Neuro-Hematology/Oncology

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Disclosures

- None

Background: Cancer-associated stroke

- About one of the population will develop a malignancy in their lifetime
- 10% of hospitalized ischemic stroke patients show a comorbid malignancy (1)
- Increase risk of venous and arterial thromboembolism (cancer-induced hypercoagulability, Trousseau syndrome)
- Higher rates of cryptogenic stroke, higher rates of PFO

1. Sanossia et al J Stroke Cerebrovasc Dis 2013

Case

- A 45 year old previously healthy woman with history of migraine with visual and sensory aura
- Acute left sided hemianopia and left sided visual loss, dizziness, and vertigo
- During 4 months prior to admission recurrent episodes of left sided visual loss, not typical for her migraine aura

Exam

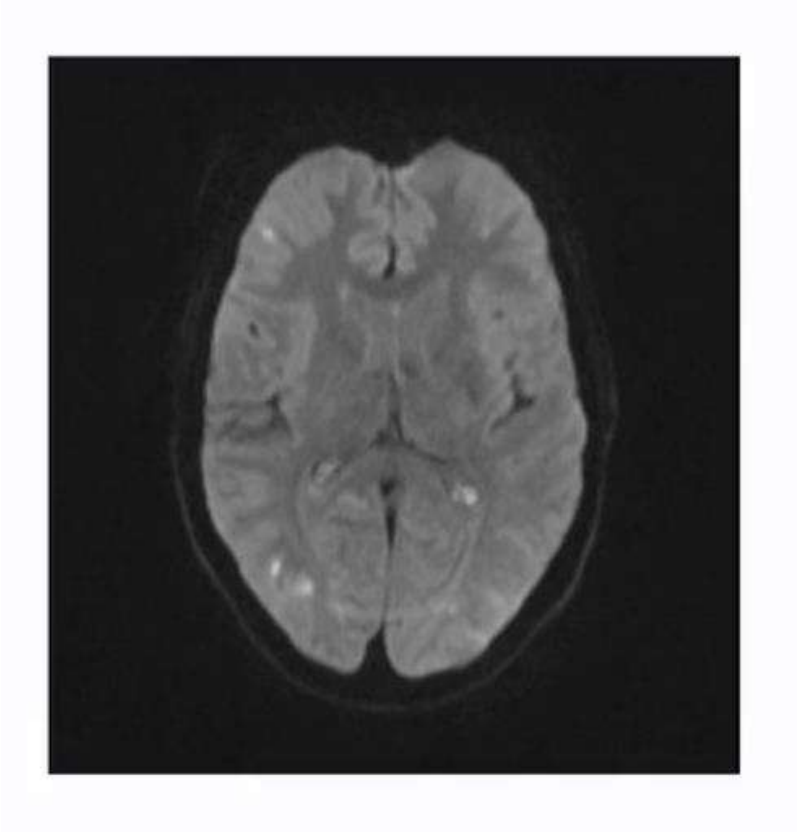
- Left sided hemianopia, no other neurological deficits
- ECG: Sinus tachycardia, blood pressure 173/94 mm Hg
- No signs of infection, blood tests including WBC were normal
- CT brain without contrast: no early signs of ischemia
- Transcranial doppler US: High peak systolic velocities, vasospasm, flow in the right posterior cerebral artery (PCA) detected

- CT-Angiography: occlusion of the right P2 with distal perfusion
- Perfusion CT brain: significant increased time-to-peak territory of the right PCA
- Reversible cerebral vasoconstriction syndrome?

