INTRAVENOUS PULSE METHYL PREDNISOLONE IN THE SUCCESSFUL TREATMENT OF SEVERE SARCOID POLYNEUROPATHY WITH PULMONARY INVOLVEMENT

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Abstract:
Severe widespread sarcoid polyneuropathy with associated pulmonary involvement was treated successfully in a 26 year old man using 'pulse' methyl prednisolone. After he had failed to respond clinically to a two months course of high-dose oral prednisolone, a regimen of intravenous methyl prednisolone 1 g once a week for eight weeks was instituted, along with 10 mg prednisolone orally daily. Neurological improvement began after the third dose with complete remission achieved after the eighth week. More than 12 months after cessation of treatment he remains in good health with no clinical or laboratory evidence of sarcoidosis. (Aust NZ J Med 1985; 15: 45-46.)
Key words: Sarcoid polyneuropathy, pulmonary sarcoidosis, intravenous 'pulse' methyl prednisolone.

INTRODUCTION

Severe neurological sarcoidosis presents a major clinical challenge to the physician as its response to oral prednisolone is at best unpredictable and usually requires a prolonged course in high doses with the risk of severe side-effects.[1] High-dose intravenous 'pulse' methyl prednisolone has been used in a number of diseases with variable success.[2-5] However no controlled studies of its use in pulmonary or extrapulmonary sarcoidosis have been reported. This case highlights the successful use of such a regimen in a patient with a severe widespread sarcoid polyneuropathy with associated pulmonary parenchymal and endobronchial involvement.

CASE REPORT

A 26 year old married building supervisor presented to his local medical officer complaining of a painful swelling in his right groin. A biospy of this revealed an inguinal lymph node infiltrated with non-caseating granulomata typical of sarcoidosis, with no acid fast bacilli visible on Zeil-Neilson stain. He was referred to the University Unit where research into sarcoidosis was in progress. By that time he had experienced four months of exertional dyspnea, profound lethargy, and parasthesia in his hands and feet. He had no past history of serious illness, was taking no medication, rarely drank alcohol, was a non-smoker, and had one child.

Clinically he had an enlarged left inguinal lymph node but no other lymphadenopathy and no abnormal signs in his thorax or abdomen. Surprisingly he had a marked patchy sensory impairment for pin-prick and light touch on the lateral aspect of his right arm from his shoulder to his elbow and also on the medial aspect of his right thigh and left leg. There was marked loss of pain, light touch, and temperature sensation on the right side of his face and scalp in the distribution of all three branches of the trigeminal nerve. There was also impairment of his right corneal reflex. Full ophthalmologic examination with a slit lamp along with Rose Bengal and Schirmer's Test was normal.

His serum angiotensin converting enzyme activity was moderately elevated, 53.5 nmol ml^{-1} min^{-1} (NR < 41 nmol ml^{-1} min^{-1} for a male), ESR 4 min in the first hour, hemoglobin 16 g per dl, white cell count 4,300 cells dl^{-1}. His serum electrolytes and calcium, 24 hour urinary calcium, chest x-ray were normal. A mantoux test to 10 and 100 units of (PPD) was non-reactive. His ECG revealed frequent atrial and nodal ectopics. His respiratory function tests, consisting of flow volume loops, carbon monoxide diffusion, arterial blood gases, and an incremental exercise test with an ear oximeter, were normal. A CT scan of his brain with fine cuts through the brain stem area was normal. A fibroptic bronchoscopy revealed an inflamed bronchial tree with biopsy-proven endobronchial sarcoid. Transbronchial biopsy of the right lower lobe contained multiple non-caseating granulomata with giant cells. No acid fast bacilli were demonstrated on Zeil-Neilson stain or grown on culture. A bronchoalveolar lavage of his right middle lobe using 100 ml of normal saline revealed a lymphocyte count of 15% (NR < 8%) consistent with a low-grade sarcoid alveolitis. A whole body gallium-67 scan read with a gamma camera at 24 and 72 hours showed increased uptake in the right parotid gland and both orbits but no increased activity elsewhere. A diagnosis of sarcoid polyneuropathy with associated pulmonary involvement was reached.

By November 1982 his dyspnea and lethargy were worse, his balance had become poor with diminished libido, anorexia, and increased thirst. His acroparasthesia had become more severe and clinically his sensory loss was more widespread with involvement of the left upper arm and forearm. He now had

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diminished power of hip flexion and abduction bilaterally. There was no weakness of muscles innervated by the trigeminal or facial nerves and his gag reflex and palatal function were at that stage normal. He was considered to have a mild proximal myopathy with the possibility of some hypothalamic dysfunction. His electromyogram, motor and sensory nerve conduction tests, and lumbar puncture were normal. By early December 1983, three months after presentation, his facial sensory impairment had extended to all trigeminal divisions on the left. His right corneal reflex remained impaired and he also had marked right palatal weakness.

