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CASE REPORT

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Microscopic polyangiitis: an incidental finding in a patient with stroke

Abubakar Tauseef[a], Muhammad Sohaib Asghar[a], Mariam Amir[a], Maryam Zafar[a], Ayesha Anum[a], Haris Alvi[b], Mustafa Dawood[c], Uzma Rasheed[d], Mohammed Akram[d] and Nisar Ahmed[d]

[a]Internal Medicine, Dow University Hospital, DUHS, Karachi, Pakistan; [b]Medicine, Dow University Hospital, DUHS, Karachi, Pakistan; [c]Internal Medicine, Greater Baltimore Medical Center, Towson, MD, USA; [d]Internal Medicine, Liaquat National Hospital and Medical College, Karachi, Pakistan

ABSTRACT

Microscopic polyangiitis (MPA) is a primary systemic vasculitis characterized by inflammation of small-sized vessels associated with the presence of anti-neutrophilic cytoplasmic antibodies. We report a case of a 39-year-old female diagnosed with microscopic polyangiitis as an incidental finding who presented with signs and symptoms of a stroke at a young age. Usually, it presents with fever, malaise, skin rash, weight loss, mononeuritis multiplex, and arthralgia/myalgia. Very rarely, it can involve meninges to cause meningeal vasculitis which can present as a febrile seizure. The most frequent neurological manifestation is peripheral neuropathy. Cerebral infarction or hemorrhage as an isolated finding is very rarely observed in the patient with MPA as was seen in our patient.

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Microscopic; incidental; finding; stroke; patient

1. Introduction

Microscopic polyangiitis (MPA) associated with the presence of anti-neutrophilic cytoplasmic autoantibodies first defined in 1994 in Chapel Hill Consensus, is an autoimmune multisystem disease which includes renal symptoms, mononeuritis multiplex, arthritis, diffuse alveolar hemorrhages, hemoptysis, hematuria, weight loss, proteinuria, skin rash, gastrointestinal bleeding, seizures, and myalgias. ANCA associated with microscopic polyangiitis has a peri-nucleic staining pattern P-ANCA caused by autoantibodies against myeloperoxidase. The absence of circulating ANCA, however, does not exclude the diagnosis. ANCA antibodies can also be positive secondary to exposure to hydralazine or propylthiouracil, in some inflammatory conditions, various infections and cystic fibrosis.

2. Case presentation

A 39-year-old obese female of Asian descent with a family history of hypertension and past medical history of diabetes mellitus, hypertension and recurrent abortions presented to us with complaints of left foot drop with numbness and tingling, rash on the bilateral forearm, legs and face with multiple joint pain more pronounced in knees and small joints of hands with morning stiffness of 2–3 minutes which was followed by drooping of right eyelid and deviation of angle of mouth after 2 days. She denied symptoms of asthma, allergy, cough, fever, alopecia, dry eyes, painless vision loss, oral ulcers, hemoptysis, or hematuria. Empirically patient was started on aspirin, folic acid, vitamin B12 and paracetamol for joint pain and other symptoms of numbness and tingling.

The physical examination was unremarkable except for a steppage gait, drooping of the right eyelid, angle of mouth deviated towards the right with facial muscle weakness on the right side. In the left lower limb, there was tenderness at the calf, the power of dorsiflexion on foot was 1/5. Ankle and knee reflexes were brisk on the left side while normal on the right side. Sensations were intact bilaterally. The laboratory findings were hemoglobin: 10.7 mg/dl, total leukocyte count: 10.2 cells/microliter, C-reactive protein (CRP): 105.7 mg/l, erythrocyte sedimentation rate (ESR): 86 mm/hour, Complement levels C3: 0.4 mg/dl, C4: 1.49 mg/dl, random blood sugar of 165 mg/dl and HBA1C of 6.0%. Urine detailed report showed moderate proteinuria (+2), while the rest of the labs were within normal limits. Magnetic resonance imaging (MRI) of the brain was done which showed multiple abnormal signal intensity areas noted in the subcortical white matter on the left side which appear isointense on T1, hyperintense on T2 and FLAIR (Figures 1 and 2). The differential considerations included microscopic polyangiitis, Eosinophilic granulomatosis with polyangiitis, multiple sclerosis, diabetic neuropathy, and antiphospholipid syndrome with systemic lupus erythematosus. Based on her history, examination and early onset of stroke, her antineutrophil cytoplasmic antibodies (ANCA) were

