CASE REPORT AND REVIEW OF LITERATURE

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A rare case of left ventricular thrombus with ischemic MCA stroke in a lady with Crohn's disease

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ABSTRACT

We report a case of Crohn's disease (CD) presenting as a thromboembolic middle cerebral artery stroke due to a left ventricular (LV) thrombus in a 50-year-old lady. The proinflammatory and procoagulant state reported in CD seems responsible for this. The patient was managed with conservative treatment, but she died quickly. The findings highlight the rare occurrence of LV thrombus in a patient of CD as well as the need for aggressive control of disease activity with disease-modifying drugs at an earlier phase of treatment.

Key words: Crohn's disease; Inflammatory bowel disease; Left ventricular thrombus; Thromboembolism; Prothrombotic state; Middle cerebral artery infarct

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INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory disorder associated with a two- to three-fold higher risk of thromboembolic events compared to subjects without CD, especially during acute exacerbations.[1] To date, the prevalence of inflammatory bowel disease (IBD)-associated cardiac intraventricular thrombus formation is not well established.[2] Intracardiac thrombus is an unusual site.

IBD is a recognized risk factor for thromboembolic complications due to multifactorial mechanisms, namely, platelet activation, increased levels of fibrinogen, coagulation factor II, V, VII, VIII, X, and XI as well as impaired fibrinolysis, and endothelial dysfunction.[3]

The risk of arterial thrombotic events in CD has been less well delineated and reported as isolated case reports in medical literature.[4] Any artery can be affected such as coronary, splanchnic, iliac, renal, or branches of the aorta.[5] No risk factor has been identified in a substantial number of patients with IBD who develops thrombosis for unknown reasons.[6]

However, thrombus formation in IBD is important because it occurs in young population, often in unusual sites and has a high mortality.[6] Embolic stroke with left ventricular

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(LV) thrombus in subjects with CD is rare and only three patients with CD have been reported so far.[7,8] The exact pathophysiology of stroke in IBD is still not clear.[9] We report an unusual case of LV thrombus with ischemic stroke in a subject with CD.

HISTORY

A 53-year-old lady was brought to the emergency ward with a history of sudden onset of left hemiparesis and dysarthria.

General examination revealed thin built, moderate anemia, emaciation, and a colostomy bag in the right iliac fossa. The pulse was irregular, low volume and the pulse rate was 100 per min. Her blood pressure was 122/78 mmHg. Her body weight was 45 kg and BMI was 17. There was a history of weight loss of 5 kg.

Neurological survey showed she had a complete left-sided hemiparesis with a power of grade three (Medical Research Council grading) in the extensor group in the upper limb and flexor group of lower limb. There was left-sided hemineglect. Keeping in mind about the need of thrombolysis, noncontrast computerized tomography (CT) brain was done immediately and it was normal.

National Institute of health stroke scale score was 11 and Alberta stroke program early CT score was ten. Although the patient arrived within the window period for thrombolysis (within 2.5 h of stroke onset), it could not be given because the patient underwent ileal resection with jejunoileal anastomosis for subacute intestinal obstruction just 2 weeks before. Magnetic resonance imaging (MRI) brain and CT abdomen are shown in Figure 1a and b, respectively. There was apical systolic murmur on cardiovascular system examination.

Routine blood examination showed hypochromic, microcytic anemia with a hemoglobin level of 8.5 g/dL, ESR of 50 mm fall in the 1st h, neutrophilic leukocytosis, and thrombocytosis with a platelet count of 5.00.000/cu.mm. There were immature platelets and it was abnormally raised (immature platelet fraction [IPF] % was 8). C-reactive protein (CRP) was raised, and it was 20 in the preoperative state and 26 in the postoperative period. Liver function tests showed hypoalbuminemia (2.5 g/dL).

Prothrombotic workup including lupus anticoagulant panel, APLA, Factor V Leiden mutation, Factor VIII, protein C, protein S activity, and antithrombin level were normal. Hyper-homocysteinemia was found, and it was 30 micromol/L (normal – 5–15 micromol/L).

ECG showed sinus tachycardia and occasional ventricular ectopics. Echocardiography showed normal LV systolic function, Grade I diastolic dysfunction with an ejection fraction of 55%. There was a pedunculated mobile mass of size 2 cm×0.5 cm at the apex of the left ventricle.

