Sensorimotor neuropathy with sulphasalazine

T.R. Price

Northwick Park Hospital, Watford Road, Harrow, Middlesex.

Summary: A case of mixed sensorimotor neuropathy associated with sulphasalazine therapy is reported. This is believed to be unique.

Introduction

Sulphasalazine produces adverse reactions in about 20% of patients. (Collins, 1968; Das *et al.*, 1973; Goldman & Peppercorn, 1975). One case of reversible sensory neuropathy has been described (Wallace, 1970) and unspecified cases of paraesthesiae are recorded (Collins, 1968). We describe a severe sensorimotor neuropathy implicating sulphasalazine, without major constitutional upset, and with delayed recovery.

Case report

A 63 year old woman suffered a first attack of severe ulcerative colitis with up to 20 bloody motions per day, and considerable weight loss. She had no other features of the disease, no neurological symptoms nor signs, and had only taken codeine. Investigation was consistent with severe colitis: stool cultures were negative and the diagnosis confirmed by biopsy and barium enema which showed extensive colitis sparing the proximal ascending colon. Therapy consisted of fluid and electrolyte replacement, prednisolone 60 mg o.d. and prednisolone enemata with sulphasalazine 1 g q.d.s. Prompt recovery occurred and she was discharged on prednisolone 15 mg o.d., sulphasalazine 1 g q.d.s. and ferrous sulphate. Ten days later she was well and had regained 2 kg. Prednisolone was reduced to 10 mg.

Two weeks later she complained of 'tingling' in the hands and feet and difficulty in walking because she could not 'find her feet'. Her colitis remained in remission. Examination and routine laboratory investigations were normal. Prednisolone was reduced to 7.5 mg. One week later she was wheeled into clinic. Paraesthesiae extended to her elbows and knees and her legs felt weak. On examination she was lucid, the cranial nerves were intact and there were no cerebellar signs. There was reduced perception of touch below

the elbows but no other neurological signs in the arms. She had a flaccid paresis of the legs affecting all muscle groups. Tendon reflexes were absent and the plantars downgoing. Perception of vibration and joint position was absent below the knees.

She was admitted and sulphasalazine discontinued. Routine investigations remained normal; erythrocyte sedimentation rate, serum vitamin B12, TPHA, VDRL, thyroid function, glucose tolerance and auto-antibodies were normal or negative.

She improved quickly so that by one week she could walk with an ataxic gait. Power was still reduced in the legs but the knee jerks were weakly present. Further progress was slower. At six weeks her left leg was objectively normal with paraesthesiae to the ankle, but in the right leg slight reduction in power remained with blunted sensation and absent ankle jerk. At three months the patient was vastly improved with paraesthesiae restricted to the toes, but power loss could still be demonstrated in the right leg and the ankle jerk remained absent. At this time she was given a test dose of sulphasalazine and was shown to be a slow acetylator.

Discussion

In previous reports of neurological disturbances attributed to sulphasalazine, the onset has been similarly delayed by about three weeks (Wallace, 1970; Smith *et al.*, 1982). This together with the rapid improvement on drug withdrawal leads us to implicate sulphasalazine rather than an infective polyneuritis as the cause of the mixed neuropathy in this woman: moreover she is at increased risk of sulphasalazine toxicity as a slow acetylator. Our patient differs from the other documented case of peripheral neuropathy in her serious motor disturbance and delayed recovery as well as in the absence of major systemic upset or encephalopathy (Wallace, 1970). However the two cases are similar in respect of the marked sensory

ataxia. One further report of two cases of delayed encephalopathy with jaundice has appeared but without peripheral neuropathy (Smith *et al.*, 1982).

Although sulphasalazine may induce a 'lupus-like' syndrome (Crisp & Hoffbrand, 1980; Carr & Locke, 1982), especially in slow acetylators, the clinical picture does not include peripheral neuropathy which would also be unusual in 'true' systemic lupus erythematosus. Those reported cases of cerebral disturbance with systemic features are perhaps best seen in the context of a drug induced lupus reaction (Rafferty *et al.*, 1982).

Sulphasalazine is sulphapyridine azo-linked to 5-

aminosalicylic acid. Colonic bacteria split the azo link, the sulphapyridine is absorbed while the 5-amino-salicylic acid is excreted in the faeces and probably represents the therapeutic moiety. Some reactions are thought to represent hypersensitivity to sulphapyridine, but most are dose related occurring at intakes above 4 g/d more commonly in slow acetylators, although there is no close correlation with serum concentrations. It is suggested that lower doses, up to 4 g/d, can be reintroduced safely in recovered subjects (Das *et al.*, 1973; Goldman & Peppercorn, 1975).

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