CONTACT Abubakar Tauseef abubakartauseef93@gmail.com Dow University Hospital, DUHS

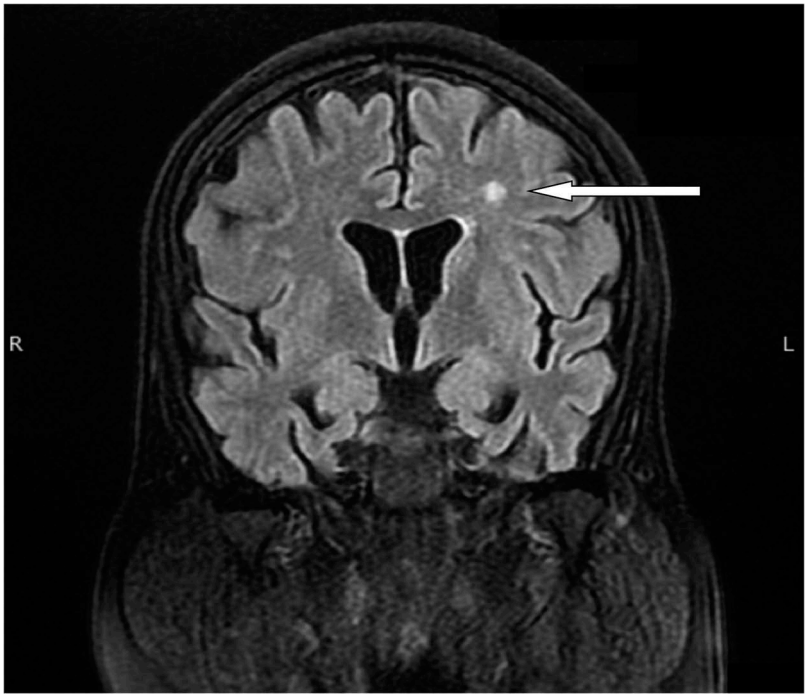

Figure 1. Magnetic resonance imaging of brain (T2) showing abnormal signal intensities.

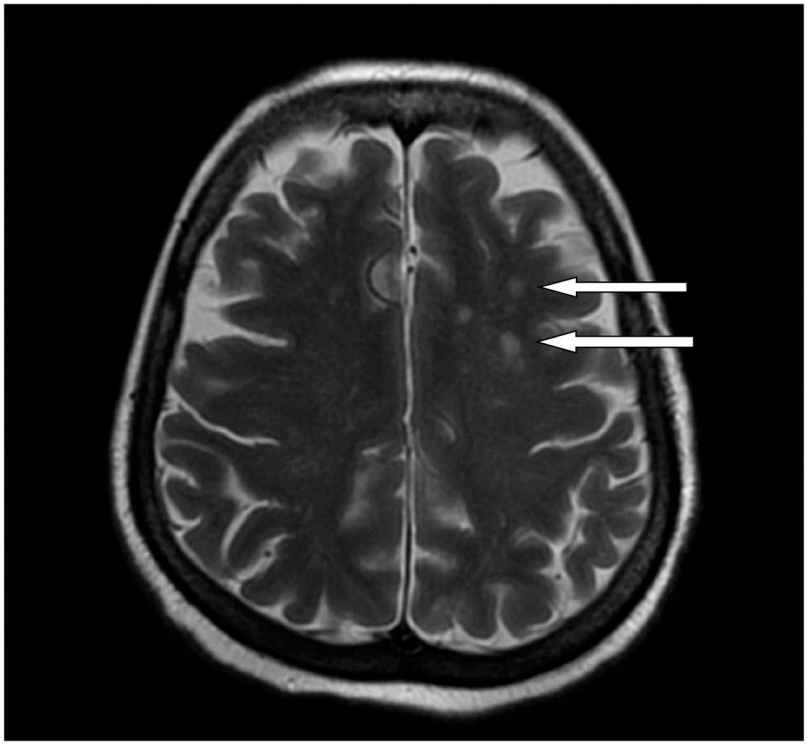

Figure 2. Magnetic resonance imaging of brain (FLAIR) showing abnormal signal intensities.