He was prescribed prednisolone 50 mg mane on 6 December 1982, and one month later there was no symptomatic improvement or change in his physical signs. In fact he had developed new symptoms with arthralgias in his left elbow, knees, ankles, neck and lumbar spine, profuse night sweats, severe pain in his bladder when it became full, as well as nocturia three times a night. His respiratory function tests were unchanged. His serum calcium was normal and there was no biochemical evidence of diabetes mellitus. As he had become Cushingoid his corticosteroid dosage was reduced to 40 mg mane. His sensory loss over the following weeks had extended in patches to involve the thorax and abdomen and in his limbs his sensory loss had come to involve proprioception and vibration sense as well. So severe was his sensory loss in his feet that on one occasion when he accidentally trod on a pin it was able to enter his foot to a depth of 2 cm before he felt it.

In view of the gravity of his symptoms and their failure to respond to an eight week course of high-dose oral prednisolone, methyl-prednisolone (1 g intravenously) was given weekly in late January 1983. This was administered on an outpatient basis *via* an intravenous infusion of 100 ml of normal saline over 30 minutes. There were no side-effects experienced during the course of therapy. He also took 10 mg prednisolone mane each day. A total of eight infusions were given with a gradual improvement in sensory loss experienced after the third week. Surprisingly, by the end of the eighth week of treatment, all his neurological signs had resolved completely and he felt well. The oral prednisolone was then ceased. By June 1983 his serum ACE had returned to normal and his full respiratory function tests including cycle ergometry were still normal.

In September 1983, 12 months after presentation, his repeat bronchoscopy was normal and bronchoalveolar lavage was only just above normal with a lymphocyte count of 11%. A repeat gallium-67 scan showed no abnormal uptake anywhere and his chest X-ray remained normal. He has remained in good health for over twelve months since cessation of steroids.

DISCUSSION

The neurological manifestations of sarcoidosis have been widely reported in the literature and it is apparent from these reports that no part of the central or peripheral nervous system is exempt from possible involvement. Trigeminal nerve involvement is usually sensory and unilateral and often associated with other cranial nerve palsies as occurred in this case where there was unilateral palatal weakness and sensory loss. Indeed dysfunction of the IX and Xth cranial nerves is reported to be the third most commonly affected cranial nerve complex and is most often unilateral. This patient also had widespread patchy sensory loss of both the trunk and limbs quite typical of that described in sarcoidosis. Neither the absence of abnormal findings in the CSF nor abnormal nerve conduction are unusual in such cases.[1]

It is worth emphasising that despite the presence of a normal chest radiograph this patient had quite florid endobronchial and pulmonary parenchymal sarcoidosis. However the lack of increased pulmonary parenchymal activity as demonstrated on two gallium scans along with repeatedly normal lung function tests suggests that his pulmonary disease was not highly active.

Oral corticosteroids have been used extensively in the treatment of neurological sarcoid with variable and unpredictable response and some patients may even remit spontaneously. However neurological involvement, particularly of the central nervous system, is usually regarded as an absolute indication for corticosteroids especially as there is no way at present of predicting the natural history of each individual case.

The use of intravenous 'pulse' methyl-prednisolone has been used in a variety of diseases *e.g.* renal allografts, rheumatoid arthritis, ankylosing spondylitis, multiple sclerosis, and diffuse proliferative lupus nephritis, and with the exception of the first, with limited or no success.[2-5] Unpublished anecdotal reports of the successful use of this form of therapy in pulmonary sarcoidosis from the National Institute of Health, Bethesda, Maryland, USA prompted its use in this case. To our knowledge no controlled clinical studies on the use of 'pulse therapy' for sarcoidosis have been completed.

It has been shown that sarcoid alveolitis, the precursor of granuloma formation in the lung, is characterised by an influx of helper T-lymphocytes with an associated stimulation of immunoglobin production by B lymphocytes.[6] In normal subjects both T and B lymphocyte function is depressed by high-dose oral corticosteroids.[7-10] However, detailed knowledge of the immunologic effects of high-dose intravenous methyl-prednisolone in sarcoidosis is not available.

It is hoped that this case report will prompt further investigation into what may prove a useful addition to the very limited armamentarium currently employed in the treatment of this disease.

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