Neurological complications of systemic vasculitis

A report of 2 cases

A. MALOON, V. U. FRITZ, C. L. KAPLAN

Summary

In up to 72% of patients with systemic vasculitis the neurological system may be involved. This may be peripheral or central (brain or spinal cord), and is usually due to infarction or a ruptured aneurysm. Diagnosis and evaluation are based peripherally on examination of a biopsy specimen or centrally on angiography. Therapy is usually with steroids and/or immunosuppressive agents. Two patients with systemic necrotizing vasculitis with unusual neurological complications are presented.

Vasculitis is a clinicopathological process characterized by necrosis and inflammation of small and medium-sized arteries throughout the body. It can exist either as a major clinical entity or as a minor factor in other primary immunopathogenetic mechanisms.

In both classical polyarteritis nodosa and allergic granulomatosis neurological involvement is characteristic of the disease. The brain or spinal cord is involved in 20-40% of cases, and the peripheral nervous system even more frequently. Leib et al. described a 72% involvement of the neurological system, either central or peripheral, in 64 patients with polyarteritis nodosa.

Two patients with systemic necrotizing vasculitis and unusual neurological complications were observed in the neurology unit of Johannesburg Hospital.

Case 1

A 61-year-old man was admitted to the neurology unit with a history of acute sensory loss in both feet and hands, inability to walk due to bilateral foot drop, and marked weakness of both legs. He had been well until 2 weeks before admission when a prostatectomy had been performed for benign hyperplasia. He had been a heavy drinker for many years, but denied abuse of alcohol. He smoked 10-15 cigarettes a day. Personal and family history were otherwise non-contributory.

On examination he was alert, co-operative, and apyexual; no lymphadenopathy was detected. There was mild pallor. Blood pressure was 180/110 mmHg and pulse rate 90/min. There was left ventricular enlargement and a left-sided fourth heart sound was heard. Otherwise the cardiovascular and respiratory systems were normal, and abdominal and rectal examination negative.

Neurological examination revealed no cranial nerve abnormality, but patchy lower motor neuron-type weakness involving all four limbs with bilateral foot drop was present. Marked generalized muscle wasting was evident, particularly affecting the intrinsic muscles of the hands and the proximal leg muscles. There was posture-related pedal oedema. The reflexes were abnormal in a patchy distribution varying from absence to hyperreflexia. A severe asymmetrical glove and stocking peripheral neuropathy to all sensory modalities was detected. Cerebellar function was normal. The patient was too weak to walk.

Laboratory investigations revealed a haemoglobin concentration of 8.0 g/dl, red cells were hypochromic and normocytic, the white cell count was 19 x 10^9/l with a normal differential count, and the erythrocyte sedimentation rate (ESR) was 118 mm/1st hour (Westergren). The platelet count was 833 x 10^9/l. Serum urea concentration was 17 mmol/l and creatinine 309 μmol/l; creatinine clearance was 31.6 ml/min. Granular casts were seen in the urine. Serum vitamin B12 and folate values were normal. All other biochemical and serological tests were normal except that total serum complement and C3 and C4 components were reduced. Cerebrospinal fluid was normal, as was a chest radiograph. Electromyography revealed evidence of a severe neuropathic disorder of axonal nature. Underlying malignancy was excluded by a full range of investigations.

Examination of a sural nerve biopsy specimen was negative, but a renal biopsy specimen revealed a focal proliferative glomerulonephritis with 25% crescents, compatible with a diagnosis of systemic polyarteritis nodosa. Prednisolone 60 mg daily was given.

The neuropathy improved. Renal function remained stable and the ESR returned to normal as did the full blood count. Hypertension was managed with β-blockers, diuretics and vasodilators. An episode of left ventricular failure at rest occurred in the ward and this was managed with intravenous diuretics. The ECG showed no acute change and there was no associated cardiac enzyme rise. The patient made a gradual recovery and with the aid of foot-drop splints and vigorous physiotherapy was eventually ambulant and discharged on 40 mg prednisolone daily.

