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IMAGING HIGHLIGHT

Non-bacterial thrombotic endocarditis: A rare manifestation of cervical adenocarcinoma

[1]Michael Chung Keat LIM, [1]Zatul Akmar AHMAD, [2]Soon Chai LOW, [1]Yin Ling WOO, [3]Norlisah RAMLI, [2]Nortina SHAHRIZAILA, [2]Chong Tin TAN

[1]Department of Obstetrics and Gynaecology, [2]Division of Neurology, Department of Medicine, [3]Department of Biomedical Imaging, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia.

Non-bacterial thrombotic endocarditis (NBTE) denotes the presence of sterile non-infective vegetation on structurally normal, or subtly degenerate cardiac valves and is often associated with advanced malignancies. In gynaecological cancer in particular, NBTE has been most commonly associated with ovarian cancer.[1,2] Here we report a rare but interesting case of NBTE in a patient with locally advanced cervical adenocarcinoma.

CASE REPORT

A 35-year-old woman presented with six months history of postcoital bleeding and persistent vaginal discharge. On examination, she was found to have a polypoidal cervical growth with pelvic magnetic resonance imaging (MRI) scan revealing a cervical mass measuring 5.7 cm x 4.6 cm with enhancement in the parametrium (Figure 1). Clinical staging and histology was consistent with Fédération Internationale de Gynécologie et d'Obstétrique (FIGO) Classification Stage IIB poorly differentiated cervical adenocarcinoma. She was then referred for concurrent chemoradiation therapy.

Two months later, she presented to a different institution with left thigh pain and swelling. A Doppler ultrasound confirmed left leg proximal deep vein thrombosis, of which she was treated with prophylactic dose of low molecular weight heparin (LMWH). Approximately four weeks later, she developed acute onset slurring of speech, mild expressive dysphasia and right-sided weakness. Multiple acute infarcts involving the left corona radiata, insular and occipital region as well as splenium of corpus callosum were seen in the brain magnetic resonance imaging (MRI) (Figure 2). MR angiography (MRA) of the brain was normal with no evidence of arterial disease andcomputed tomography (CT) venogram was also normal with no cerebral venous thrombosis. Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) were performed with no evidence of valvular vegetations, mural thrombus or patent foramen ovale. Repeat abdominopelvic CT scan showed an unchanged cervical mass, but multiple paraaortic nodes consistent with disease progression and hypodense lesions on the spleen and left upper pole of kidney suggestive of infarcts (Figure 3). Of note, the thrombophilia screen, serum homocysteine, thyroid function test, anti-cardiolipin antibody and anti-dsDNA antibody were within normal limits.

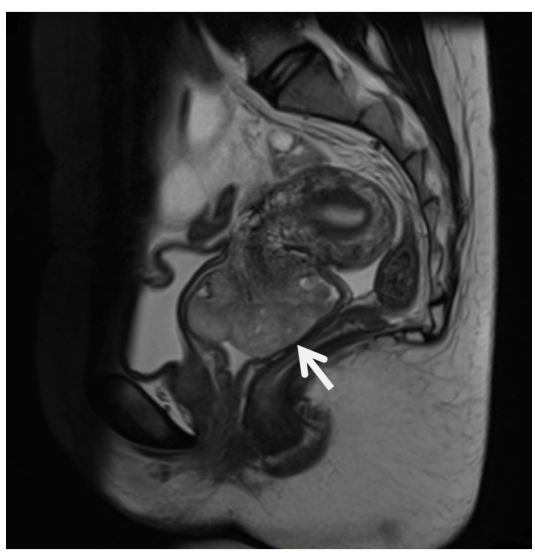

Figure 1. T2 weighted magnetic resonance imaging of the pelvis showing the 5.7 cm x 4.6 cm cervical cancer mass (white arrow) causing distension of the upper vagina but no extension to the uterus.

Address correspondence to: Dr. Michael Chung Keat Lim, Department of Obstetrics and Gynaecology, Faculty of Medicine, University of Malaya,50603 Wilayah Persekutuan Kuala Lumpur, Malaysia.Tel: +603-79492059, Email: michael.lim@ummc.edu.my

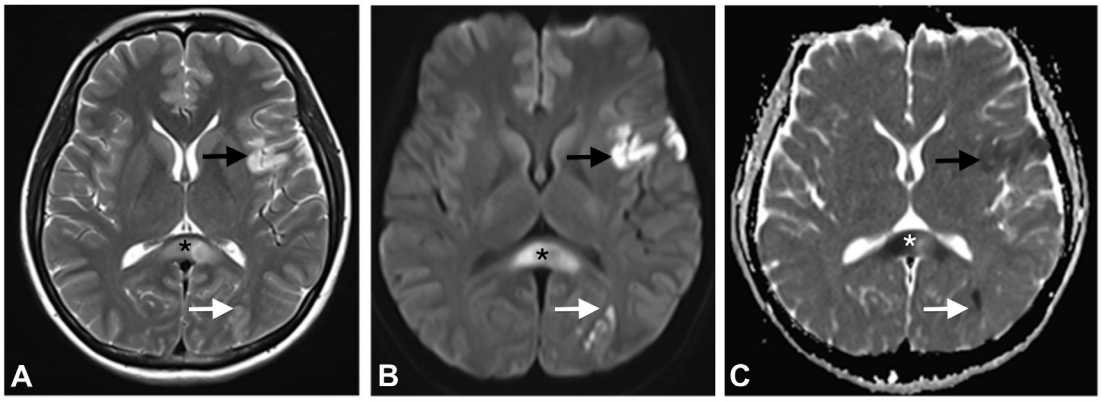

Figure 2. Axial MRI of the brain A) T2 weighted axial view showing multiple hyperintense lesions at left insular (black arrows), splenium of corpus callosum (asterisk) and left occipital regions (white arrows). B) Diffusion weighted imaging and C) apparent diffusion coefficient showing restricted diffusion at those regions in keeping with acute infarcts

In view of the multifocal systemic arterial infarcts and the background of advanced malignancy, a diagnosis of NBTE was made. She was anticoagulated with therapeutic doses of enoxaparin. Palliative chemotherapywas also initiated with carboplatin and paclitaxel aimed at a total of 6 cycles every 21 days. She madefull neurological recovery with no residual deficits. There was no further neurological event over the follow up period of one year.

