

STROKE AS A FIRST PRESENTATION OF MALIGNANCY

Dr Farheen Niazi¹, Dr Puneet Kakar², Dr Ratneshwari Jha³, Reena Dhama⁴, Farook Edoo⁵

^{1,2,3,4,5}Epsom and St Helier NHS trust London, UK

Corresponding Author: Dr Farheen Niazi Registrar stroke medicine Epsom and St Helier NHS trust London, UK Email: farheenniazi@gmail.com Place of study: Epsom and St Helier NHS trust, UK

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ABSTRACT

Stroke is a frequent complication in patients with cancer occurring in nearly 15% of the cases. However cerebrovascular disease as the first presentation of malignancy has rarely been reported.

We report two such cases who were admitted with acute stroke but were later on found to be having malignancy. Routine workup was unrewarding in both patients. Both patients developed pulmonary embolism as well during hospital stay suggesting hypercoagulable state as likely etiology. Reaching to the final diagnosis was an arduous journey but can help guide other clinicians facing similar cases. Non Hodgkins B cell lymphoma and Carcinoma Gall bladder were the final diagnosis in our patients. Therefore, we recommend workup for malignancy if no likely cause is found on routine extensive workup before labelling stroke as cryptogenic stroke. Ultrasound abdomen was particularly rewarding in our patients.

Key words: Stroke, Malignancy, Ischaemic stroke, Cancer

INTRODUCTION

Stroke is a frequent complication in patients with cancer occurring in nearly 15% of the cases. However cerebrovascular disease as the first presentation of malignancy has rarely been reported¹.

We hereby report two of such cases where final diagnosis was actually a malignancy but presented with acute stroke and where we did routine extensive workup for the etiology of stroke but was unrewarding.

CASE 1

83 years old female was admitted with history of left sided visual field loss. She had risk factors of stroke in form of hypertension, hypercholesterolaemia. She also had Polymyalgia rheumatica and was on steroids.

On examination she was conscious alert with normal vital signs. Neurological examination was all normal except for right homonymous hemianopia.

Her investigations showed anaemia with Haemoglobin of 8 with MCV 68. Her ESR was raised to 124 and CRP was 259.8. Her CT brain scan confirmed a left occipital infarct as shown in Figure 1.

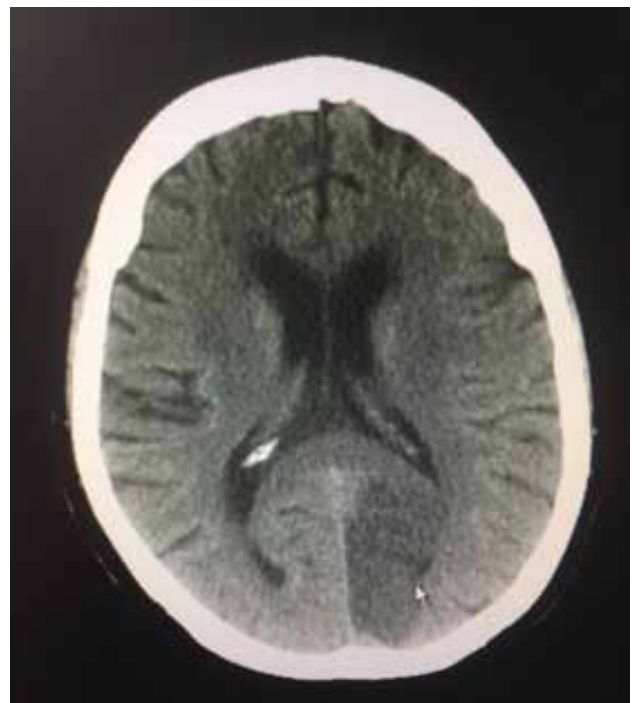


Figure 1. CT scan brain showing left occipital infarct. Her anaemia was investigated. Her OGD was normal. Her colonoscopy revealed angiodysplasia of colon, argon plasma coagulation was done on caecum.