Four weeks after discharge he suffered an acute right hemiparesis and dysphasia. He was readmitted and found to have an ESR of 100 mm/1st hour (Westergren). His urine sediment was active but urea and creatinine values remained stable. The dose of prednisolone was increased to 80 mg daily, and he gradually improved and was discharged once more.
Case 2

A 39-year-old schoolteacher presented at Johannesburg Hospital with a history of an episode 3 years previously of nasal polyps, asthma and large patchy vasculitic skin lesions of palms, soles, elbows and calves. Confirmation of allergic vasculitis was obtained by examination of a biopsy specimen and the patient was treated with corticosteroids for 8 months. Six months later he developed a recurrence of vasculitic lesions on the fingers, and an interstitial pulmonary infiltrate. Steroids and cytostatic therapy were started. Shortly thereafter he developed vasculitic lesions of the finger tips and elbows. There was acute exacerbation of the disease and the patient complained of a sudden onset of severe, excruciatingly painful backache associated with pain and weakness of the left leg. He subsequently complained of occipital headache, became mildly confused, and was admitted to the neurology unit of the Johannesburg Hospital.

On examination the patient was mildly confused and complained of severe low back pain. There was minimal neck stiffness and Kernig's sign was positive. Although he was obtunded and screamed uncontrollably with pain he appeared to be fully orientated and speech and cranial nerves were intact. Cerebellar, extrapyramidal and motor and sensory function of both upper limbs appeared normal on examination. There was decreased sensation in the L4-S1 distribution of the right leg with reflexes decreased in the corresponding segments. Blood pressure was 110/75 mmHg and the cardiovascular, abdominal and respiratory systems were normal except for mild bronchospasm. The only residual features of vasculitis were vasculitic nodes on the right index finger, right thumb, left index finger, left and right elbow.

A clinical diagnosis of spinal subarachnoid haemorrhage was confirmed when a lumbar puncture revealed grossly blood-stained cerebrospinal fluid (CSF) under a pressure of 200 mmH₂O. Results of other laboratory investigations were within normal limits.

The patient stabilized initially but 2 days later had a second spinal subarachnoid haemorrhage. Lumbar puncture then revealed a CSF protein value of 7.2 g/l, glucose of less than 1.5 mmol/l, 920 neutrophils, 200 lymphocytes and 8700 red blood cells. Although no bacterial growth was present the patient became pyrexial and antibiotics were given in addition to prednisolone 80 mg daily. However, his clinical condition deteriorated and he developed total paralysis of the left leg with reflexes decreased in the corresponding segments. Blood pressure was 110/75 mmHg and the cardiovascular, abdominal and respiratory systems were normal except for mild bronchospasm. The only residual features of vasculitis were vasculitic nodes on the right index finger, right thumb, left index finger, left and right elbow.

Diagnosis and evaluation are based on examination of biopsy specimens and angiographic findings. Biopsy has been performed on sural nerve, muscle, kidney and skin. Biopsy specimens of muscle showed abnormality in 35% of patients in the series of Maxeiner et al.⁷ Sural nerve biopsy specimens are most useful if the sensory latency is abnormal. Angiography provides information on medium-sized arteries. Travers et al.⁸ performed abdominal aortography and selective mesenteric angiography on 17 patients and identified a form of polyarteritis nodosa which was more severe and associated with a worse prognosis.

Therapy must be directed at both the encephalopathy and the hypertension so often present. The prognosis is usually favourable, and our first patient made a good recovery. The overall prognosis is good, given time and appropriate therapy. Cohen et al.⁹ treated 36 patients with corticosteroids alone and 14 patients with corticosteroids plus either cyclophosphamide or azathioprine. The disease was controlled in patients receiving 60 mg prednisolone daily. The use of cytotoxic agents was limited to a period of less than 1 month because of side-effects and the death of 1 patient. Fauci et al.¹¹ used cyclophosphamide only when the dose of corticosteroids was being tapered off. Leib et al.¹² evaluated 64 patients with polyarteritis nodosa and concluded that the prognosis was better when immunosuppressive agents were added to the corticosteroid therapy, but their role can only be determined by a comparative prospective study. This may be a difficult task to accomplish. The importance of tissue biopsy and angiography to confirm the difficult diagnosis of systemic vasculitis should be emphasized; early corticosteroid therapy may prevent the ongoing occlusive vascular process which eventually accounts for the high morbidity and mortality of this disease.

**Discussion**

The involvement of the nervous system in systemic necrotizing vasculitis may be central, peripheral or both. The first manifestation is usually a peripheral neuropathy, and this was demonstrated in our first patient. A wide spectrum of peripheral nervous system involvement may result from vasculitic infarction. Central nervous system deficits tend to occur much later in the course of the disease; both of our patients had manifestations of central nervous system involvement. The first had a right hemiplegia; the second had a spinal subarachnoid haemorrhage with complete recovery but ultimately died of a central subarachnoid haemorrhage.

