

SHORT REPORTS

Neurotoxicity—a Side-effect of Sulphones

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Several reports have appeared on a number of side-effects following the use of sulphones, more especially in the field of haematology (3, 6) and dermatology (2, 3, 5), but also as concerns hepatitis (6), nephrotic syndrome (1), as well as psychotic episodes (4) and peripheral neuropathy (5, 7).

A 60-year-old man with a typical dermatitis herpetiformis diagnosed in 1947. He had been taking sulfapyridine once or twice daily during the period 1948-1956, when he became tired and weak, suffered from tinnitus and cyanosis of the lips. He was then given aldesulphone sodium 0.666-1.3 g daily and his condition improved rapidly. In 1968 he began to suffer from numbness and a tingling feeling in his toes and fingertips, which gradually spread proximally. For this condition he was treated with diaphenylsulphone (100-125 mg daily) until 1972. During the treatment the paresthesia became more intense and spread to knees and elbows, accompanied by a feeling of coldness, but without a subjective loss of strength. The patient got cyanosis of the lips and he became irritable and psychologically unbalanced. In 1969 he lost consciousness while driving a car and injured several persons. He was then forced to stop taking sulphones in 1972 and instead received Prednisone 10-25 mg daily. The paresthesia gradually disappeared completely and his psychological condition improved, but the skin disease remained active. He was hospitalized in the Department of Dermatology, Rikshospitalet, in 1975 and he was tested with diaphenylsulphone 150 mg daily and put on gluten-free diet. After a couple of days he developed distal symmetrical paresthesia in the extremities, which spread centripetally, with his nails turning brown, and also

cyanosis of the lips. The dose was then reduced to 50 mg/daily, with the result that the paresthesia gradually abated and after the medication was stopped the paresthesia disappeared completely in the course of 3 days. The neurologist did not find any reliable objective results: EMG did not show pathological signs. On the other hand, achylia and chronic inflammation in the mucous membrane of the stomach and the small intestine was detected.

COMMENTS

In three published cases of peripheral motor neuropathy (5, 7), a symmetrical peripheral loss of strength appeared distally in the extremities, as well as atrophy of muscles (in particular of the interosseal muscles) and weakened or even completely suspended deep reflexes 3-10 months after the patients had been treated with 300-400 mg diaphenylsulphone daily. Our patient developed symptoms of polyneuropathy, mainly as paresthesia of the distal extremity, gradually spreading in a proximal direction.

When the dose was reduced to 1/3, an improvement could be detected, as in the case of one of the patients reported (5), and on stopping the medication, the paresthesia disappeared. This, and the fact that ca 300 000 American soldiers in Asia daily took 25 mg diaphenylsulphone prophylactically against falciparum malaria without one single case of neurotoxicity being reported, would seem to indicate that neurotoxicity is dose-related (6, 7). By means of autoradiography, sulphones have been found in affected nerves (7) and in some cases, neurotoxicity has been reported in leprosy patients treated with sulphones, but as we know that leprosy affects the peripheral nerves, these findings cannot with absolute certainty be considered as side-effects due to sulphones. In the case of an acute overdose of diaminodiphenylsulphone in a child of 22 months, cyanosis and agitation occurred pre-mortally. Post mortem, the brain was found hyperaemic with small haemorrhages and recent thrombi.

which could be explained effectively as being caused either by sulphone or by methaemoglobin-aemia and grave anoxaemia.

REFERENCES

1. Belmont, A.: Dapsone-induced nephrotic syndrome. *JAMA* 200: 262, 1967.
2. Browne, S. G.: Desinsitization for Dapsone dermatitis. *Br Med J II*: 664, 1963.
3. Catalone, P. M.: Dapsone agranulocytosis. *Arch Dermatol* 104: 675, 1971.
4. Hedstrand, H.: A case of acute side-reactions to diaminodiphenyl sulphone (DDS). *Acta Dermatovener (Stockholm)* 48: 528, 1968.
5. Hubler, W. R. & Solomon, H.: Neurotoxicity of sulphones. *Arch Dermatol* 106: 598, 1972.
6. Millikan, L. E. & Harrell, E. R.: Drug reactions to the sulphones. *Arch Dermatol* 102: 220, 1970.
7. Saqueton, A. C. et al.: Dapsone and peripheral motor neuropathy. *Arch Dermatol* 100: 214, 1969.

Keratoderma Blennorrhagica in a Woman with Relapsing Polychondritis

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This 62-year-old woman who in 1967 had had an operation on a serous ovarian cystoma without signs of malignancy suffered bilateral pareses of u. abducens in August 1972. Medical examination revealed, besides the pareses, an erythrocyte sedimentation rate of 100 mm/h, which had probably been present even in 1967, and hepatomegalia. X-ray of the stomach showed deformation of the duodenal bulb, without ulceration. The patient appeared again in November 1973, with acute iridocyclitis and secondary glaucoma on both eyes and a few days after the eye symptoms had started, her right ear became swollen, red and very painful. Penicillin gave no cure. After one month the other ear was also affected. On betamethasone therapy, 3 mg/day, the condition of ears and eyes improved and she was symptom-free within 2 months. She interrupted steroid therapy one month later due to epigastric pains. This was followed by fever, 39–40°C, without other symptoms. On betamethasone 1.5 mg/day she was afebrile. In the autumn of 1974 cutaneous lesions appeared with scal-

ing crusty erosions on acral areas and on elbows and knees.

In March 1975 on admission to the dermatological ward the lesions corresponded to those of keratoderma blennorrhagica (see Figs.). Livedo reticularis and ecchymoses were present in addition. The right ear was red, scaling, enlarged and painful on palpation. Physical examination revealed the liver 5 cm below the costal arc and weakness of the right leg, with peroneal palsy. The right knee was swollen with hydrops.

Laboratory examinations. *Blood:* Haemoglobin 12.8 g/100 ml, white blood cell counts 12 100 (neutrophils 73%, eosinophils 1%, lymphocytes 25% and monocytes 1%), thrombocytes 185 000. Erythrocyte sedimentation rate 110 mm/h. *Serum:* iron 9.6 μ M; transferrin 22 μ M; creatinine 0.8 mg/100 ml; uric acid 5 mg/ml; liver tests (bilirubin and enzymes) normal; proteins: normal immunoglobulins IgG, A and M, orosomucoid 129 mg/ml, anti-nuclear antibody titre homogeneous 1/25–1/100, rheumatoid factor negative (before steroids positive); seroreactions for syphilis and gonorrhoea



Fig. 1.