Two weeks later…

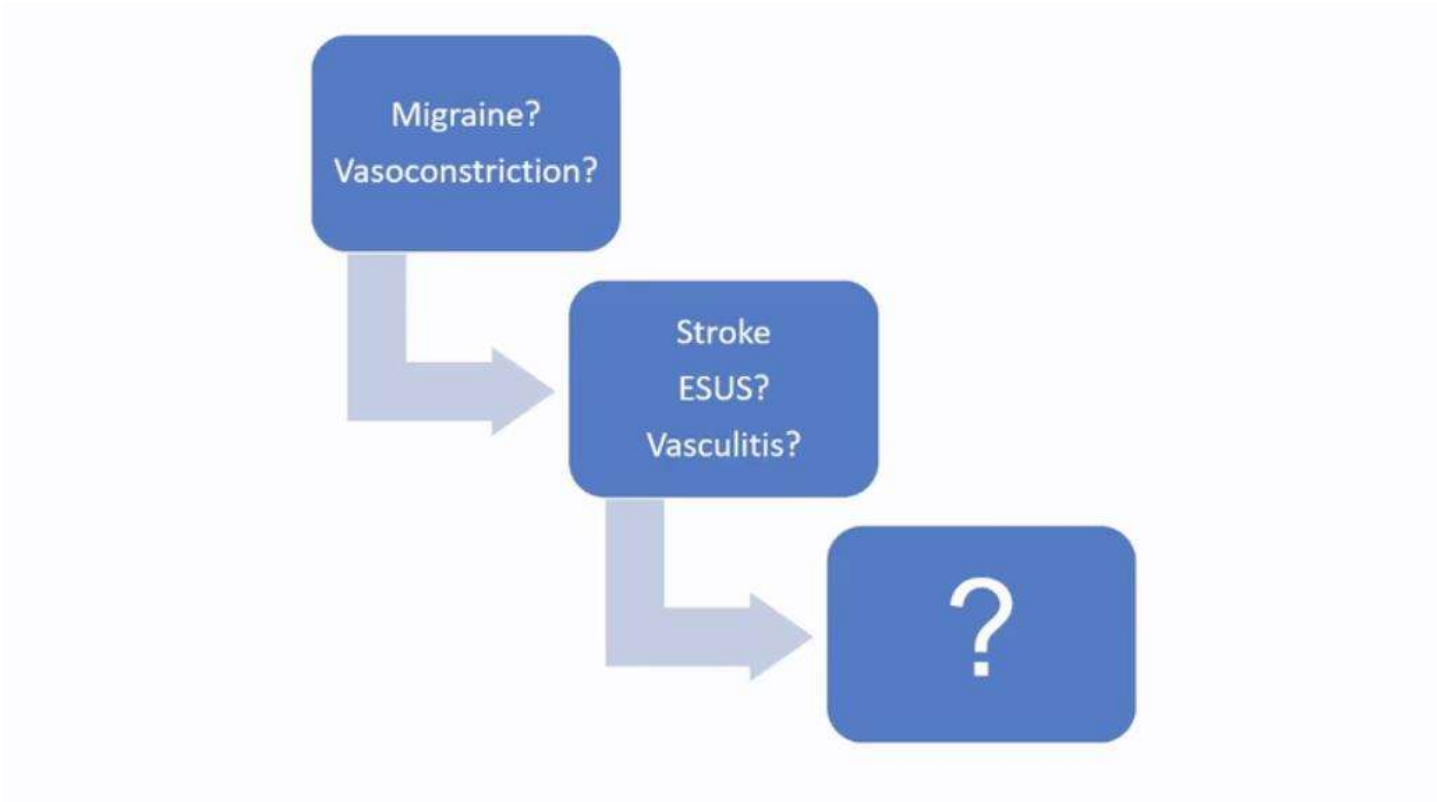
- Not fully recovered from visual loss, problem concentrating, fatigue
- On secondary prevention with ASA and statin
- Echocardiogram and Holter ECG unremarkable

MRI Brain



MRI Brain

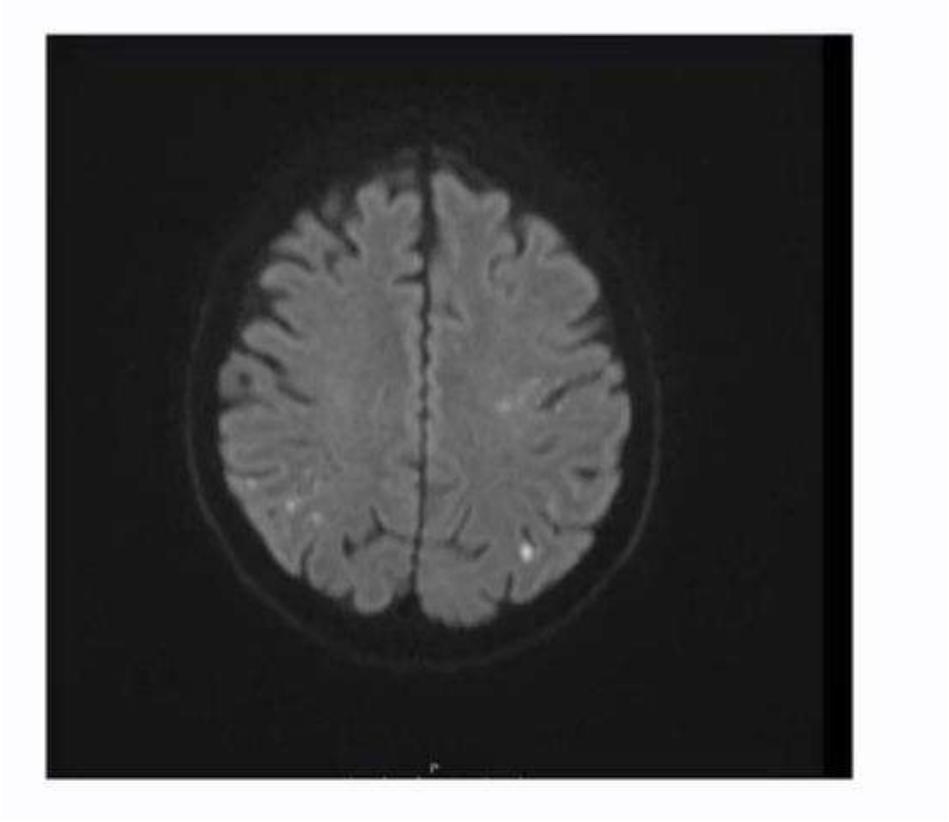
MRI brain 14 days later restricted diffusion right PCA territory, small cortical and subcortical areas restricted diffusion posterior and anterior circulation bilaterally (scattered emboli?), MR Angiography no new occlusions, right PCA P2 high grade stenosis


