benign etiologies such as thrombosis and stenosis from central venous access catheters and pacemaker leads. Only a handful of cases have been reported in the gynecologic cancer literature, mostly in recurrent cervical cancer (Biswal et al., 1995; Charles and Savage, 1980; Griffin et al., 2004; Inoue et al., 1988; Puleo et al., 1986). One report exists of SVC syndrome associated with uterine carcinosarcoma but there appear to be no reported cases associated with uterine serous carcinoma (Kimura et al., 1999).

The risk of developing metastatic lymphadenopathy with uterine serous carcinoma is well described. Using SEER data, Mattes et al. found that 44.5% of FIGO stage IIB uterine papillary serous cancer patients developed lymph node metastases to the pelvis and/or para-aortic lymph nodes (Mattes et al., 2015). Thus the development of our patient's lymphadenopathy, particularly with the presence of LVSI, was not surprising but the growth and degree of infiltration were particularly severe.

The management of the non-catheter associated cases of SVC syndrome in gynecologic malignancies has been inconsistent, ranging from intravenous heparin to thrombolysis with TPA. Every case was treated with some form of radiotherapy. Emergent management of SVC syndrome is largely centered around radiation therapy and corticosteroids. Corticosteroids reduce the swelling that may accompany radiation and allow for effective relief of symptoms while radiation targets the source of obstruction. In severe cases, intravascular stents can provide effective relief of symptoms within 24–48 h, though this method has not been reported in patients with gynecologic malignancies (Biswal et al., 1995; Charles and Savage, 1980; Griffin et al., 2004; Inoue et al., 1988; Puleo et al., 1986). In patients with non-emergent SVC syndrome caused by a malignancy, the mainstay of treatment is chemotherapy to decrease the tumor burden.

In our patient, stenting of the brachiocephalic veins led to initial improvement in her symptoms while radiation likely improved tracheal compression and contributed to success of extubation. Our patient did not undergo chemotherapy but this might have been a viable alternative or addition to radiotherapy given the volume of disease in her chest and mediastinum. Platinum-based chemotherapy for recurrent uterine serous carcinoma has a response rate of 50% and 30% of uterine serous carcinomas overexpress Her-2/neu. A randomized phase II study of paclitaxel, carboplatin and trastuzumab in advanced stage and recurrent uterine serous carcinoma yielded an improvement in median progression free survival of 8.6 months in those who had not been previously treated (Fader et al., 2018). Other trial considerations at our

institution in a patient with better performance status would include SBRT with immunotherapy.

In conclusion, the clinical course of our patient highlights the need to prevent nodal metastases and their sequelae in uterine serous carcinoma patients. Although the outcome of developing metastatic disease might have been the same despite adjuvant therapy, encouraging patient follow-up, possibly with the help of patient navigation may have altered her decision to refuse adjuvant treatment. The signs and symptoms of SVC syndrome need to be recognized early to allow for optimal treatment when the tumor burden is smaller. Steroids and radiation therapy are standard palliative treatment options for SVC syndrome due to metastatic disease but the decision making around radiation vs chemotherapy should take into account the volume of disease to be treated, the expected time to response and management of acuity of symptoms.

Author contribution

AL and SDY contributed to the drafting of the manuscript. RA, YH and SDY critically revised the manuscript for content.

Declaration of Competing Interest

The authors declared that there is no conflict of interest.

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