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Case report

Amnesia and brain atrophy with focal white matter lesion in a 30-year old male with Crohn's disease

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SUMMARY

Central nervous system (CNS) manifestations in Crohn's disease (CD) have been well recognized over the years and have been regarded either as an extraintestinal disease manifestation or as therapeutic side effects. Focal white matter lesions in CD patients have been demonstrated using magnetic resonance imaging (MRI).

A 30-year-old patient with small bowel Crohn's disease diagnosed 3 years ago came to the outpatient clinic complaining of amnesia in relation to familiar names, for the last 2 years. Physical and neurologic examination were both negative. Laboratory tests were within normal limits. Anticardiolipin antibody, lupus anticoagulant, the widely known list of risk factors for ischemic stroke, possible sources of emboli such as carotids and heart, deficiencies of protein C, activated protein C, protein S and antithrombin III leading to hypercoagulation were negative. Circulating immunocomplexes and p-antineutrophil cytoplasm autoantibodies (p-ANCA) were not detected.Neurological examination revealed amnesia and brain magnetic resonance images (MRI) showed cortical atrophy and a focal lesion in the paraventricular deep white matter of the left frontal lobe.

This is, to our knowledge the first report of a young CD patient with amnesia and MRI demonstrable brain atrophy with focal white matter lesion.

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INTRODUCTION

Central nervous system (CNS) manifestations in Crohn's disease (CD) have been well recognized over the years.[1,2] In a series of 253 CD patients 84 of them had evidence of neurologic or neuropsychiatric entities.[3] These entities have so far been regarded either as extraintestinal disease manifestations or as therapeutic side effects.[2] The reripheral nervous system is rarely affected in CD[3] and it is noteworthy that patients with extensive ulcerative colitis (UC), but not with CD, have an increased risk of brain cancer.[4]

Brain focal white matter lesions in CD patients have been demonstrated using magnetic resonance imaging (MRI)[5]. No correlation of these lesions with multiple sclerosis (MS) or other neuropsychiatric disorders has so far been established.

Herein we present a 30-year-old patient with CD and amnesia who was diagnosed with brain atrophy and a focal deep white matter lesion.

Abbreviations used in the text:

CNS *= central nervous system*

MRI *= magnetic resonance imaging*

IBD *= inflammatory bowel disease*

CD *= Crohn's disease*

UC *= ulcerative colitis*

MS *= multiple sclerosis*

TPN *= total parenteral nutrition*

CASE REPORT

A 30-year-old patient diagnosed 3 years ago with small bowel Crohn's disease came to the outpatient clinic complaining of amnesia, for the last 2 years. The amnesia had to do with names of familiar persons and had worsened during the last couple of months. The patient had never before been to a psychiatrist or a neurologist and his family history was negative for any such kind of diseases.

Medical treatment included sulfasalazine P.O. 3g/day, methylprednizolone 8mg P.O. every second day and azathioprine 100mg/day P.O. In the last year chimeric anti-TNFa monoclonal antibody (Remicade) intravenous infusions had been added. Because of low-normal vitamin B_{12} and folic acid serum levels, continuous supplementation with these elements was added last year. The patient never received total parenteral nutrition (TPN), never smoked and was not an alcohol misuser.

The patient had never had severe disease relapses and at the time he visited the outpatient clinic the disease was in complete clinical and endoscopic remission. Moreover, no apparent disease extraintestinal manifestations were evident.

Physical examination did not reveal anything of interest. Laboratory tests, including peripheral blood test, immunohistochemistry and biochemical analysis were within normal limits. Possible sources of emboli, such as carotids and heart were excluded. Neurological examination revealed amnesia but otherwise was unremarkable. Plantar reflexes were downgoing, no signs of cerebral dysfunction and no sensory disturbances were evident. In the Mini Mental Scale Examination (M.M.S.E.) the overall score was 29 from 30.

Brain magnetic resonance imaging (MRI) was performed using conventional spin echo, T1-weighted sequence, Turbo spin echo T2-weighted sequence and Inversion Recovery Turbo spin echo sequence, T1-weighted in three planes. MRI clearly showed cortical atrophy (Figure 1) and also a focal white matter lesion (foci) in the deep white matter (Figure 2). Conventional spin echo T1, pre or post contrast medium sequences did not show the focal lesion. The patient is being followed up with memory tests once a year and with brain MRI every 4 years.

