Transient remission of systemic manifestations following intraarticular triamcinolone hexacetonide injection in a boy with systemic juvenile idiopathic arthritis

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Intraarticular corticosteroid therapy is widely used in the management of children with juvenile idiopathic arthritis (JIA) to obtain rapid symptomatic relief of inflammation and functional improvement. Several corticosteroid preparations are available for intraarticular injection, with triamcinolone hexacetonide (TH), which is the least soluble molecule, being generally preferred due to its ability to provide a longer duration of response with a lower rate of systemic absorption from the joint. Occasionally, however, unexpected systemic effects of intraarticular injection of different corticosteroid preparations, including TH, have been observed in children with JIA (1-6). We describe a boy with systemic JIA who experienced transient remission of extra-articular manifestations following intraarticular TH injection.

A 3-year-old boy was admitted to his local hospital with a 1-month history of intermittent high spiking fever, evanescent macular rash and polyarthritis. A diagnosis of probable systemic JIA was made and he was given nonsteroidal anti-inflammatory drug therapy. Because control of symptoms was not achieved, prednisone therapy 1 mg/kg/day was started, which led to progressive clinical improvement. Prednisone dose was tapered within 2 months to 1 mg/kg - 0.3 mg/kg every other day, but had to be increased again to 1 mg/kg/day 1 month later due to a disease flare. Four months after the beginning of corticosteroid therapy, while receiving prednisone 1/mg/kg/day the child experienced back pain of acute onset. Vertebral X-ray and magnetic resonance imaging studies revealed a severe body crushing of the eighth lumbar vertebra. Because a corticosteroid iatrogenic effect was suspected, prednisone therapy was rapidly tapered and eventually discontinued, and the boy was referred to us.

On admission he had fever (38.7°C), erythematous macular rash and swelling, intense pain, and functional limitation of both wrists and ankles. Laboratory studies revealed increased erythrocyte sedimentation rate (ESR) at 83 mm/h and C-reactive protein (CRP) at 202 mg/l. Initial treatment included ibuprofene (40 mg/day) and intravenous immunoglobulins (2 g/kg), which, however, did not affect either systemic or joint symptoms. We then decided, with the aim of improving articular complaints, to perform an intraarticular injection of TH in both wrists and ankles. A total of 40 mg of TH were injected (5 mg in each wrist and 15 mg in each ankle) corresponding to 2.2 mg/kg. This was followed by prompt improvement of pain and function of the injected joints and, unexpectedly, by sustained remission of fever (Fig. 1) and cutaneous rash. Moreover, 3 days after the intraarticular injections, the ESR and CRP dropped to 68 mm/h and 78 mg/l, respectively. The boy was discharged with ibuprofene, oral methotrexate (10 mg/m^2/ week), ferrum, calcium, calcidiol, and alendronate. Moreover, he was immobilized with corset. After discharge, he remained free of systemic symptoms for three weeks, when he had recurrence of fever, though at a lower grade, and increase of ESR and CRP to 75 mm/h and 155 mg/l, respectively. Two months later, arthritis in the cervical spine and wrists recurred and thus the methotrexate dose was increased to 15 mg/m^2/ week.

Systemic absorption of intraarticular corticosteroids is a well recognized phenomenon. Laaksonen *et al*. (1) described alterations in plasma cortisol levels, which persisted for at least 4 weeks, following intraarticular corticosteroid injection in children with JIA. Similar findings were subsequently obtained by Huppertz and Pfuller (5), who found universal depression of morning peak cortisol concentration that returned to normal within 10 to 30 days in 22 patients following TH injection. Additional examples of systemic effects of absorbed steroids following intraarticular injection in children are the occurrence of depression (3) and the observations of transient (12 to 36 hours) fall in the serum salicylate levels (2), and transient remission of atopic dermatitis (4) and active iritis (6). Of note, using microwave thermography following intraarticular corticosteroid injection of the knee in adults with rheumatoid arthritis, MacDonald *et al.* (7) were able to provide objective evidence of suppression of inflammation in the uninjected knee. In conclusion, the transient remission of systemic manifestations observed in our patient represents a previously unreported example of the systemic effect of intraarticular TH in JIA.

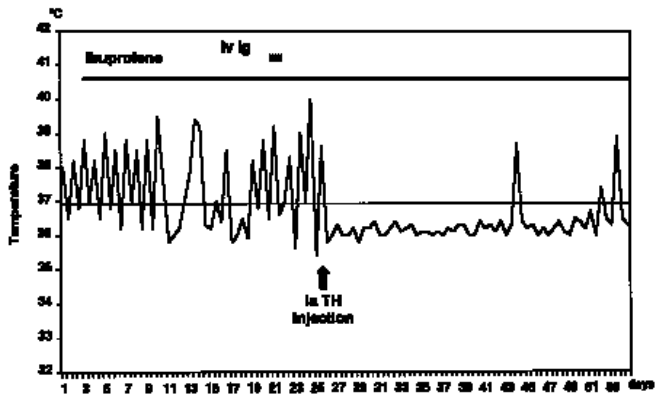

Fig. 1. Time course of fever before and after the intraarticular injection of triamcinolone hexacetonide. iv Ig: intravenous immunoglobulins; ia TH: intraarticular triamcinolone hexacetonide.

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