

# Ischaemic Stroke as the First Presentation of Occult Squamous Cell Cancer

Hina Zia Mirza<sup>1</sup>, Beyla Jamil Zuberi<sup>1</sup>, Tayseer Mohammad Zein<sup>2</sup> and Zein Mirghani<sup>3</sup>

## ABSTRACT

A 39 years old female presented with sudden onset of left sided weakness and CT scan brain confirmed an ischaemic stroke. Extensive investigations looking for the underlying cause were un-rewarding. She presented few days later with confusion and fever and was found to have multiple new cerebral infarcts, disseminated intravascular coagulation, rectal mass and liver metastases. Biopsy of metastatic liver lesion identified the primary tumour to be of squamous cell origin. Such a rare presentation as ischaemic stroke of a very rare squamous cell carcinoma of rectum has not been reported before.

**Key words:** *Ischaemic stroke. Squamous cell carcinoma. Rectal cancer.*

## INTRODUCTION

Thromboembolic strokes related to malignancy are rare and usually associated with adenocarcinoma.<sup>1</sup> Lung cancer was the most common primary tumour followed by brain and prostate.<sup>2</sup> Rectal squamous cell carcinoma is a rare tumour. The incidence of this malignancy has been reported to be 0.25 to 1 per 1000 colorectal cancers. It has a slight female preponderance and a prognosis worse than that of adenocarcinoma.<sup>3</sup>

We describe the case of a 39-year-old woman presenting with acute ischaemic stroke due to occult squamous cell carcinoma of rectum.

## CASE REPORT

A 36-year-old Pakistani female presented with sudden onset of inability to move the left side of her body. She had past history of gestational diabetes. She was not hypertensive, non-smoker and not taking oral contraceptive pills. Family history revealed that her father died of cancer of rectum. On examination, she had dense left hemiplegia with left upper motor neuron type of seventh nerve palsy. Her complete blood count, urea and electrolytes, random sugar and coagulation profile were normal. ECG showed no evidence of atrial fibrillation or ischaemic changes. CT scan of brain showed large right temporo-parietal infarction. CT angiogram of brain was also normal. Transthoracic and transesophageal echocardiogram (TEE) were normal. Carotid Doppler examination showed normal common carotid, internal

and external carotid arteries. Her ESR was high (80 mm after first hour) and C-reactive protein was also high (151.8 mg/l). Total cholesterol, LDL and HDL were normal. Her ANA, ANCA and anti-cardiolipin IgM Ab was negative. Thrombophilia screen including antithrombin 3, protein S (chromogenin and total) and Factor-V Leiden were negative. Lupus anticoagulant was weakly positive. Urine homocysteine and RPR for syphilis were negative. She was put on antiplatelet and anticholesterol agents and received physiotherapy. Three days later, she presented again with restlessness, acute confusional state and fever for 24 hours duration. Her WBC count was high with neutrophilia, prolonged PT/PTT and high FDP suggestive of DIC and multi-organ failure. Repeated blood cultures were negative. CSF examination was normal and CSF culture was negative. CT scan and MRI brain (FLAIR, DW1, T1, T2 sequences) with contrast showed multiple infarcts in both cerebral hemispheres, left cerebellar hemisphere and midbrain (Figure 1). MR venography and MR angiography were normal. CT scan of chest was normal. CT scan of abdomen showed multiple focal lesions of variable sizes in liver and spleen with non-homogenous contrast uptake suggestive of metastases (Figure 2). CT scan of pelvis showed a midline posterior rectal mass, 3x4 cms in size (Figure 3). Sigmoidoscopy was performed but was inconclusive due to poor preparation of the patient. She received intravenous antibiotics, transfusions of blood, platelets and FFPs. Alpha-fetoprotein was normal but carcinoembryonic antigen was high (151.2 ng/ml, normal value upto 10) and CA125 was very high (2574 u/L, normal value upto 34). Liver biopsy showed liver metastases of poorly differentiated squamous cell carcinoma with massive necrosis. Immunohistochemistry for CEA and CA125 was negative but cytokeratin staining was densely positive confirming squamous cell origin (Figure 4). The patient died on the 9th day of admission. Postmortem examination was not carried out.

