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## Chemotherapy Port Induced SVC Thrombosis in a patient with non-Metastatic Breast Cancer

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## **Chemotherapy Port Induced SVC Thrombosis in a patient with non-Metastatic Breast Cancer**

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# Chemotherapy Port Induced SVC Thrombosis in a Patient with Non-metastatic Breast Cancer

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## Abstract

Cancer patients are at a higher risk of complications such as venous thromboembolism (VTE). This risk increases in patients who receive chemotherapy. Despite the increased risk, common locations for VTE are similar to those in patients without cancer. Chemotherapy-port-related thrombosis represents a rare complication due to the location and frequent use of access (with Heparin flushes) as part of the standard care. Attention should be made to this rare complication, which may progress to superior vena cava (SVC) syndrome. SVC syndrome typically presents in females around the age of 57 years old. Management of this syndrome can be difficult and generally requires the initiation of systemic anticoagulation therapy. Here, we present a rare case of a 45-year-old female who presented to the Emergency Department with right arm swelling, found to be secondary to her chemo port thrombosis, causing SVC syndrome.

**Keywords:** SVC syndrome, Breast cancer, Port thrombosis

## 1. Introduction

SVC syndrome has been found to be a complication associated with cancer patients, with a further increase in the development of this syndrome if patients receive chemotherapy through indwelling catheters. Patients with SVC syndrome can present acutely due to the rapid rate of clot development without the body's ability to adjust and develop collateral circulation. Treatment consists of treating the underlying cause, such as removal, replacement, or thrombolysis of the catheter itself, followed by the use of anti-coagulation. Here, we discuss a case of a chemo port associated with SVC syndrome in a 45-year-old female with inflammatory breast cancer, who ultimately required urgent removal of her central venous catheter and initiation of systemic anticoagulation therapy.

## 2. Case report

A 45-year-old Hispanic female with a past medical history of inflammatory breast cancer of the left breast

status post adjuvant chemotherapy followed by a modified radical mastectomy, presented to the Emergency Department (ED) with a chief complaint of neck swelling for 5 days with associated facial swelling, RUE swelling, and pain with cervical rotation. At the time of presentation, the patient complained of an intermittent headache over her frontal and occipital area rated 8/10 in severity with associated blurry vision for one day. She denied shortness of breath, chest pain, nausea, vomiting, or abdominal pain.

In terms of the patient's past oncologic history, she was diagnosed with biopsy positive ductal adenocarcinoma that was ER/PR negative with HER2 IHC +3 positive with Ki 67 < 10%. The patient completed 6 cycles of Taxotere, Carboplatin, Herceptin, and Perjeta (TCHP) chemotherapy 4 months prior to the current presentation with the use of a chemotherapy port, which she tolerated well. Following neoadjuvant chemotherapy, the patient underwent left radical mastectomy 2 months prior to the current admission and after surgery, she had cancer staging of ypTis (DCIS) N0

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(i+) Mx. In the interim, the patient was compliant with receiving port flushes with heparin every 6 weeks. The patient was initiated on maintenance therapy of Herceptin and Perjeta the day prior to admission through the peripheral line due to her swelling. She did not receive treatment with Tamoxifen. The patient denied tobacco or illicit drug use, and her family history was negative for malignancy or deep vein thrombosis.

Physical exam was significant for facial and neck swelling. Laboratory studies were significant for normocytic anemia with a hemoglobin of 8.7 g/dL (reference range 12.0–16.0), and a hematocrit level of 28.9% (reference range 36.0–46.0) with a mean corpuscular volume of 83.3 fL (reference range 80–100). Prothrombin time was 12.9 s (reference range 12.2–14.9), PTT was 27.5 s (reference range 21.3–35.1), and INR was 1.0 (reference range  $\leq 1.1$ ). Chest XR was notable for new minimal blunting of bilateral costophrenic angles posteriorly, most indicative of trace pleural effusions. Venous ultrasound of the right upper extremity was notable for focal occlusion of the dome of the right internal jugular vein proximally by deep vein thrombosis with occlusion of the right chemotherapy port, and with focal thrombus in the distal basilic vein. The patient was admitted for further management of the focal occlusion of her right internal jugular vein.

