Crohns disease with central nervous system vasculitis causing subarachnoid hemorrhage due to aneurysm and cerebral ischemic stroke

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Abstract

Cerebral vasculitis secondary to Crohn's disease (CD) seems to be a very rare phenomenon. We report a 39-year-old male who presented with headache, vomiting, and left-sided weakness in the known case of CD. Cross-sectional imaging (computed tomography and magnetic resonance imaging,) showed right gangliocapsular acute infarct with supraclinoid cistern subarachnoid hemorrhage (SAH). Cerebral digital substraction angiography (DSA) showed dilatation and narrowing of right distal internal carotid artery (ICA). Left ICA was chronically occluded. His inflammatory markers were significantly raised. Imaging features are suggestive of cerebral vasculitis. Arterial and venous infarcts due to thrombosis are known in CD. Our case presented with acute subarachnoid hemorrhage in supraclinoid cistern due to rupture of tiny aneurysm of perforator arteries causing SAH and infarction in right basal ganglia. Patient was treated conservatively with immunosuppression along with medical management of SAH.

Key Words

Aneurysm, cerebral ischemia, Crohn's disease, extra-intestinal manifestations, subarachnoid hemorrhage, vasculitis

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Introduction

Crohn's Disease (CD) is an idiopathic intestinal disorder of unknown cause.[1] Secondary vasculitis represents a rare extraintestinal manifestation of CD. Appropriate and prompt diagnosis is often delayed by uncertainties about the relationship of the vasculitis manifestation and CD.[2] Presentations may include headaches, hemiparesis, and intermittent loss of orientation.[3] Work-up can reveal elevated inflammatory markers, abnormal cerebral spinal fluid, and magnetic resonance imaging (MRI) abnormalities. However, these findings are often variable mimicking other primary central nervous system (CNS) processes.[4] As in this case, it is imperative to diagnose Crohn's-associated vasculitis early. As a result, early immunosuppresive therapy may be started to prevent further neurologic compromise.

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Case Report

A 39-year-old male who presented with acute onset headache, vomiting, and left-sided weakness. There was no sensory dysfunction, unconsciousness, or seizures. No risk factors like hypertension, diabetes, or dyslipidemia.

One year back, patient presented with acute intestinal perforation. He had undergone emergency laparatomy. Right colectomy performed along with resection of terminal ileum. CD was diagnosed on histopathology and patient started on steroids.

Physical examination revealed reduced muscle power (left upper limb 0/5, left lower limb 2/5), increased muscle tone, reflexes 3/4 on left side while normal on right side. Mental status testing and cranial nerves were intact.

Laboratory investigation revealed significantly raised erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP).

Imaging findings

Computed tomography (CT) and MRI of the brain showed right gangliocapsular acute infarct [Figure 1]. There was acute subarachnoid hemorrhage (SAH) seen in the supraclinoid cistern on right side [Figure 2]. On magnetic resonance

angiography (MRA), right ICA supraclinoid segment showed dilatation, whereas left ICA showed occlusion in supraclinoid segment with diffuse narrowing. A1 segment of right Anterior cerebral artery ACA is dilated [Figure 3].

Cerebral digital substraction angiography (DSA) showed dilatation of supraclinoid right ICA, fusiform dilation of A1 segment of right ACA, tiny aneurysm on one of the medial lenticulostriate artery near its origin from A1 segment of right ACA, and non-visualization of its distal segment due to severe vasospasm from SAH (causing acute right gangliocapsular infarction). Left anterior cerebral artery (ACA) and middle cerebral artery (MCA) were opacified across Acom [Figure 4a]. Left ICA was chronically occluded in supraclinoid segment [Figure 4b]. There were bridging pial collaterals from left ACA reforming left MCA cortical branches. B/L carotid bifurcations were normal.

He was managed conservatively for SAH with nimodipine (cerebral vasodilators), Tab. paracetamol for headache, and Tab. Atorvastatin. Systemic steroid therapy was continued as before.