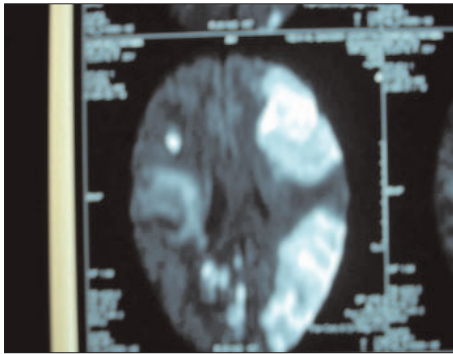
<sup>1</sup> Department of Internal Medicine / Neurology<sup>2</sup>, Al-Qasimi Hospital, Sharjah, UAE.

<sup>3</sup> College of Medicine, University of Sharjah, UAE.

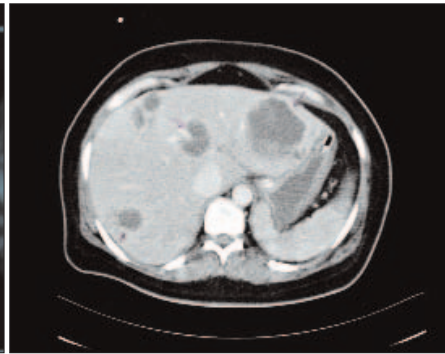
Correspondence: Dr. Beyla J. Zuberi, P.O. Box 7272, Dubai, UAE.

E-mail: [beylazuberi@gmail.com](mailto:beylazuberi@gmail.com)

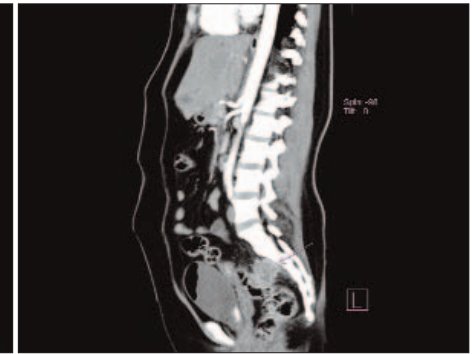
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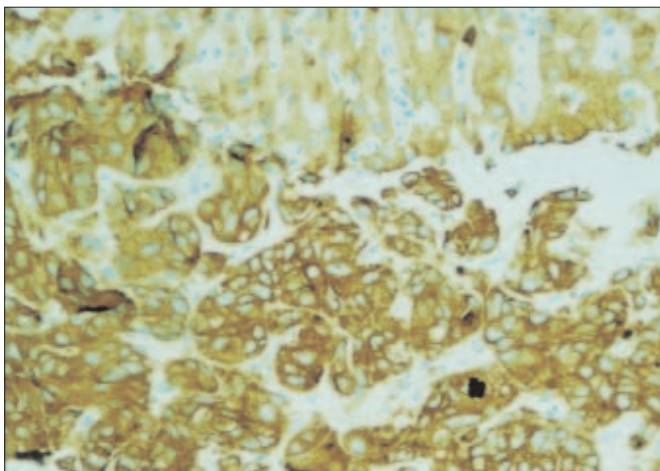
**Figure 1:** MRI of brain (axial FLAIR image) showing multiple infarctions.



**Figure 2:** Liver metastases of various sizes.



**Figure 3:** Posterior rectal mass seen in saggittal CT scan.



**Figure 4:** Immunohistochemistry staining of metastatic liver growth is intensely positive for cytokeratin confirming squamous cell origin.

## DISCUSSION

Ischaemic stroke rarely occurs as the first manifestation of malignancy. There are two possible mechanisms by which malignancy can cause ischaemic stroke. One possible mechanism is thromboembolism associated with malignancy which was first described by Trousseau in 1865, as a “migratory thrombophlebitis as a presenting sign of visceral malignancy,” a condition that is referred to as Trousseau's syndrome.<sup>4</sup> It is strongly associated with adenocarcinomas, particularly pancreatic, gastric, ovary, prostate and lung. These thromboembolic phenomena could be venous or arterial, secondary to hypercoagulability of malignancy or may be the sequela of embolization of occult tumour itself.<sup>5</sup> Non-bacterial thrombotic endocarditis (NBTE) is another mechanism of arterial thromboembolism encountered in patients with neoplastic disease. It is characterized by sterile vegetations composed of platelets and fibrin that adhere to valvular structures and are susceptible to embolization.<sup>6</sup>