The commonest central nervous system presentation is usually diffuse encephalopathy with or without seizures, but focal presentations of infarct or haemorrhage are also frequent. The basic vascular change is characteristically patchy. Intimal proliferation or thrombosis may occur with resultant infarction as in our first case. Weakened necrotic vascular walls may granulate, scar and form multiple small aneurysms. When these aneurysms occur in the spinal cord or the brain they may rupture, causing a cerebrovascular accident in the form of an intracerebral haematoma or a subarachnoid haemorrhage. This is the likely pathogenesis of the lesion in our second patient. Spinal subarachnoid haemorrhages are very rare and complete recovery of function with minimal residual deficit as in case 2 is most unusual.

Abnormal laboratory findings of relevance are: elevated ESR, leucocytosis, anaemia, thrombocytosis, haematuria, proteinuria, circulating immune complexes and low titres of rheumatoid factor. Eosinophilia is not present in classic polyarteritis nodosa but 30% of patients have hepatitis-B antigenaemia (HAA+). Audio antigens are not a feature.

REFERENCES

Peritonitis in juvenile chronic arthritis

A report of 2 cases

E. BHETTAY, A. J. G. THOMSON

Summary

Peritonitis is a rare extra-articular manifestation of juvenile chronic arthritis (JCA) which, although mentioned in passing, seems not to have been documented previously. Two patients with systemic-onset JCA, 1 of whom had peritonitis in the early weeks of onset while the second developed peritonitis 10 years after onset, are described.

Peritonitis is a rare extra-articular manifestation of juvenile chronic arthritis (JCA). It is not mentioned in some monographs,1,2 while in several others3-12 episodes of abdominal pain are attributed to mesenteric adenitis or peritonitis. Documented evidence for peritonitis is lacking.13 We report the occurrence of peritonitis in 2 patients with systemic-onset JCA.

Case reports

Case 1

A 3½-year-old girl developed fever and arthritis involving the right hip, left elbow and left ankle for which penicillin and aspirin were prescribed. Two weeks later she was admitted to hospital because of severe neck pain, and reluctance to swallow or chew. On admission to hospital she was thin and apprehensive, and she had a swinging fever. There was an active arthritis of the left wrist and right ankle. She also complained of pain near the angle of the jaw. A few small, discrete cervical lymph nodes were palpable, and a few subcutaneous nodules could be felt along the dorsal spine. The pulse rate was 160/min, no cardiac murmurs were heard, and the chest was clear. She had abdominal pain, with marked abdominal distension and generalized tenderness. The liver was not enlarged, but the spleen was palpable 1 cm below the costal margin. The leucocyte count was 3,0 x 10⁹/l and the erythrocyte sedimentation rate (ESR) 110 mm/1st h. The chest radiograph was clear and the ECG was normal. Ampicillin and cloxacillin were started for a presumed primary pneumococcal peritonitis. The patient's temperature seemed to settle initially, but because of persisting abdominal distension and tenderness, and recrudescence of fever, an appendix abscess was suspected.

Sixteen days after admission, laparotomy revealed a gelatinous exudate all over the peritoneum, a normal appendix, and multiple lymph nodes showing nonspecific inflammatory changes. Antibiotics were discontinued; a low-grade fever and arthritis persisted. She was given salicylates followed 2 days later by prednisone, which resulted in dramatic improvement. The peritonitis resolved rapidly.

Over the ensuing 14 years her arthritis has persisted, but her disease has now been in remission for 2 years.

Case 2

A 13-year-old boy developed systemic-onset JCA at the age of 3½ years. In addition to antituberculosis therapy for calcified hilar lymph nodes, he was given aspirin and later indomethacin. For 24 months during 1975-1977 d-penicillamine was given, followed by gold sodium thiomalate until December 1981. In June 1982 he was re-investigated for tuberculosis because a pleural rub was heard. Chest pain due to costosternal and costovertebral arthritis had been troublesome intermittently and caused some chest deformity and pulmonary restriction. Since October 1982 he had been treated with chloroquine, sulindac, and a small daily dose of prednisone with isoniazid prophylaxis.

In March 1983 he was admitted to hospital with a swinging fever and a painful right hip. He was placed in traction, and