Her echocardiogram showed mild pulmonary hypertension and moderate to severe Aortic stenosis. Her liver function tests showed deranged ALT of 181 which was initially attributed to Statins use. An ultrasound abdomen was done which showed heterogenous Hypoechoic round lesion at splenic hilum measuring 2.5cm. It was the deranged LFTs which led us to do ultrasound abdomen and led us to underlying diagnosis.

She kept on spiking high grade intermittent fever for which all relevant investigations were done including septic screen, blood cultures which showed no growth, serum immunoglobulins, serum electrophoresis, serum autoantibodies and serum complement levels which were normal.

CT abdomen showed solid mass in spleen with extensive lymphadenopathy in the upper abdomen and Lymphoma was suspected.

She also developed shortness of breath and hypoxia during hospital stay, CTPA was done and showed Segmental Pulmonary embolus within a branch of right upper lobe artery.

She was started on therapeutic dose of Dalteparin CT guided lymph node biopsy confirmed High grade B cell Lymphoma.

CASE 2

A 62 years old lady with no previous comorbidities except for DVT leg for which she was on Rivaroxaban presented to us with left arm weakness and facial droop was diagnosed as having right lacunar stroke. After few months she was readmitted with multiple episodes of aphasia, one episode rendering her completely aphasic.

MRI brain confirmed new stroke and showed areas of restricted diffusion bilaterally in both anterior circulations and posterior circulation as shown in figure 2.

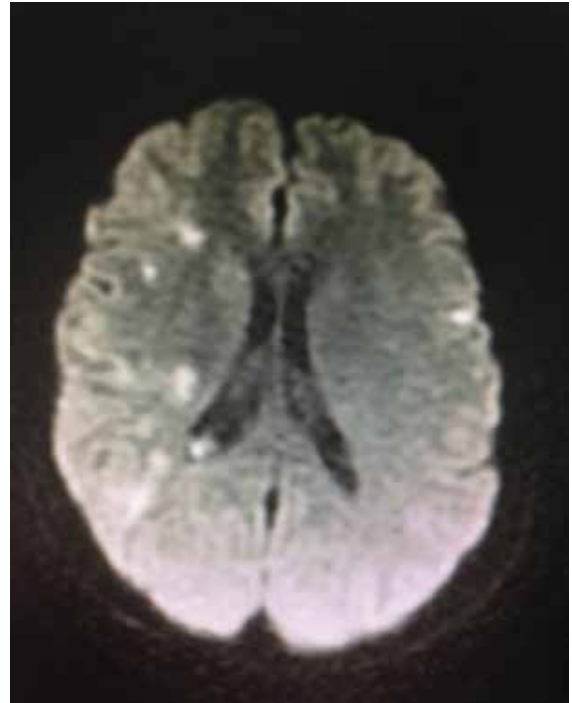


Figure 2. MRI brain DWI sequence showing bilateral infarcts.

All the workup for recurrent stroke including Anticardiolipin antibodies IgG and IgM, Thrombophilia and vasculitic screen was negative.²⁴ hours and 5 days ECG monitoring was normal. Transthoracic Echocardiogram was normal. Bubble contrast echocardiogram showed PFO.

Ultrasound abdomen was done during the course of hospital stay which showed a mass lesion involving the fundus of the gallbladder and the adjacent liver. It also showed small hypoechoic lesions in the adjacent liver. Carcinoma of the gallbladder with metastases was suspected.

CT abdomen and pelvis confirmed large mass of mixed density in the gallbladder fossa with a thick enhancing rim and another 2 cm well-defined low density lesion in the liver. Possibility was of gallbladder malignancy, liver lesion was suspicious for a metastatic deposit.

She was Started on Therapeutic Dose Dalteparin. PEG tube inserted

While on Dalteparin therapeutic dose developed extensive left femoral vein DVT extending into left iliac vein upto iliac bifurcation. IVC filter was placed.

