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What is This?
Immune-Complex Allergic Vasculitis in Association with the Development of Transverse Myelitis

A Case Report

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ABSTRACT

A severe vasculitis, probably therapy related, in a sixty-four-year-old man being treated for possible subacute bacterial endocarditis, was associated with the development of transverse myelitis. It is hypothesized that the vasculitis affected the small vessels to the spinal cord in the same way that systemic vasculitis can also cause a transverse myelitis.

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Introduction

Transverse myelitis is a disorder of spinal cord function in which both the sensory and motor systems are affected up to a particular level, with no gross local mechanical disturbance found. It has been estimated to have an incidence of about 4.6 cases per million per year. Various causes have been described, including most commonly a parainfectious origin, or in association with multiple sclerosis, or with spinal cord ischemia. Rarely it has been described in association with vasculitis secondary to collagen vascular disease or systemic arteritides. It has not, until now, been documented in relation to vasculitis occurring with an allergic reaction.

Case Report

A sixty-four-year-old man presented to another hospital with a two-day history of fever and general unwellness. Four months previously he had undergone mitral and aortic valve surgery with tilting disc artificial replacements; prior coronary angiography findings were normal. During his subsequent otherwise uneventful recovery he had received a pacemaker following increasingly bradycardic atrial fibrillation. Since discharge he had been well with administration of warfarin, digoxin, a calcium antagonist, an angiotensin converting enzyme inhibitor, and a loop diuretic. He was known to have hypertension in the past. There was no other relevant medical history, recent vaccination, or foreign travel. No one else in the family had been unwell; he had no pets; he was a nonsmoker.

At the current presentation to hospital he had a normal blood pressure and a temperature of 39°C, with no tachycardia. There was no lymphadenopathy. Examination of the chest revealed clear lungs, prosthetic heart sounds with murmurs of mild aortic and mitral regurgitation. He was known to have hypertension in the past. There was no other relevant medical history, recent vaccination, or foreign travel. No one else in the family had been unwell; he had no pets; he was a nonsmoker.

While awaiting the results of blood cultures, a provisional diagnosis of bacterial endocarditis was made; the patient was given intravenous antibiotics (gentamicin, rifampicin, and vancomycin) and admitted to the ward. In retrospect, the negative blood culture results and the unremarkable echocardiography make the diagnosis of endocarditis unlikely. Over ten days, the fever settled and the patient's symptoms improved somewhat. Over the initial few days after commencing the antibiotics, he developed diarrhea and pains in the lumbar region, although he had no history of back pain. Concurrent with these symptoms he noticed a peripheral palmar and plantar exfoliative erythema. This persisted and extended to the trunk so that the patient exhibited a generalized exanthematous rash. The administration of gentamicin was discontinued after fourteen days of therapy; despite this, over the subsequent fourteen days the rash became more prominent and hemorrhagic, typical of an immune-complex-mediated reaction (Figure 1).

Twenty-eight days after admission, the patient described a gradual onset of pain in the distribution of T10, followed by sensory loss in the same area. Over the next seven days he developed flaccid loss of motor power, up to and including hip movement. Reflexes in the upper limbs were reduced, those in the lower limbs were now completely absent, and the Babinski test was negative. Bladder and bowel function appeared normal. Electromyelography of the quadriceps and tibialis anterior muscles and nerve conduction studies yielded normal findings. Lumbar and thoracic radiography, CT, bone scan, and myelography were also unremarkable, excluding mechanical compression of the spinal clonal immunoglobulin M (IgM) gammopathy type lambda, with a high IgG (24.3 g/L). Tumor markers, including carcinoembryonic antigen, Ca19-9, and prostate-specific antigen, were normal. Blood and sputum cultures on numerous occasions were all negative for bacteria. Urine was negative for Bence-Jones protein; twenty-four-hour urine indicated a raised protein excretion. Chest radiography indicated evidence of the recent operation, a slightly enlarged heart with normal lung fields. An electrocardiogram showed atrial fibrillation at a rate of 80 bpm, not requiring pacing. Transthoracic echocardiography confirmed mild incompetence of both prosthetic valves. Abdominal ultrasound and computed tomography (CT) revealed splenomegalgy.
Figure 1.
Upper thigh, showing vasculitic rash, which was present over the entire trunk and limbs.

cord. Nuclear magnetic resonance studies were not undertaken because of the presence of the pacemaker.

The patient was transferred to this clinic. Further tests to elucidate the cause of the transverse myelitis were carried out. Blood tests taken at this time showed a slightly reduced hemoglobin (6.1 mmol/L), normal platelet count, and mild lymphocytosis (total white count 8.6 g/L; 50% mononuclear cells; 1% eosinophils). Bone marrow examination showed a substantial increase in white cell production with a left shift and a slight increase in megakaryocytopenia. There were increased plasma cells and some mature and immature eosinophils. There was a mildly raised urea (9.4 mmol/L) and creatinine (124 mmol/L). Urine microscopy demonstrated renal casts.