A CT angiogram of the neck and chest was significant for an occlusive thrombosis in the left hemiazygos vein draining into the superior vena cava, and nonocclusive thrombosis of the internal jugular vein, mid and distal left subclavian vein, and proximal left axillary veins. Vascular Surgery and Hematology Oncology teams were consulted, and the patient was initiated on a therapeutic dose of unfractionated heparin for her occlusions.

A fluoroscopy study was completed to determine the patency of the chemotherapy port, which demonstrated confirmation of complete occlusion of both lumens of the port flush. Four days following admission, the patient underwent IR-guided removal of her chemotherapy port. The patient had a follow-up Left Upper Extremity Venous Duplex ultrasound which was significant for negative DVT findings in the left upper extremity and positive findings for superficial thrombophlebitis. Throughout her admission, she reported symptomatic improvement each day in terms of her swelling and physical exam findings. The patient was discharged on oral Apixaban 5 mg twice daily with close outpatient Hematology Oncology clinic follow-up and plans to continue chemotherapy via peripheral line administration. Upon follow up, the patient had complete resolution of her symptoms.

### 3. Discussion

Despite the thrombogenic tendency of most malignancies, especially in patients who are actively receiving chemotherapy treatment, the incidence of chemo port-related thromboses has been shown to be rather low. In a study involving over 51,000 individuals who underwent chemo port placement, only 1.81% of these patients developed an upper extremity venous thrombotic event (VTE).<sup>1</sup> Additional studies have demonstrated a variable incidence of 1.75%–30.2% for patients who develop VTE secondary to catheters.<sup>2</sup> Nevertheless, removal of the catheter is not always required according to studies that have demonstrated a low incidence (3.4%) of patients who require catheter removal because of VTE.<sup>3</sup> Our patient represents one of the few individuals with a chemo port-related VTE requiring the removal of her catheter.

Many trials have investigated whether patients with indwelling catheters may benefit from prophylactic warfarin (at either a fixed dose or titrated to achieve an INR goal of 1.5–2); however, these studies have not demonstrated a significant reduction in VTE.<sup>3</sup> This evidence is further emphasized by the American College of Chest Physician guidelines, stating there is no indication for chronic systemic anticoagulation as prophylaxis for VTE in patients who have indwelling catheters placed.<sup>4</sup>

It has been shown that VTE secondary to chemo ports has become more frequent in individuals who use their chemo port for blood draws and anti-cancer treatment. In a retrospective study reviewing 80 patients with SVC syndrome, 21% of these patients had VTE due to their chemo port. In this study, the average age of presentation was 57.7 years old and approximately 54% of the patients were females.<sup>5</sup> When comparing our patient's demographics and age, she was slightly younger than the anticipated age for this phenomenon and represented the majority as a female who developed SVC syndrome.

Specific risk factors have been identified when it comes to determining cancer patients who are at a higher risk for the development of VTE. These factors include genetic mutations, age, gender, ethnic background, grade and level of metastatic disease, as well as specific types of cancer. In particular, patients with pancreatic and brain malignancies have been categorized as higher risk, with patients diagnosed with lung and colon cancer moderate risk, and patients with breast and prostate cancer considered to be a low risk.<sup>6,7</sup> As our patient was diagnosed with breast cancer, she remained at a lower risk for the development of thrombotic events per this risk stratification. One study demonstrated that patients

diagnosed with breast cancer who underwent chemotherapy treatment were found to have a 47% higher chance of developing thrombosis. Alternatively, the breast cancer patients who did not receive chemotherapy were found to have a 26% increase in thrombotic events. In this study, there were no significant differences in thrombotic events between patients who did versus did not proceed with surgical intervention (mastectomy or lumpectomy).<sup>8</sup>

Patients with chemo ports can develop thrombosis via two different mechanisms, such as occlusion or stenosis of the vein. This may occur due to thrombus development at the tip of the catheter, manipulation at the implantation site, malpositioning of the implanted port, or traumatic vessel injury of the vein.<sup>9–11</sup> Patients with a short catheter may have malpositioning of the tip into the subclavian or brachiocephalic vein (smaller diameters) which can lead to the development of a fibrin sheath and thus increase the resistance of blood flow when the chemo port is used.<sup>9</sup> Our patient had her chemo port inserted to streamline receiving infusion therapy for her inflammatory breast cancer. Catheters can be inserted in cancer patients to avoid frequent sticks for blood draws and infusions; however, it is essential to remember the serious risk factors of these chemo ports.