She also developed acute shortness of breath during hospital stay, CTPA confirmed Pulmonary embolism in

form of segmental pulmonary emboli within right lower lobe and Lingula and left lower lobe.

Gall bladder biopsy was taken and GB malignancy proven. She was referred to acute Oncology and Palliative care.

DISCUSSION

Both the patients were interesting because of the fact that they first presented with stroke and were later on found to be having a malignancy. Stroke as a first presentation of malignancy is a rare phenomenon¹.

There are many ways in which stroke occurs in cancer as mentioned in different studies. Coagulopathic conditions involve disseminated intravascular coagulation, thrombocytopenia, nonbacterial thrombotic endocarditis, and cerebral intravascular coagulation².

Complications of chemotherapy, radiation therapy, direct tumor effects include intratumoral hemorrhage, arterial and venous sinus invasion by tumor mass or leptomeningeal infiltrates, and tumor emboli, all can occur².

Finally, septic infarction from fungal or bacterial sepsis and infectious vasculitis can manifest in cancer patients immunocompromised by malignancy or cancer therapy².

In many cases a combination of mechanisms is causative, and both hemorrhagic and ischemic stroke can occur².

Cancer-associated hyper-coagulation as a relevant stroke etiology was confirmed in many studies^{3,4}. In a study it was found that patients with elevated d-dimer levels in the absence of other conventional stroke etiologies and/or infarction in multiple vascular territories or small embolic infarction are the ones with increased risk for stroke³. Same study also suggested that patients presenting with lung or pancreatic cancer as well as patients with metastatic disease are at highest risk for cancer-associated stroke³. They also proposed that diagnostic workup should include a

broad laboratory assessment of hypercoagulability including d-dimer levels in all patients with cancer+stroke³.

It was interesting to note here that our both patients developed pulmonary embolism as well. It has been suggested in few studies that patients with suspected cancer-associated hypercoagulability should also be screened for other thromboembolic complications especially deep vein thrombosis which it is of therapeutic significance⁴. Our second patient had a DVT prior to having stroke. Also interesting was to note was the fact that our second patient developed first stroke while she was on oral anticoagulant Rivaroxaban and again developed extensive DVT of leg while on therapeutic doses of Dalteparin(LMVH) suggesting a severe hypercoagulable state.

Therefore, we suggest that in patients with stroke in which the usual workup is negative, before labelling them as cryptogenic stroke, workup/ screening for hidden malignancy should be undertaken. This holds particularly true if there is suspicion of hypercoagulable state, especially if D dimers are very high, if there is evidence of DVT/PE, stroke has affected multiple arterial territories, thrombophilia screen is negative and there is evidence of anaemia and inflammatory markers are raised. Ultrasound abdomen was particularly rewarding in this regard. Our both patients were diagnosed on ultrasound abdomen.

REFERENCES

1. Taccone FS, Jaengette SM, Bleic SA. First ever stroke as initial presentation of systemic cancer. *J Stroke Cerebrovasc Dis.* 2008 Jul; 17(4):169-74
2. Katz JM, Segal AZ. incidence and etiology of cerebrovascular disease in patients with malignancy. *Curr Atheroscler Rep.* 2005;7(4):280-8.
3. Horowitz N, Brenner B. Thrombophilia and cancer. *Pathophysiol Haemost Thromb.* 2008;36:131-6.
4. Schwarzbach CJ, Schaefer A, Ebert A, Held V, Bolognese M, Kablau M et al. The importance of cancer associated hypercoagulation as a possible stroke etiology. *Stroke.* 2012;43:3029-34.

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Farheen Niazi; Study concept and design, protocol writing, data collection, data analysis, manuscript writing, manuscript review

Puneet Kakar; Study concept and design, data collection, data analysis, manuscript writing, manuscript review

Ratneshwari Jhai; Study concept and design, data collection, data analysis, manuscript writing, manuscript review

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