investigated. Titers of C-ANCA/PR-3 ANCA (Proteinase-3) were 1.4 and titers of P-ANCA/MPO ANCA (Myeloperoxidase) was 58.2 while the rest of the autoimmune workup including Anti-nuclear antibody, Anti-double stranded DNA antibody, Anti-smooth muscle antibody, Anti-smith antibody, Anti-Cardiolipin IgG and IgM, Anti beta-2 glycoprotein IgG and IgM, and Lupus anticoagulant all were negative.

The patient was diagnosed with P-ANCA positive microscopic polyangiitis as an incidental finding in an obese female with a stroke. Sural nerve biopsy was carried out which revealed nerve bundle fibers showing mild inflammatory cell infiltrate comprising lymphocytes which are positive on immune-histochemical stain CD3. No other biopsies were done in this patient. She was started on corticosteroids in the induction phase, followed by a maintenance phase then

cyclophosphamide with Mesna was given. The patient was scheduled for physiotherapy and followed up in an ambulatory setting on a two-weekly basis.

3. Discussion

Friedrich Wohlwill in 1923 on observing two patients coined a term of "microscopic form of periarteritis nodosa", which was distinct from classical polyarteritis nodosa. This name was further replaced by the term 'microscopic polyangiitis (MPA)' in 1994 in Chapel Hill Consensus Conference. MPA is an idiopathic autoimmune primary systemic vasculitis characterized by inflammation of the small-sized blood vessels and the presence of circulating anti-neutrophilic cytoplasmic antibodies (ANCA). As ANCA is frequently seen in patients with MPA, it is often classified as a form of ANCA-associated vasculitis, an important subset of the primary systemic vasculitis that includes Wegener's granulomatosis (WG), Churg-Strauss syndrome (CSS), and renal-limited vasculitis in addition to MPA [1].

MPA is a multi-systemic disease in which renal symptoms are frequent, but the disease is also associated with general symptoms including arthritis, mono-neuritis multiplex, and other manifestations that are also seen in various vasculitis [2]. The rarity of abnormal angiogram findings and the high frequency of P-ANCA are characteristic of MPA. In most cases, the outcome is comparable with those of other systemic vasculitis, but relapses are frequently observed in patients with MPA [2].

The pathogenesis of MPA is usually explained in the literature in two steps [3–5]. In the first step, neutrophils are primed by exposure to low-levels of pro-inflammatory cytokines, such as interleukin-1 or tumor necrosis factor-α [3]. This process leads to surface expression of myeloperoxidase, followed by adherence of neutrophils to the endothelial surface of blood vessels or glomeruli. In the second step, neutrophils are activated by interaction with MPO-ANCA, either through binding of its substrate [4] or interaction with Fc receptors of the neutrophil [5]. MPA usually manifest with signs of kidney inflammation including proteinuria or hematuria (seen in 80% of patients), weight loss (seen in greater than 70% of patients), skin rash (seen in greater than 60% of the patients), signs of nerve damage (seen in greater than 60% of the patients) and on and off fever (seen in up to 55% of the patients). In addition, MPA can also present as gastrointestinal bleeding, abdominal pain, seizures, arthralgia, myalgias and rarely testicular pain [6]. In patients having MPA, the most common kidney manifestation is rapidly progressive glomerulonephritis (RPGN) reported in 80–100% of patients [2,6], clinically ranging from asymptomatic urinary sediment to end-stage renal disease [7].