DISCUSSION

Cancer-associated thrombosisis a common contributor to morbidity and mortality of cancer patients andmost events are venous in origin although arterial thromboembolism can also occur and accounts for 10 to 30% of thrombotic complications in cancer patients.[3] The pathophysiology behind cancer-associated hypercoagulable state is complex and often multifactorial, with different patients and different tumour types conferring different thromboembolic risks. NBTE is a rare manifestation of cancer-associated thrombosis with the mitral and aortic valves being the most commonly involved sites.[1,3]

A diagnosis of NBTE is often associated with advanced malignancies and can be difficult to establish antemortem due to the non-specificity of symptoms andits occurrence in advanced systemic disease. At post-mortem, NBTE was detected in 0.9 to 1.3% of all cancer patients.[3] Malignancies that have been associated with NBTE include pancreas, lung, stomach, ovary, cervix, endometrium, colon, breast, kidney, gallbladder, prostate, bile duct, lymphomas, sarcomas, melanomas and leukaemias.[4] In gynaecological cancer, NBTE is often associated with ovarian cancer with histological findings often typical of mucin-secreting adenocarcinoma, and rarely cervical cancer.[1]

When there is a high index of suspicion, TTE followed by TEE (if the former was negative), should be performed to search for vegetations.[5] Interpretation of echocardiography is subjective and can be unreliable in certain cases. Two-

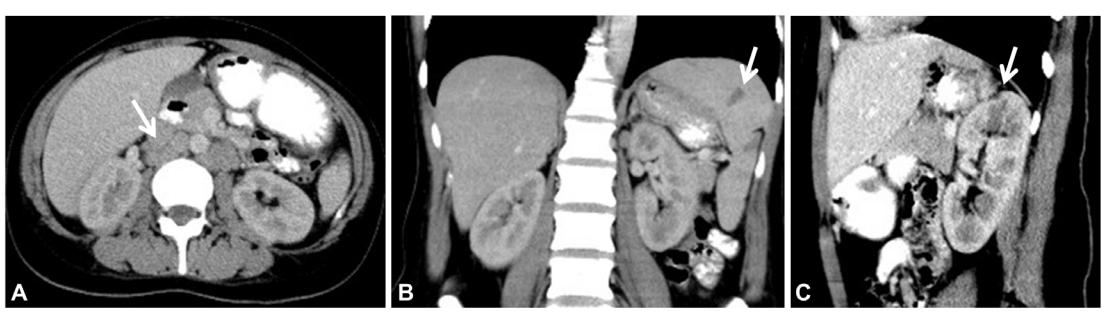

Figure 3. A) Axial CT of abdomen and pelvis showing multiple paraaortic nodes (white arrow) B) coronal and C) left parasagittal view showing multiple hypodense wedge-shaped lesions on the spleen (white arrow) and left upper pole of kidney (white arrow) suggestive of infarcts.

dimensional-echocardiography has been reported to be sensitive in less than 45% of cases.[6] In our patient, both the TTE and TEE were normal. It is hypothesised that the non-infective cardiac vegetation may have resolved or was technically difficult to detect on echocardiography. Despite the normal findings of the echocardiogram, cardiac emboli remains the most likely cause of our patient's presentation rather than *in-situ* thrombosis asthis is evident by the multi-organ arterial infarcts. Other potential causes of cancer-associated stroke were unlikely based on the normal MRA, CT venogram and thrombophilia screen. Her good response to LMWH and a normal MRA also favours cardiac emboli over arteritis of small arteries with *in-situ* thrombosis.

Compared to vegetations in infective endocarditis, the smaller fibrin-platelet rich thrombi in NBTE are easily dislodged since there is little inflammatory reaction at the site of attachment.[2] Systemic embolization to multiple organs is common, and the rate of embolization to the brain ranges from 14 to 91%.[7] NBTE produces neurological symptoms by occluding cerebral vessels of various sizes resulting in ischaemic infarction, and can be multifocal in nature. Speech impairment or aphasia is one of the most common focal neurological signs and may be due to ischaemic occlusion of the branches of middle cerebral artery.[7] Other major organs that can be involved include the heart, lung, spleen and kidney.[6] In the current case, the diagnosis of NBTE was further supported by findings of splenic and kidney infarcts on the abdominopelvic CT scan.

The mainstay of treatment for NBTE is to treatthe underlying disease and decrease embolization risk through adequate anticoagulation with unfractionated heparin or LMWH.[8,9] The CHEST guidelines recommend treatment with full dose unfractionated intravenous or subcutaneous heparin (Grade 1C evidence) and note that little benefit has been observed with vitamin K antagonist in this setting.[9] However, the evidence is mainly based on case reports or observational studies and no recommendations are made by CHEST, with regards to the optimal duration of anticoagulation. On the other hand, Dearborn *et al*. recommends that anticoagulation should be continued until the cancer is in remission or in cases where there are adverse effects or unacceptable complications such as bleeding.[5] Future prospective studies are warranted to further investigate the effect of the newer anticoagulation agents such as direct thrombin and/or Xa inhibitors.

Keywords: Endocarditis, non-infective; Adenocarcinoma; Uterine cervical neoplasm

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