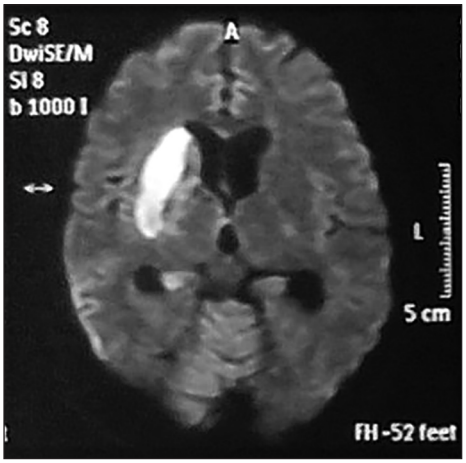

Figure 1: Magnetic resonance imaging (MRI) diffusion weighted imaging showing acute infarct in right gangliocapsular region

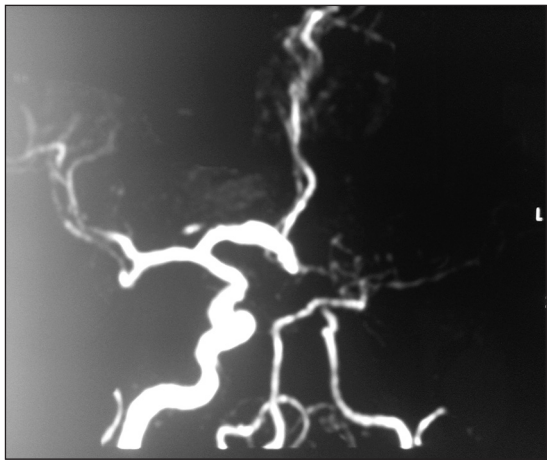

Figure 3: Magnetic resonance (MR) angiography of circle of willis showing right ICA supraclinoid segment dilatation. Left ICA occlusion in supraclinoid segment with diffuse narrowing. A1 segment of right ACA is dilated with a tiny aneurysm from medial lenticulostriate branch

During the hospital stay, neurological symptoms gradually improved. On discharge, after 3 weeks, he started on aspirin (75 mg). Nimodipine was stopped, Atorvastatin and steroid were continued. On 3-month follow-up, there was no new symptom seen, but unfortunately patient expired after 3 months due to reperforation of the bowel leading to severe hemoperitoneum and shock.

Discussion

Etiopathogenesis

Increased platelet activation leading to multifocal micro infarction in mesenteric vasculature is the primary event in the pathogenesis of CD.[5] This and disorders of factor V, Viii, fibrinogen, and decreased antithrombin iii levels results in a hypercoagulable state, which may be responsible for thromboembolic episodes leading to various neurological deficits.[6] Alternative explanations include the presence of circulating immune complexes[7] as a consequence of vasculitis,[8] associated auto-antibodies including anti-neutrophilic cytoplasmic (ANCA) and antiphospholipid antibodies[9,10] or prolonged dehydration and immobilization secondary to active disease.[11] Cerebral venous and arterial

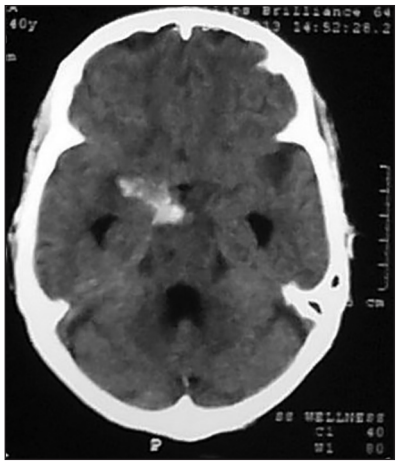

Figure 2: Plain computed tomography (CT) scan of brain showing subarachnoid hemorrhage in supraclinoid cistern