Histopathological examination revealed transmural involvement of the intestinal wall with non-caseating, non-confluent granulomas (Figure 1c). There was deep fissuring into muscularis propria with strictures, cryptitis, crypt abscess, serosal vascular congestion as well as fibrinous exudates supporting the diagnosis of CD.

Contrast-enhanced cardiac MRI confirmed the presence of LV thrombus (Figure 1d). Preoperative CECT abdomen revealed stricture with intestinal obstruction, enterolith with no significant lymphadenopathy. The grossly resected ileal sample showed thick intestinal wall, creeping fat, stricture, shortened mesentery, focal ulceration, and enterolith.

She was treated with antiplatelets, subcutaneous low-molecular weight heparin (LMWH), intravenous albumin infusion, Vitamin B12, and folic acid supplementation as well as supportive care.

Opinion from gastroenterologist was taken for immunomodulatory therapy and nutritional rehabilitation. They advised to continue supportive care. They were not in favor of giving immediate immunomodulatory therapy because of risk of infectious complications.

Cardiology opinion was taken for fibrinolytic therapy and they advised to give subcutaneous LMWH only. They did not advise fibrinolytic therapy because of the risk of hemorrhagic transformation of the cerebral infarct.

However, the patient died suddenly within 1 week of admission due to cardiopulmonary failure following fatal ventricular arrhythmia.

DISCUSSION

Thrombosis is a well-recognized complication in subjects with IBD and it is a prime cause of morbidity and mortality of the patient. Venous sinus thrombosis is the more common type of stroke in IBD as compared to arterial stroke as observed in a previous study of 7199 patients with IBD with only seven cases of cerebrovascular disease.[10] Only a few pieces of literature are available and summarized here. Among cases of stroke in CD, the risk is three-fold in those below 50 years as compared to elderly.[11] The risk is more common in women compared to men.[12] The age of onset of stroke of our patient with CD is relatively young and this emphasizes the fact that CD is an important but underrecognized cause of stroke in the young. Most arterial thromboembolic phenomena have been reported in the postoperative period.[11]

