

Case Report

## Concomitant Arterial and Venous Thrombosis Associated with Advanced Cervical Cancer: A Case Report

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### Abstract

Cervical cancer is a common cancer associated with high morbidity and mortality among women in Sri Lanka and worldwide. Venous thromboembolism (VTE) is a well-known complication of malignancy and chemotherapy. However, arterial thrombosis in the presence of cancer is not as widely encountered as venous thrombosis and the concurrent occurrence of venous and arterial thrombosis remains a rarity. Here we report a case of concomitant venous and arterial thrombosis in a middle-aged woman with advanced cervical carcinoma.

**Keywords:** *Cervix, Malignancy, Thrombosis*

### INTRODUCTION

Cervical cancer is the second commonest cancer in women in Sri Lanka with an incidence of 10.4 per 100000 population and is associated with high morbidity and mortality due to delayed presentation and delayed diagnosis<sup>1</sup>. Human Papilloma virus (HPV) infection is strongly indicated as a causative factor of cervical cancer. Venous thromboembolism (VTE) is more common among cancer patients than in the general population. The concomitant occurrence of venous and arterial thrombosis is rare in clinical practice. This case report highlights the rare occurrence of concomitant venous and arterial thrombosis in a middle-aged woman who presented with deep vein thrombosis (DVT) and an ischemic stroke and was later found to have an advanced cervical cancer.

### CASE REPORT

A 49-year-old woman presented with acute onset weakness of left upper and lower limbs and slurring of

speech for one day. She denied experiencing numbness, imbalance, dysphagia, urinary or faecal incontinence. There were no familial risk factors for thrombotic events. On examination, her Glasgow Coma Scale (GCS) was 15/15. She had motor weakness of both upper and lower extremities on left side with power 3/5. Her sensory system was intact. On further evaluation, she had mild slurring of speech, but swallowing was not affected. She was **haemodynamically stable and didn't have** cardiac murmurs or carotid bruit. A localized tender swelling was noted in her right calf with a positive Homans' signal though the patient had not noticed the calf swelling previously. Vaginal examination revealed an irregular cervix with contact bleeding.

Full blood count showed a normocytic normochromic anaemia (Hb 9.9 g/dl). ESR was 55 mm /1<sup>st</sup> hour. Her non-contrast computed tomography (NCCT) of the brain showed a small infarction in the anterior limb of the right-side internal capsule. The doppler study of lower extremities showed a thrombus extending from right midcalf up to popliteal fossa with surrounding soft tissue oedema. Carotid doppler study did not reveal a



clinically significant carotid artery stenosis. Her renal and liver functions, fasting blood sugar and fasting lipid profile were all within normal limits and thrombophilia screening was negative. 2D echocardiogram revealed normal valves and normal sized chambers with an ejection fraction of 60%. There was no intracardiac thrombus to suggest a cardiac cause for the ischemic stroke. The contrast enhanced computer tomography (CECT) of the brain, chest, abdomen and pelvis showed an advanced invasive cervical carcinoma with regional lymph node infiltration (Stage 111A).

She was initially treated with subcutaneous enoxaparin 1 mg/kg body weight twice a day for 5 days and a vitamin K antagonist (warfarin) was introduced while monitoring the international normalized ratio (INR). Warfarin was titrated up until the INR was stable between 2.0 and 3.0. A multidisciplinary approach was arranged to incorporate expert opinions of relevant subspecialties in the clinical decision-making process. She was referred to the Cancer Institute Maharagama where she was treated with a combination of aggressive chemotherapy and radiation followed by surgery.

## DISCUSSION

Thrombotic events are common among cancer patients with the annual incidence being 0.5% compared to 0.1% in the general population<sup>2</sup>. The Virchow triad consisting of hypercoagulability, abnormalities of the blood flow and vascular endothelial abnormalities, is a well described phenomenon which explains the pathophysiological processes leading to thrombotic events<sup>3</sup>. Increased platelet aggregation, reduced responsiveness to prostacyclin and elevated levels of platelet specific substances such as thrombospondin create a hypercoagulable environment<sup>3</sup>. Furthermore, procoagulant proteins such as fibrinogen and tissue plasminogen activator inhibitors increase in the blood while the activity of fibrinolytic system is reduced. Angiogenesis as a direct effect of increased vascular endothelial growth factor (VEGF) may induce turbulence of the blood flow. Many of these mechanisms act synergistically leading to a higher tendency to form venous thrombi in cancer patients as seen in our patient who developed DVT.