In this patient, the first episode of ischaemic stroke could be due to occult tumour embolization as the patient's coagulation profile was normal at that time. The cause of multiple cerebral infarcts in the second admission could

be due to disseminated intravascular coagulation (DIC) secondary to malignancy or infection with *Streptococcus Bovis* endocarditis which is commonly associated with colonic cancer.<sup>7</sup> Repeated blood cultures were negative which are against DIC secondary to infection. The possibility of NBTE causing multiple embolic cerebral infarcts could still be a possible mechanism in our patient as vegetations may be too small to be visualized by transesophageal echocardiography.<sup>8</sup> Carcinomas that have been described in association with NBTE are usually adenocarcinomas, commonly pancreas, lung, stomach, ovary, colon, breast, kidney, gallbladder, prostate, and bile duct. NBTE and even DIC are often asymptomatic until major embolic events occur and the malignancy is often advanced by the time of diagnosis.<sup>9</sup>

In another study, the frequency of ischaemic and haemorrhagic stroke in tumour patients was found to be similar to that in the non-cancer population.<sup>10</sup> It was concluded that cerebrovascular risk factors do not significantly vary between cancer and non-cancer patients and the higher frequency of thrombotic events in cancer patients may reflect a coagulation disorder, commonly found in patients with malignancy.

In a recent published study from Portugal, almost 6% of ischaemic stroke patients had a concomitant malignancy. In most of them, cancer was the only cause of the stroke found. Patients with stroke and malignancy exhibited raised D-dimer, fibrinogen, and ESR levels, suggesting the prothrombotic state was a principal mechanism underlying stroke. D-dimer and ESR assessments may be useful in identifying underlying disorders in ischaemic stroke.<sup>11</sup>

## REFERENCES

1. Kwon HM, Kang BS, Yoon BW. Stroke as the first manifestation of concealed cancer. *J Neurol Sci* 2007; **258**:80-3.
2. Cestari DM, Weine DM, Panageas KS, Segal AZ, DeAngelis LM. Stroke in patients with cancer: incidence and etiology. *Neurology* 2004; **62**:2025-30.
3. Theodosopoulos TK, Marinis AD, Vassiliou JG, Samanides LD. Aggressive treatment of metastatic squamous cell carcinoma of

- the rectum to the liver: a case report and a brief review of literature. *World J Surg Oncol* 2006; **4**:49.
4. Khorana AA. Malignancy, thrombosis and Trousseau the case for an eponym. *J Thromb Haemost* 2003; **1**:2463-5.
  5. Bick RL. Cancer-associated thrombosis. *N Engl J Med* 2003; **349**:109-11.
  6. Borowski A, Ghodsizad A, Cohnen M, Gams E. Recurrent embolism in the course of marantic endocarditis. *Ann Thorac Surg* 2005; **79**:2145-7.
  7. Abul Y, Odbasi Z, Koli N, Oktay A, Kortan V. *Streptococcus bovis* endocarditis associated with rectal carcinoma and its neurological complications. *Eur J Gen Med* 2006; **2**:83-7.
  8. Wickremarachi M, Hughes T, Wharlow C. Three strokes and a heart attack in a fit and relatively young woman. *Pract Neurol* 2004; **4**:228-37.
  9. Scozzafava J, Hussain MS, Ahmed N, Khan K. Recurrent strokes in a 46 years old woman; rapidly progressive non-bacterial thrombotic endocarditis. *CMAJ* 2006; **175**:140-5.
  10. Stefan O, Vera N, Otto B, Heinz L, Wolfgang G. Stroke in cancer patients: a risk factor analysis. *J Neuro-oncol* 2009; **94**:221-6. Epub 2009 Mar 12.
  11. Alvarez-Pérez FJ, Verde I, Usón-Martín M, Figuerola-Roig A, Ballabriga-Planas J, Espino-Ibañez A. Frequency and mechanism of ischaemic stroke associated with malignancy: a retrospective series. *Eur Neurol* 2012; **68**:209-13.