Migraine?
Vasoconstriction?
Stroke
ESUS?
Vasculitis?
?

Three weeks later…

- Dysathria, right sided sensory loss
- MRI widespread embolizations in the anterior posterior circulation
- DAPT, low molecular - weight heparin (LMWH), full dose
- Corticosteroids
- TEE unremarkable
- Cerebrospinal fluid unremarkable

MRI Day 30



4 weeks later…

- CT Chest/abdomen/pelvis : diffuse thickening minor curve of the gastric wall/pyloric region-lymph nodes in the abdomen, mediastinum

- FDG-PET: hypermetabolic, plus thyroid glands

- Diagnosis: 4 weeks later: gastric adenocarcinoma, spread to lymph nodes and thyroid gland.

- Deteriorated, large infarction of the right middle cerebral artery and embolic infarction both left anterior and posterior circulation
- Before oncologic treatment could be initiated
- Palliative care: died 10 weeks after first symptoms

Patient History

- Symptoms indicative of malignancy including substantial anorexia/weight-loss, unexplained recurrent fever, excessive night sweats, dysphagia, abdominal pain, enlarged lymph nodes, persistent cough, hemoptysis, history of cancer, unexplained anemia or chronically high inflammatory markers (note: this would usually prompt evaluation for cancer regardless of stroke history)
- Abdominal pain, other localized pain
- Unexplained weight loss, fatigue, elevated temperature, excessive night sweats

Clinical examination findings:

- Palpation of breast, testes, superficial lymph nodes and dermatology consultation for skin cancer
- Lumbar puncture - both to make alternative diagnoses such as infectious disease and vasculitis and to find meningeal malignancy. Include cytology and flow cytometry
- Organ-specific work-up according to risk-profile, findings and symptoms