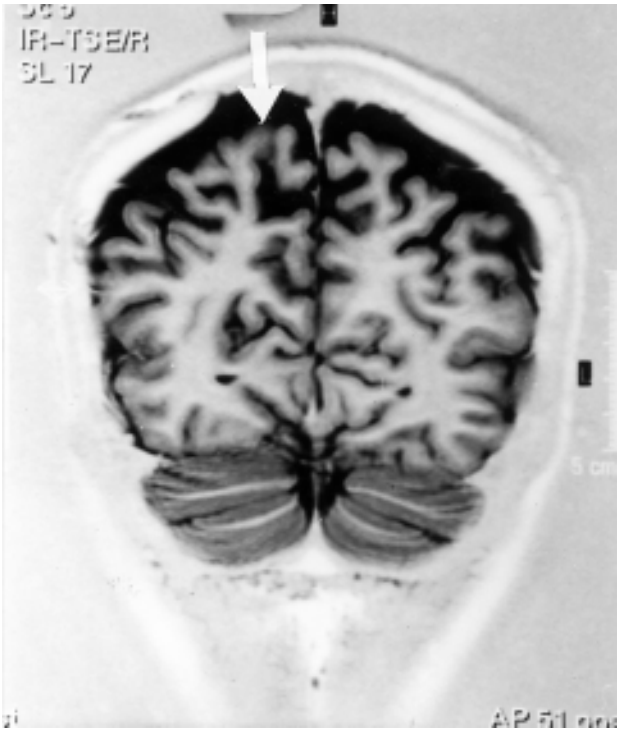

Figure 1. Cortical atrophy (arrow) in MRI (T1 weighted image, coronal plane) in a 30-year-old patient with Crohn's disease and amnesia.

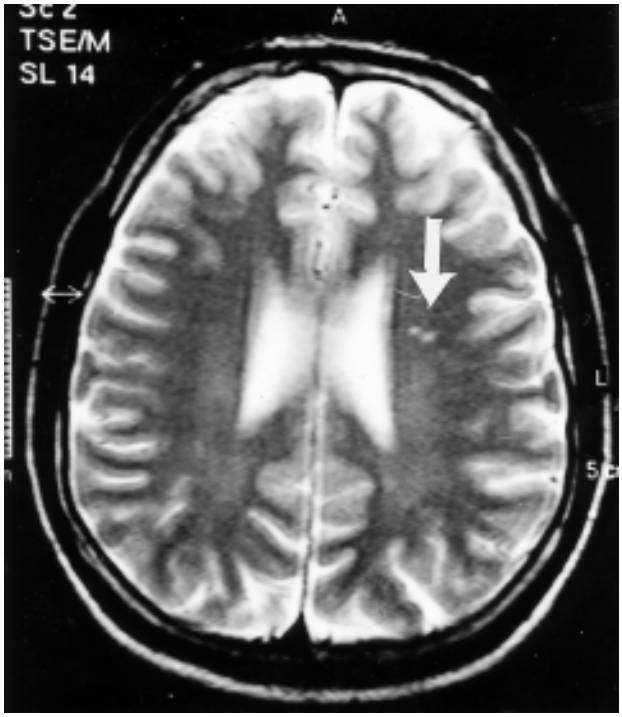

Figure 2. White matter focal lesion (foci) (arrow) in MRI (T2 weighted sequence, axial image) in a 30-year-old patient with Crohn's disease and amnesia.

DISCUSSION

The reported CNS manifestations in CD patients include symptomatic cerebral vasculitis[6], acute brain ischemia (stroke) following arterial or venous thrombosis,[7-9] subacute combined degeneration of the spinal cord due to folic acid and vitamin B_{12} malabsorption, leading to hyperhomocystinemia in one case,[10] and several CNS deficits. These deficits include psychiatric disorders, major depression being the most important and focal neurological deficits[1]. During long term total parenteral nutrition (TPN) progressive encephalopathy, possibly related to selenium deficiency[11] and signal abnormalities on MRI in the basal ganglia in patients with an increased manganese during long term TPN are well known.[12] Non-alcoholic Wernicke encephalopathy and beri-beri due to thiamine deficiency have occasionally been mentioned.[13]