Patients who develop catheter-related SVC syndrome can be managed in two ways. First, patients can have their catheter removed and replaced by a new, functional catheter.<sup>4,12,13</sup> Alternatively, patients can have a thrombolytic medication administered into the non-functional catheter to lyse the occlusion, which can be a less invasive and a less costly option.<sup>4,12,13</sup> As there is no clear evidence that removal of indwelling catheters will improve outcomes for patients, patients may undergo removal only if their catheter is no longer warranted, represents a clear source of infection, or if it is no longer working properly.<sup>4,14</sup> In some cases, patients may have a contraindication to antithrombotic therapy, have a life-threatening thrombotic event where their limb may be compromised, or may have a chronic occlusion that limits vein accessibility, and in these cases, patients may benefit from removal instead of thrombolytic therapy.<sup>4,15</sup> In our patient's case, she began to experience neurological symptoms that placed her in a higher risk category in addition to her extensive intrathoracic venous occlusion on imaging, and her requirement for long-term central venous access. Due to all of these factors, it was more beneficial for the patient to have her chemo port removed instead of receiving thrombolytic therapy.

Regardless of whether patients undergo removal of their chemo port, if they have cancer-related VTE,

systemic anticoagulation is warranted.<sup>16,17</sup> Our patient was initiated on parenteral unfractionated heparin for 4 days before IR-guided removal of her chemo port, consistent with American College of Chest Physicians (ACCP) guidelines who recommend removal of the catheter approximately three to five days following anticoagulation therapy.<sup>16</sup> Studies have demonstrated no significant difference in treatment of upper extremity DVT with warfarin versus low-molecular-weight heparin;<sup>18</sup> however, current evidence demonstrates for patients with cancer-associated thrombosis, low molecular weight heparin is superior when compared to warfarin.<sup>19</sup> In this particular patient population, recent studies have also included non-vitamin K oral anticoagulants for the treatment of cancer-related thrombosis for both prophylaxis and treatment.<sup>20</sup>

Treatment duration for these patients remains a controversial subject, where some clinicians recommend a total of 3 months of treatment following catheter removal, whereas others prefer a shorter duration depending on the severity and case-by-case basis.<sup>16</sup> Ultimately, our patient had improvement in her symptoms with an image-proven complete resolution of her thrombosis. Due to her clinical improvement, she was discharged with a three-month course of Apixaban, following recent updates to the guidelines to utilize NOACs as treatment of cancer-related thrombosis.

Although port-related thrombosis represents a somewhat low incidence complication especially with low risk factors, any unusual signs or symptoms need to be investigated. Our case was unique due to lowered risk factors to develop thrombosis when compared to older patients with other malignancies, which included the patient's age and type of cancer. However, she developed a catheter related thrombosis that progressed quickly to SVC syndrome, an oncologic emergency.

A low threshold and more thorough examination is required when unusual complaints are raised. Multiple attempts to access the port could have potentiated this complication. We recommend utilizing peripheral lines rather than ports for any blood draws to avoid manipulating the port as much as possible, and to ensure the patient is scheduled for heparin flushes in order to decrease risk.

#### 4. Conclusion

Currently, evidence supporting the use of systemic anticoagulation therapy for preventative measures of cancer-related thrombosis is lacking. Patients with SVC syndrome secondary to their chemo port can present acutely and may require

immediate removal or replacement of the catheter. Management consists of treating the underlying cause, and in our case, removal of the catheter and anticoagulation was the appropriate treatment. Additional research is warranted regarding the most appropriate use of chemo ports and management of cancer-related VTE. It would be beneficial for each hospital to establish local practice guidelines for cancer-related VTE as well as establish measures to prevent such complications in cancer patients.

### Conflicts of interest

There is no conflict of interest.

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