Laboratory tests

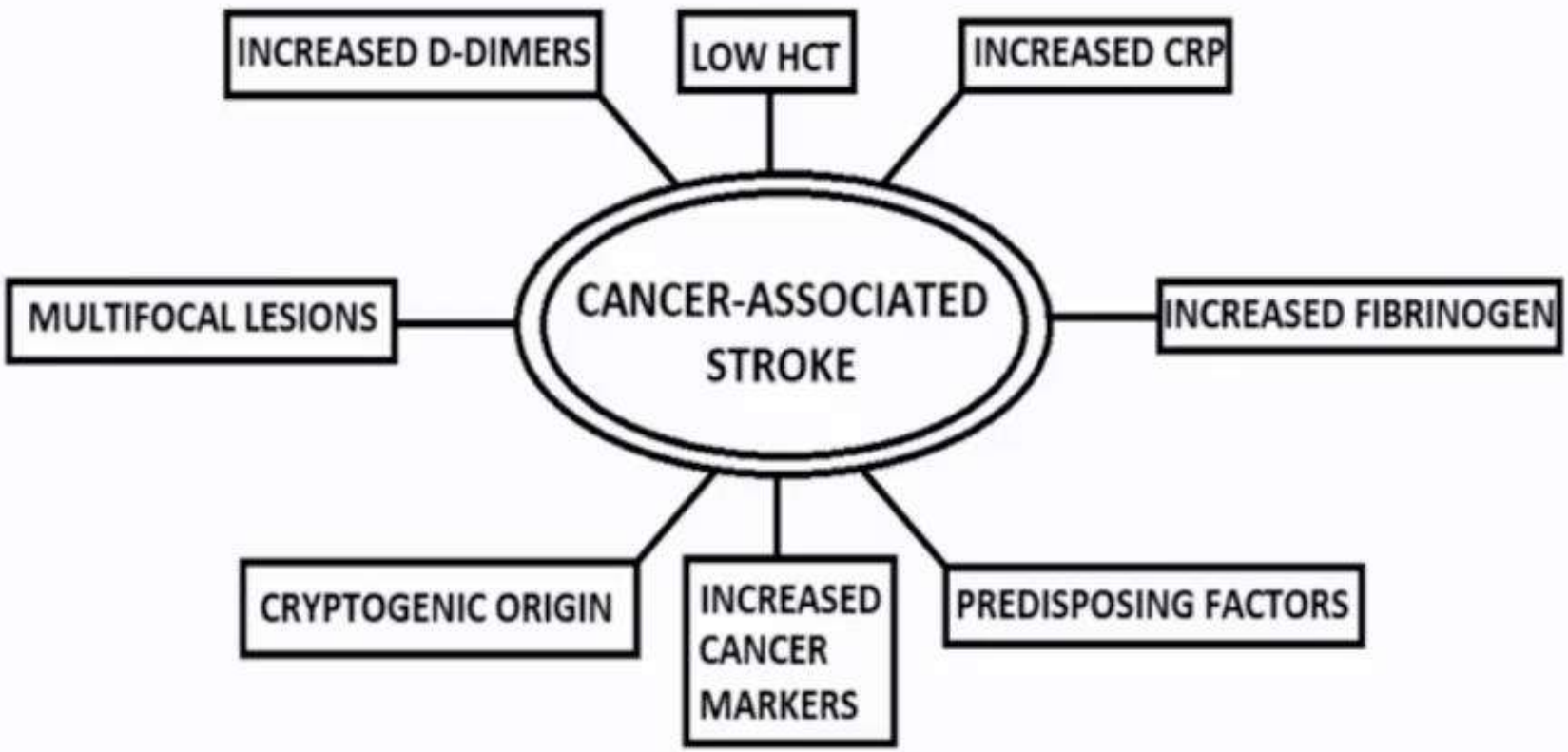
- Complete blood count including white blood cell count differential
- PT/INR, APTT, D-dimer, fibrinogen - to identify prothrombotic states, raised D-dimer in particular has been implicated as a quite specific marker for occult cancer in ischemic stroke
- CRP – non-specific for chronic inflammation
  Creatinine, urea and estimation of GFR - part of routine workup but uremia can be indicative of infrarenal obstruction in widespread malignancy
- Coagulation assay (in case of PFO venous coagulation disorders should be included)
- Liver function tests including ALP - for liver malignancies/metastasis and/or skeletal metastasis
- Consider serum markers of malignancy

Laboratory tests continued

- Lactic acid dehydrogenase (LDH) - unspecific marker of cellular demise often raised in metastatic cancer and hematologic cancer
- lonized Ca2+ - for skeletal metastasis
- Serum protein electrophoresis - for signs of chronic inflammation and hematologic malignancy
- Anemia work-up to further differentiate

Imaging

- Transesophageal echocardiography - valve vegetations or intracardiac thrombus (marantic endocarditis?)
- CT of the chest, abdomen and pelvis (consider including neck unless previously visualized during stroke workup) with and without intravenous contrast
- Mammography
- Consider 18-F FDG PET CT to look for malignancy not apparent on standard CT
- Consider MRI with vessel-wall imaging to look for signs of intracranial vasculopathy



Dardiotis et al., Int J Oncol 2019 Mar;54(3):779-796

Treatment – Secondary Prevention

- Treat underlying malignancy
- Secondary stroke prevention: ASA
- Consider low molecular weight heparin, alternatively DOAC
- ASA if additional atherosclerosis/vascular risk profile
- Close monitoring/adjustment

Cancer-associated stroke

- Suspect if cryptogenic stroke, multiple vascular territories, no cardiac embolic source, progression with secondary prevention
- Screening for cancer
- Adenocarcinomas- lung cancer, breast cancer, prostate cancer, gynecological cancers
- No RCT's secondary prevention (low molecular heparin /DOAC)
- Do not exclude patients with cancer from acute stroke treatments
- Treatment has to be individual-based and tailored, close monitoring, effect of anti-neoplastic treatment

1.Aloizouet al, J Clin Med 2022

Thank you

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