In MPA patients, pulmonary involvement can be seen in 25–55% of the cases. The classic pulmonary manifestation of MPA is diffuse alveolar hemorrhage [8,9] which usually present with dyspnoea, cough, hemoptysis, and pleuritic chest pain [10]. Neurologic involvement in MPA is quite common, observed in 37–72% of patients [2,11,12]. Among neurological manifestations, Peripheral neuropathy occurs more frequently than central nervous system involvement. Necrotizing vasculitis can be seen on sural nerve biopsy in up to 80% of affected patients as was seen in our patient, while nerve conduction studies typically show acute axonopathy [13]. Some studies suggest that relapse rates of peripheral neuropathy in MPA patients are close to the bottom line [13,14]. Central nervous system involvement is observed in only 17% of the cases ranging from patchy meningitis [15] to cerebral hemorrhage or infarction [11,16]. Cerebral infarction or hemorrhage as an isolated finding is very rarely observed in the patient with MPA as was seen in our patient [16]. MPA diagnosis is mostly clinical but ANCA antibodies are used to support the diagnosis [2,7], the absence of circulating ANCA does not exclude this diagnosis. ANCA associated with MPA generally has a perinuclear staining pattern (P-ANCA) caused by antibodies against myeloperoxidase (MPO-ANCA), which can be detected by using enzyme-linked immunoassays (ELISA) technique. ANCA antibodies can also become positive in other conditions like inflammatory diseases [17], drug induced ANCA-associated vasculitis (secondary to exposure to hydralazine or propylthiouracil) [18], cystic fibrosis [19], and various infections [20,21].

Our case describes a 39-year-old female with a past medical history of diabetes mellitus, hypertension and recurrent abortions who presented to us with the complaints of left foot drop, rash, joint pain more in knees and small joint of hands, followed by drooping of eyelid and deviation of angle of mouth after 2 days. Examination revealed steppage gait, facial muscle weakness of right side and calf tenderness. Laboratory tests included increase Erythrocyte sedimentation rate, increased C-reactive protein and positive P ANCA-anti myeloperoxidase (MPO). On Sural nerve biopsy nerve bundle fibers showing inflammatory cell infiltrate with lymphocyte positive on immune-histochemical stain CD3. All these features were suggestive of non-granulomatous polyangiitis. MRI brain showed multiple abnormal

signals in the subcortical areas of the left side of the brain, suggestive of stroke in a middle-aged female patient due to fragile vessels, because of the underlying vasculitis.

Treatment of microscopic polyangiitis (MPA) is principally with corticosteroids and other immunosuppressive agents like cyclophosphamide and consists of induction and maintenance of remission. The treatment of relapsed MPA is the same as that of remission induction. For the treatment of refractory disease Intravenous Immunoglobulin is used [22]. To monitor disease activity the level of ANCA can be monitored. However, ANCA levels do not correlate consistently with disease activity. In one study, ANCA levels became undetectable in 83% of patients after treatment; however, ANCA levels increased in 57% of patients at a mean period of 7–8 weeks prior to relapse. The reappearance of anti-MPO antibodies has positive predictive value for relapse respectively [23].

In **conclusion**, we describe a patient with Microscopic Polyangiitis (MPO) and involvement of the central nervous system vessels leading to ischemic stroke in a young female. All the laboratory investigations were in favor of a vasculitic phenomenon. Furthermore, peripheral nerve biopsy depicted non-specific vasculitic changes. The patient showed a rapid response with therapy and was scheduled for a follow-up with immunosuppressants and physiotherapy. So, we recommend that in a patient with suspected stroke at a younger age, the possibility of vasculitis should be ruled out as by doing this, we can pick the diagnosis at an earlier stage and the patient can be managed accordingly.

Disclosure statement

No potential conflict of interest was reported by the authors.

ORCID

Muhammad Sohaib Asghar http://orcid.org/0000-0001-6705-2030
Uzma Rasheed http://orcid.org/0000-0003-0596-7766

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