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Treatment of proliferative sparganosis with mebendazole and praziquantel

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Mebendazole (methyl-5-benzoyl benzimidazole-2-carbamazole) a broad spectrum anthelmintic structurally related to thiabendazole, has been found effective in the treatment of several nematode and cestode infections (KEYSTONE & MURDOCH, 1979). *Taenia saginata, T. solium* and *Hymenolepis nana* are sensitive to standard oral doses of 300 mg twice daily for three days or, in the case of *H. nana,* seven to ten days (KEYSTONE & MURDOCH, 1979; PEÑA CHAVARRIA *et al.,* 1977). More recently infections associated with larval stages of *Echinococcus granulosus* and *E. multilocularis* haves uccessfully been treated with high doses of mebendazole. Most trials have used 40 mg/kg/day for periods ranging from one to six months. Mebendazole appears to eradicate *E. granulosus* but only to control or slow the growth of *E. multilocularis* (BEKHTI *et al.,* 1977; BEARD *et al.,* 1978). Despite occasional reports of transient episodes of diarrhoea, colicky abdominal pain, slight headache and dizziness, the drug's lack of side effects even when given in large doses for prolonged periods has been confirmed in almost all clinical trials (KEYSTONE & MURDOCH, 1979; BEKHTI *et al.,* 1977; BEARD *et al.,* 1978).

Proliferative sparganosis is a rare disease produced by *Sparganum proliferum* (STILES, 1908), a unique proliferating larva found only in man and probably in baboons and vervets (KUNTZ *et al.,* 1970). Most of the published cases have come from Asia (five reported from Japan by TASHIRO, 1923 and more recently, one from Taiwan by LIN *et al.,* 1978); two additional cases have been reported, one from Florida, USA (STILES, 1908) and the other from Prague, Czechoslovakia (FAUST & RUSSELL, 1964).

Little is known of the agent's life-cycle and biological characteristics or of the host-parasite relationship in *S. proliferum* infections. Furthermore no antiparasitic drugs have ever been used for the treatment of this condition.

We report the results of the use of mebendazole and praziquantel in the treatment of a fatal case of proliferative sparganosis in Venezuela. The patient was a 35-year-old man with a seven-year history of slowly spreading papular and nodular lesions covering most of his body, sparing only face, palms, soles and genitalia. Several large subcutaneous abscesses developed from which necrotic material and many pleomorphic larvae were recovered. Skin punch-biopsies from the nodular lesions revealed cross-sections of worms with the features of sparganum. Formalin-fixed and live larvae examined at the Tropical Medicine Institute in Caracas were identified as *S. proliferum.* Initial laboratory studies revealed a moderate normochromic, normocytic anaemia, leucocytosis with eosinophilia, increased ESR and mild haemoglobinuria and proteinuria. The patient had no evidence of associated illness, and had not received previous immunosuppressive drugs. Specific and non-specific immune responses seemed unaltered. Further clinical and parasitological details will be reviewed elsewhere.

A four-month course of mebendazole at a dose of 40 mg/kg/day was completed. Tolerance was good except for the appearance of mild headache, dizziness and occasional vomiting. Clinically, the patient improved greatly. Cutaneous nodular lesions appeared to stabilize and several deep, chronic soft-tissue abscesses gradually healed up. Previously abnormal laboratory tests returned to normal except for the persistence of a moderate anaemia of the type associated with chronic systemic disorders, hypergammaglobulinaemia, increased erythrocyte sedimentation rate and proteinuria. However, new lesions continued to appear; larvae obtained at different periods were still alive, infective and morphologically unaltered. Furthermore, survival of larvae cultured *in vitro* in a modified Minimal Essential Medium (MEM) supplemented with 10% bovine serum and antibiotics (NOYA *et al.,* 1980), remained unchanged. Therefore, we decided to look at the efficacy of other anthelmintic compounds.

Praziquantel (Embay 8440) a new type of acylated isoquinole-pyrazine derivative has proved highly active against trematodes and cestodes both *in vitro* and *in vivo* (THOMAS, 1977; GROLL, 1977). Although standard single oral doses of 5 to 25 mg/kg have been effective for *T. saginata, T. solium* and *H. nana* infections, doses of 25 mg/kg are necessary to cure infections with *Diphyllobothrium latum* (GROLL, 1977; BYLUND *et al.,* 1977). Experimentally, plerocercoid larvae of *D. latum* are killed at a concentration of 600 mcg/ml of praziquantel. Such high levels are only obtainable with doses of 50 to 100 mg/kg (BYLUND *et al.,* 1977). Reported side effects consisting of abdominal pain, headache, dizziness and, in one instance, urticaria are transient and rare. No significant effects on respiration, pulse rate and blood pressure have been reported (GROLL, 1977; MCMAHON & KOLSTRUP, 1979).

Our patient received 40 mg/kg/day of praziquantel in six divided doses. Treatment was

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repeated on three occasions over a period of two weeks. Tolerance was poor. Intense nausea, vomiting and severe gastritis appeared whenever the dose given exceeded 600 mg, being somewhat milder at lower doses; symptoms were sufficiently severe to require parenteral hydration, antiemetics and antiacid treatment.

Two unexpected side effects were generalized cutaneous parestesias ("burning" sensation) and large muscle tenderness to pressure lasting for several hours after drug administration. Finally, sinus tachycardia with a rate above 140 beats per minute was observed approximately 30 minutes after each dose, the heart rate gradually returning to basal levels after approximately two and a half hours. Blood pressure remained within normal limits. Clinically and electrocardiographically there was no evidence of cardiomyopathy. Treatment was discontinued in view of the patient's intolerance of the drug and its apparent lack of influence on the progress of the disease. Furthermore, survival, infectivity and anatomical integrity of the larvae obtained remained unchanged.

We are not aware of any previous report on such adverse effects in subjects treated with praziquantel. Further experiments will be carried out to assay the *in vitro* and *in vivo* efficacy of both praziquantel and mebendazole against *Sparganum proliferum*, as well as to assay the potential cardiovascular toxic effects of high doses of praziquantel in experimental animals.

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