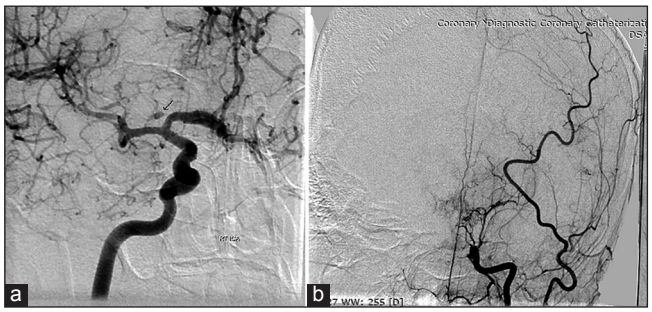

Figure 4: (a) Digital substraction angiography (DSA) showing dilatation of supraclinoid right ICA, fusiform dilation of A1 segment of right ACA, tiny aneurysm on one of the medial lenticulostriate artery near its origin from A1 segment of right ACA and non-visualization of its distal segment due to severe vasospasm from subarachnoid hemorrhage (SAH) (b) showing left ICA was chronically occluded in supraclinoid segment with bridging pial collaterals

events have been described. Cerebral arterial occlusions tend to occur in larger vessels including the internal carotid,[12] retinal,[13] and middle cerebral arteries,[14] as well as affecting branches of the posterior circulation.[15] Most patients have active CD at the time of presentation. Ischemic optic neuropathy has been described in CD implicating involvement of the posterior ciliary arteries.[16] Myelopathy[6] and multiple sclerosis has been described in CD.[17]

Hemorrhagic disorders unrelated to venous thrombosis or to cerebral vasculitis[18] are rarely described in inflammatory bowel disease. There are two pathologically verified cases of acute hemorrhagic leukoencephalitis (AHL) with ulcerative colitis (UC) [19] but not with CD. Disseminated intravascular coagulation (DIC) with generalized and focal cerebral and systemic manifestations was described in four patients with CD and one with UC.[20]

Incidence

In comparision with many of the systemic manifestation of Inflammatory Bowel Disease (IBD), neurologic involvement occurs less frequently in CD. Lossos and colleagues reported out of 638 patients, cerebrovascular disorders occurred in two UC and two CD patients (< 0.5%).[21] Talbot and colleagues reviewed the records of 7,199 patients with UC or CD and noted the presence of whole body vascular complications in 1.3% patients, out of which less than 0.15% patients develop cerebrovascular events.[22] For uncertain reasons, vascular complications occur less frequently in CD than UC[23] And to our knowledge, there is no reported case of Subarachnoid hemorrhage due to aneurysm in CD. Also, extraintestinal manifestation including cerebral vasculitis occur more often in female CD than in male patients,[24] as our case is a male patients which is also uncommon.

Clinical and imaging findings

Neurologically, CD patients present with different manifestations like cerebrovascular disease, myelopathy, peripheral neuropathy, myopathy.[21]

On cross-sectional imaging, multiple lesions are detected like infarct, ischemic changes, vascular irregularities, vascular occlusions. On DSA, multiple stenosis with vascular irregularities and occlusions are seen which are compatible with cerebral vasculities.[3]

Cerebrovascular complications in CD may emerge in a variety of forms. Large artery disease, such as carotid artery stenosis, with consequent cerebral infarction has been reported in individual with CD.[25]

To our knowledge, SAH due to aneurysm has not been reported in CD patients till date.