Examination of the cerebrospinal fluid showed a moderate lymphocytic pleocytosis with 3% IgG-producing lymphoid cells and a moderately raised protein and an increased level of normal IgG. Serology and cerebrospinal fluid titers for Legionella, Mycoplasma, Candida, syphilis, human immunodeficiency virus, hepatitis (A, B, C), Borellia burgdorferi, coxsackie virus A and B, herpes simplex, variella zoster, human herpes virus type 6, cytomegalovirus, and Epstein-Barr virus were all negative. In addition, the specific polymerase chain reactions for herpes simplex and varicella zoster from the cerebrovascular fluid were negative.

Autoantibodies, including antidouble-stranded DNA, antinuclear, anticytoplasmatic, antimitochondrial, and antismooth muscle, were undetectable or present at low undiagnostic titers. The complement protein C3 was decreased (0.38 g/L) and the IgE was minimally increased (0.226 IU/L). The initial monoclonal gammopathy was now a polyclonal gammopathy. Vitamin B12 and folate levels were within normal limits.

Antibiotic therapy was discontinued and the patient was treated with prednisolone, initially 100 mg per day, reducing to zero within a week. There was improvement in the sensory and motor function within the first twenty-four hours and complete recovery after ten days. Follow-up at five months indicated the IgE was still minimally raised, there were no residual neurologic deficits, there was no evidence of the skin rash, and the renal function was now normal.

Discussion

This patient had features typical of a transverse myelitis, which occurred during the course of a severe allergic reaction. Shortly after commencing antibiotic therapy, the patient exhibited a typical drug-related exanthematous rash together with evidence of involvement of other organs. Despite this, antibiotic therapy was continued for the presumed (and later excluded) subacute bacterial endocarditis. The rash worsened and, after a total of four weeks following initial admission,
became typical of immune-complex vasculitis. At the same time, he developed the clinical signs and symptoms of acute transverse myelitis.

During investigation of the cause of the transverse myelitis, mechanical compression was excluded; there was no evidence of multiple sclerosis; no severe metabolic disorders related to myelitis were detected; and no malignant disease was discovered. Ischemic insults from emboli to the spinal cord vessels are unlikely, for the patient was anticoagulated throughout. Myelitis can also be related to infection; it can occur during acute infection or as a parainfective or postinfective virus-induced immune myelitis. The pathology of myelitis in the context of infection is thought to relate either to direct cell lysis in the cord or to an abnormal host reaction to the virus or virus-associated antigens. From the findings in the cerebrospinal fluid in this case, previously described nonviral causes are unlikely; in addition, negative titers to viruses that have previously been described in association with myelitis were found. Lastly, the long time interval between onset of the potentially viral symptoms and the occurrence of the paraplegia (thirty days) makes a postinfectious cause unlikely.

It has been hypothesized that transverse myelitis in older patients could be related to arterial disease, but in our patient the normal-appearing coronary angiogram suggests that he did not have widespread atherosclerosis. Typically in transverse myelitis secondary to such a vascular cause as opposed to an infectious origin, the sensory level is at the high or middle thoracic region; at this level, blood supply to the spinal cord is more limited. In our patient the sensory level was at T10. Myelitis related to atherosclerotic disease also tends to be irreversible.

The patient in our case exhibited several signs of an extensive vasculitis related to a severe allergic reaction to antibiotics. Although not biopsied, because of the need for continuing high-dose anticoagulation, clinically the exanthematosus rash was typical of cutaneous vasculitis, where vascular damage is believed to result from immune-complex deposition in vessel walls. From the finding of casts in the urine and the slightly worsened renal function, which improved with cessation of antibiotics and treatment with corticosteroids, there was evidence that other organs were involved in the reaction. It is hypothesized that the vessels to the spinal cord may also have been involved in the generalized vasculitis and that this may have been the cause for the transverse myelitis. Myelitis in association with autoimmune vasculitis has been described. From the history and laboratory findings, myelitis secondary to underlying autoimmune disease, such as systemic lupus erythematosus or panarteritis nodosa, is unlikely. However, the vessels to the spinal cord could have been affected secondary to the generalized severe allergic vasculitis in a similar manner, causing the transverse myelitis and the temporary paraplegia.

**Conclusion**

The exclusion of other causes and the rapidity and completeness of the response when further antibiotic therapy was withheld and corticosteroid treatment was started suggest that the cause of the patient's transverse myelitis was vasculitis secondary to a severe allergic reaction, which has not previously been described.

**References**


