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Short communication

Intraarticular and intraperitoneal administration of etoposide in haematological malignancy

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Summary. Etoposide is frequently used in the treatment of a wide variety of malignant disorders. Administration is usually by intravenous infusion, but etoposide can also be given by mouth [3], by intraarterial infusion [2] and by direct instillation into the pleural cavity [1]. Two patients are described who were treated with injections of etoposide into the peritoneal cavity and knee joint, respectively.

Case 1

A 55-year-old man was diagnosed as having myelofibrosis. Two years later a splenectomy was performed because he was requiring increasingly frequent blood transfusions. Post-operatively rapid hepatic enlargement was noted and ascites developed. The abdomen became grossly distended and painful. Treatment with hydroxyurea and diuretics was commenced, and this led to a slight decrease in hepatic size. The ascites, however, proved resistant to treatment over a period of 4 months, and the patient was severely disabled by the abdominal distension and pain. Transformation to acute myeloid leukaemia was noted at this stage. The ascites was thought, at least in part, to be due to peritoneal seeding by haemopoietic tissue. Etoposide (50 mg) was injected into the peritoneal cavity and over the next 48 h a 7-l diuresis occurred associated with a marked reduction in abdominal swelling and discomfort. Etoposide (100 mg) was injected twice more over the next 72 h with a further diuresis and reduction of ascites. The patient died 2 weeks later from the systemic disease with no re-accumulation of ascites.

Case 2

A 77-year-old woman was admitted to hospital with a 48-h history of painful swelling of the left knee. Examination revealed a large effusion into the joint, and no movement of the knee was possible because of pain. A full blood count and subsequent bone marrow aspirate revealed a diagnosis of acute myeloid leukaemia. Aspiration of the joint fluid revealed many blast cells containing Auer rods. No urate or pyrophosphate crystals were present. Treatment with systemic chemotherapy or radiotherapy to the knee was refused by the patient. An intraarticular injection of 5 mg etoposide was given. After 24 h there was a slight but definite reduction in the effusion and some movement of the joint was possible. A second injection of 10 mg was given with a further sustained reduction in symptoms. The patient died 1 month later from pneumonia.

Discussion

In case 1, intraperitoneal administration of etoposide caused a marked reduction in ascites, and hence symptoms, where more conventional treatment had failed. Intraperitoneal etoposide has been previously used in the management of ovarian carcinoma [5]. However, experimental animals have been shown to develop fibrosis following administration of etoposide by this route, and caution has thus been advised for its use in humans [4]. In the patient described here, no local reaction after injection occurred but the follow-up period was very short.

In case 2, pain in the knee was the dominant symptom in a patient with acute myeloid leukaemia, and injection of etoposide into the joint provided good symptomatic relief. No adverse local reaction was noted. There is no previous report of this method of administration of etoposide.

Intraperitoneal and intraarticular injection of etoposide had particular appeal in these patients, as it provided effective local relief of symptoms without any systemic toxicity. This approach to treatment could be considered either where systemic chemotherapy is contra-indicated or where it has been used without success in the treatment of localised symptoms.

References

1. Jones JM, Olman EA, Egorin MJ, Aisner J (1985) A case report and description of the pharmacokinetic behavior of intrapleurally instilled etoposide. Cancer Chemother Pharmacol 14: 172–174
2. Kokron O, Olbert F (1983) Intra arterial infusion therapy for pulmonary tumours. Rec Res Cancer Res 86: 128–136
3. Phillips NC, Lauper RD (1983) Review of etoposide. Clin Pharmacol 2: 112–119
4. Stahelin H (1976) Delayed toxicity of epipodophyllotoxin derivatives (VM 26 and VP 16-213), due to a local effect. Eur J Cancer 12: 925–931
5. Zimm S, Clearly S, Lucas W, Weiss R, Markman M, Andrews P, Schiefer M, Howell SB (1986) Phase I pharmacokinetic study of intraperitoneal cisplatin and etoposide. Proc Am Soc Clin Oncol 5: 49

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