Differential diagnosis mainly includes

1. Arteriosclerotic cerebrovascular disease[26]
2. Other systemic vasculitides affecting CNS[27]
3. Primary CNS vasculitis[4]
4. Multiple sclerosis[4]

The arteriosclerotic cerebrovascular disease is ruled based on normal carotid bifurcation, normal ICA origins with no further evidence of arteriosclerotic disease like normal arch, 39 years of age.[26]

Other systemic vasculitis affecting CNS: Vasculitides constitute a heterogenous group of diseases characterized by inflammation and necrosis of the blood vessel wall. According to the Chapel Hill Consensus Conference (CHCC), the primary systemic vasculitides may be classified into three main groups: those affecting predominantly large-sized vessels, medium-, and small-sized vessels. Large vessels including the aorta are affected in giant cell arteritis (GCA), Takayasu arteritis. Medium vessels are affected in classic polyarteritis nodosa (PAN), Kawasaki disease. All other systemic vasculitides affect small vessels. It may be separated in those with antineutrophil cytoplasmic antibodies (ANCA) positive and negative. ANCA-positive vasculitides include Wegeners granulomatosis, Churg-Strauss syndrome, microscopic polyarteritis. ANCA-negative vasculitides include cryoglobulinemic vasculitis, Behcet syndrome. Immune complex deposits are seen in the vasculitic variants of systemic lupus erythematosus (SLE) and rheumatoid arthritis, and with cryoglobulinemic angiitis.[27]

Laboratory findings suggestive of a systemic vasculitis include an acute inflammatory response with raised ESR and increased values of CRP. Anemia, thrombocytosis, elevated liver enzymes, and low complement are frequent associated findings. Complement consumption preferentially is present in vasculitides associated with immune complexes. If a cerebral manifestation occurs in the course of a systemic vasculitis, an acute inflammatory response has to be expected. In PACNS, serum findings usually are normal, but CSF studies reveal inflammatory findings. These include a mild lymphomonocytic pleocytosis or protein elevation in more than 90% of patients. Laboratory tests in suspected vasculitis should search for systemic inflammation including specific antibodies.[27]

Imaging techniques play a crucial role in securing the diagnosis of a vasculitis, and in demonstrating cerebral involvement. In large-vessel angiitis, conventional DSA is the gold standard for the demonstration of vessel stenoses or aneurysms.[28] MRI performed with and without contrast medium is the investigation of choice to detect and monitor cerebral involvement.[29] Measurements should include ADC-maps, diffusion and perfusion measurements, and gradient echo sequences. In cerebral vasculitis, both ischemic and hemorrhagic lesions of different ages as well as findings of focal or diffuse inflammation are observed.[30] Color duplex sonography, computerized tomography angiography (CTA), and MRI with MRA may show vessel wall alterations when the lumen is still unaffected on angiography. Also, 18-fluorodeoxyglucose positron emission tomography (PET) is very sensitive in revealing inflamed vessels.[31]

Primary angiitis of the CNS (PACNS). The diagnostic criteria for the diagnosis of primary angiitis of the CNS are[32]

1. Acquired neurological deficit unexplained after complete evaluation.
2. Diagnostic cerebral angiogram with narrowing of vessels, areas of dilation and/or beaded vessel appearance, displacement of vessels or vessels occlusions.
3. No evidence of systemic vasculitis or any other condition that mimic the angiogram findings.

For diagnosing multiple sclerosis, the 2010 McDonald criteria for diagnosis of multiple sclerosis should be fulfilled.[33]

Treatment and prognosis

Ischemic stroke is managed conservatively with anti-coagulants, anti-platelets, and statins.[34] SAH due to aneurysm in CD is not reported till date. However, we decided to manage conservatively as tiny aneurysm was inaccessible either by endovascular or open micro-neurosurgical access. So we managed with nimodipine to prevent spasm and paracetamol for the headache.

Conclusion

Although rare, cerebral arterial and venous infarcts due to thrombosis have been reported in the literature. Petechial hemorrhages related to these infarcts have also been reported; however, SAH due to aneurysm has not been reported so far. CD has significant female prevalence. Cerebro-vascular complications are also known to occur more commonly in females. Our case is unique in this respect too with male patient of CD presenting with SAH due to aneurysm, unrelated to thrombo-embolism.

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