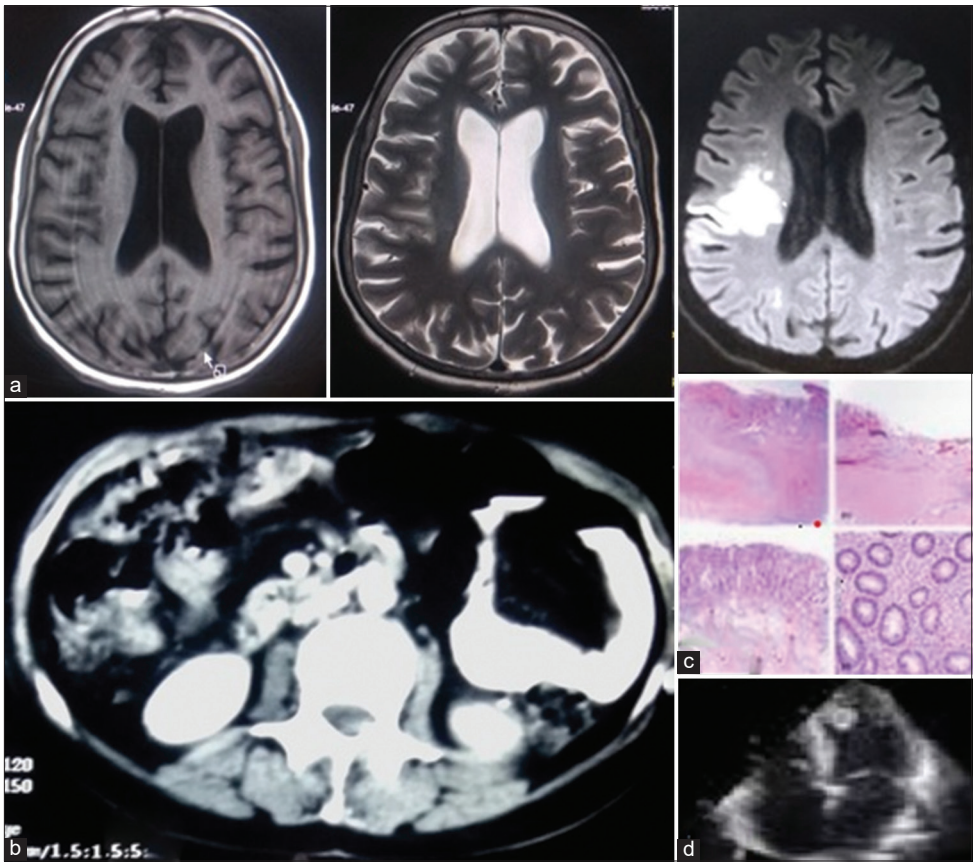

Figure 1: (a) Images of MRI brain of the patient with T1, T2, and DWI sequences. DWI showing acute infarct in right middle cerebral artery territory; (b) Images of Contrast CT Abdomen showing thick edematous bowel loops; (c) Transmural involvement, noncaseating, non-confluent granulomas, deep fissuring into muscularis propria with strictures, cryptitis, and crypt abscess, serosal vascular congestion; (d) 2D-Echo showing clot in left ventricle

Surgery for CD can be complicated by an enhanced inflammatory response as measured by CRP.[13] Other risk factors for arterial stroke as reported in previous studies in active CD include Vitamin B6 deficiency, leading to hyperhomocysteinemia and iron deficiency anemia.[14,15] Thrombocytopenia and anemia have been observed as potential risk factor for stroke in laboratory analysis.[16]

Our patient developed acute ischemic stroke in the right anterior circulation on the fourteenth postoperative day, and this was associated with heightened CRP level than preoperative phase. An active disease with pancolitis was present and it was evidenced from the post-operative clinical status, raised ESR, leukocytosis, high CRP, thrombocytosis, raised IPF, hyperhomocysteinemia as well as iron deficiency anemia.

All stages of the coagulation cascade are thought to be operative in the pathogenesis of IBD.[17] This is the basis for the use of heparin in IBD with thromboembolic complications as well as decreased incidence of thromboembolic complications in patients with von Willebrand disease and hemophilia.[18] Platelet leukocyte aggregates (PLAs) are increased in subjects with IBD compared to healthy and inflammatory controls.[19] PLAs cause microinfarction and promote thrombus formation by increasing the production of tissue factor.[20]

MRI is the gold standard investigation for the assessment of cardiac mass.[21] We did contrast-enhanced cardiac MRI to exclude pseudothrombus-like cardiac tumors (myxoma or fibroma) and vegetations. There are no standard guidelines for the management of ischemic stroke in subjects with IBD. However, Simmons et al., said patients should be treated with aspirin within the first 24–48 h of stroke onset.[22,23]

Joshi et al., suggested all cases of stroke in subjects with IBD should be treated with aspirin and modification of atherosclerotic risk factors.[20] Prophylactic doses of LMWH are widely used in subjects with IBD if there is accelerated disease activity, evidence of gastrointestinal complications, during surgical intervention, or episodes of sepsis as recommended by the British Society of Gastroenterology.[24]

Anticoagulants to prevent further thrombotic episodes are controversial because of the risk of bleeding though patients have been treated with anticoagulants without bleeding.[25] Heparin induces activation of the fibrinolytic system.[26] The use of disease modifiers in CD in the perioperative period needs to be patient centric as a surgery carries the risk of infectious complications.[27]

Kwak et al., showed early immunomodulatory therapy is more effective than conventional therapy in inducing remission but not in preventing relapse.[28] We treated our patient with antiplatelets (aspirin), subcutaneous LMWH, albumin infusion, Vitamin B12, and folic acid supplementation. We intended to use immunomodulatory therapy in our subject, but the patient died with a rapid downhill course following an attack of fatal ventricular arrhythmia.

This case report highlights few things that are rare but important from the perspective of diagnosis to management. LV thrombus in our subject with CD is a rare occurrence. Moreover, cerebral arterial thromboembolic phenomenon seen in our patient is rare in comparison to the more common incidence of venous sinus thromboembolism in subjects with CD. Only three cases of cerebral arterial thromboembolic stroke with LV thrombus in subjects with CD have been reported so far. LV thrombus with normal LV ejection fraction is also uncommon and is very likely due to PLA rather than cardiac causes.

Limitations of the study

Platelet-leukocyte aggregation study could not be arranged in our case because of the lack of resources.

This is a single case report. Series of cases are required to draw conclusion about the management strategy.

CONCLUSION

Subjects with CD are susceptible to have LV thrombus even in the presence of normal LV ejection fraction and this may rarely be accompanied by thromboembolic ischemic stroke. Caution should be exercised in identifying the cardiac source of embolism in subjects with CD presenting with acute stroke. Further study is required to establish whether immunomodulatory and fibrinolytic therapy will be of benefit in the critical state.

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