Chronic portal-systemic encephalopathy after ileostomy and colonic resection,[14] nonfamilial Turcot's syndrome associated with CD and duodenal ulcer[15] and fatal reno-cerebral oxalosis induced by xylitol[16] have also been also reported. Sulfasalazine associated encephalopathy, suggesting a hypersensitivity reaction to sulfasalazine or one of its metabolites has been reported, but for ethical reasons no rechallenge was performed.[17,18]

Sulfasalazine induced encephalopathy is diagnosed during the first days or weeks of drug administration and usually presents with asterixis, flapping tremor, confusion or even delirium and brain imaging techniques reveal extensive white matter lesions rather than white matter foci as in this case. Infliximab CNS-related symptoms were not apparent in this patient during the almost twelve-month infusion program and this drug, as well as the whole therapy, continues to date.

Optic nerve involvement in CD includes optic neuropathy and severe bilateral retinal arteritis and phlebitis.[19,20] The lack of clear evidence about the relationship of CD with multiple sclerosis (MS) does not allow combining the clinical phenotype of these diseases.[21] Nonspecific symptoms such as headaches, seizures and pseudotumor cerebri can also be added to this long list.[1,22]

Central neurological disorders could either be part of extraintestinal symptoms in CD or precede diagnosis.[1,2] It also seems that their first manifestation does not go along with disease exacerbation. Aetiopathogenesis of these conditions is not always clear and several hypotheses have so far been made regarding altered CNS vascularization or tissue damage. An autoimmune phenomenon affecting small vessels of the central and peripheral nerves has also been suggested as causing these complications.[23]

Amnesia has never previously been reported in CD, and in our case could be the result of this clearly shown cortical atrophy. The differential diagnosis of a patient presenting with dementing illness includes dementia of the Alzheimer type, Pick's disease, diffuse Lewy body disease, Huntington's disease, multi-infarct dementia, hydrocephalus, neurosyphilis viral encephalitides and HIV-related dementia. Rare demyelinating diseases at an advanced stage may also present with intellectual dysfunction such as progressive multifocal leucoencephalopathy, adrenal leukodystrophy, metachromatic leukodystrophy, Canavan's disease and others. Finally systemic diseases may present with cerebral pathology such as vitamin B_{12} deficiency, chronic metabolic or endocrine diseases and substance abuse. The history, physical examination, neuroradiologic findings and laboratory tests easily exclude most of the above conditions in our patient.

On the other hand the role of these white matter lesions remain obscure in CD patients. The differential diagnosis of lesions presenting with increased signal in T2-weighed MRI of the brain, include among others, demyelinating disease of the CNS, ischemic lesions, and infectious causes. The history excludes conditions that cause microvascular disease such as hypertension or diabetes. The history, physical examination and laboratory work up similarly does not show evidence of systemic or localized infection. In the specific age group (20's to 30's) the commonest cause of this radiologic picture would be multiple sclerosis. Indeed, a higher incidence of multiple sclerosis has been reported in patients with a coexisting autoimmune disease, including inflammatory bowel disease[25]. In addition, CD was diagnosed in a patient with known multiple sclerosis[26]. It has been reported that the concurrence of MS and IBD was greater than expected but, although MS and IBD may share common predisposing factors, not enough information is available to speculate about possible aetiopathogenetic mechanisms.[27] However, the history of the patient is negative for attacks with neurologic signs and/or symptoms such as optic neuritis, hemiparesis, diplopia, etc, and the phyical examination did not reveal any focal neurologic signs and neyrophysiologic testing, including somatosensory evoked potentials, was normal. In any case, it is exceedingly rare for multiple sclerosis to manifest itself as a dementia with no other associated abnormalities.

There is a paucity of controlled trials assessing the impact of mind, CNS and neuromodulation on the over-

lying active immune response in intestinal mucosa.[28] Bowel-brain interactions in this inflammatory process deserve closer attention, which may highlight new therapeutic interventions in several groups of patients who may respond to adjunctive treatment for inflammatory bowel disease (IBD) such as hypnosis, meditation, neuropeptide receptor modulation and cortisone-releasing factor (CRF) modulation.The true clinical impact of these MRI abnormal signals in relation to disease phenotype has yet to be clarified in inflammatory bowel disease (IBD). This single reported case of a young CD patient with pure amnesia may be a unique opportunity to increase emphasis and focus on disease outcome and quality of life.

This is, to our knowledge, the first report of a young CD patient with amnesia and MRI demonstrable brain atrophy with focal white matter lesion.

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