Arterial thrombosis in the presence of malignancy is a well-known complication but not

encountered as frequently as venous thrombosis<sup>3</sup>. The exact mechanism remains obscure but local inflammatory process and elevated coagulation molecules may contribute by expanding the already existing atherosclerotic plaques<sup>3</sup>. Rarely tumour embolization occurs. Cytotoxic chemotherapy may also play a role. Our patient didn't have common risk factors for arterial thrombosis such as diabetes, hypertension, dyslipidaemia or cigarette smoking.

Concurrent venous and arterial thrombosis in a patient with a cancer seems to be rare and medical literature on this topic is scarce. The rarity of this clinical scenario made us look for an underlying cause for the increased thrombotic state which resulted in the discovery of an advanced cervical cancer in an otherwise healthy patient. Therefore, it is imperative to have judicious clinical decision making to identify underlying aetiology when uncommon or atypical clinical scenarios are encountered.

The management of concurrent arterial and venous thrombosis in a cancer patient should be done with caution and a multidisciplinary approach should be strongly considered. Despite there being guidelines on management of isolated venous and arterial thrombosis in cancer patients, there are no guidelines addressing the management of concurrent arterial and venous thrombosis. The safety and efficacy of thrombolysis with intravenous alteplase in patient presenting within the window from the onset and fulfilling the eligibility criteria are not well established<sup>4</sup>. If the patient has a reasonable life expectancy (> six months) in the absence of contraindications, the patient may benefit from thrombolysis. Malignancy should not be considered an absolute contraindication for thrombolysis<sup>5</sup>. But our patient presented well outside the window period and therefore, thrombolysis was not considered.

2019 International Clinical Practice Guidelines for the treatment and prophylaxis of venous thromboembolism in patients with cancer recommends low molecular weight heparin (LMWH) either 1mg/kg twice a day or 1.5 mg/kg once a day for the initial treatment of VTE when creatinine clearance (CrCl) is more than 30 ml/min<sup>6</sup>. A divided dose (twice a day) regimen can be considered in a fragile patient at risk of haemorrhage. Unfractionated heparin is recommended if CrCl is less than 30 ml/min. For a patient who does not have a high risk of gastrointestinal or genitourinary bleeding, a regimen of direct oral anticoagulants (DOACs) Rivaroxaban or Edoxaban (started at least after 5 days of parenteral anticoagulation) can also be used for the initial

treatment of established VTE if the creatinine clearance is more than 30 mL/min<sup>6</sup>. In the Hokusai VTE cancer trial, it was shown that oral edoxaban was not inferior to subcutaneous dalteparin (LMWH) with respect to the composite outcome of recurrent venous thromboembolism or major bleeding in patients with cancer who had either acute symptomatic or incidental VTE<sup>7</sup>. LMWH is preferred over vitamin K antagonists for the early (up to 6 months) and long term (beyond 6 months) maintenance. DOACs are emerging as a safer option for maintenance in patients with low risk of bleeding. Vitamin K antagonists are preferred if CrCl is less than 30 ml/min. LMWH or DOACs should be used for a minimum of 6 months to treat established VTE in patients with cancer<sup>6</sup>. After 6 months, termination or continuation of anticoagulation (LMWH, DOACs or vitamin K antagonists) should be based on individual evaluation of the risk-benefit ratio, tolerability, drug availability, patient preference and cancer activity.

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## CONCLUSION

This case highlights a rare presentation of a concomitant arterial and venous thrombosis in a previously asymptomatic patient with advanced cervical cancer. Clinicians must carry a high degree of suspicion to promptly identify the underlying aetiology in patients with rare presentations of cancer to achieve a favourable outcome.

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