Severe heparin osteoporosis in pregnancy

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Summary

A case of severe osteoporosis following administration of low dose subcutaneous heparin in pregnancy is reported. Possible reasons for the condition are suggested which caution against the indiscriminate use of subcutaneous heparin in pregnancy.

KEY WORDS: Hirschsprung's disease, thrombo-embolism.

Introduction

Ante-natal thromboembolism is an important cause of maternal morbidity and mortality. Self-administered subcutaneous heparin has been recommended for use during pregnancy and for the first 6 weeks of lactation, in high-risk patients (Spearing *et al.*, 1978). However, pregnancy may increase the risk of skeletal demineralization from prolonged heparin therapy (Wise and Hall, 1980). We report a case of severe osteoporosis with low dose heparin treatment during pregnancy.

Case report

A 29-year-old woman presented in February, 1981 with left pleuritic chest pain of sudden onset, preceded by 3 days of left calf pain. She smoked 20-30 cigarettes daily, and had taken an oral contraceptive pill for 7 years. Investigations revealed the presence of multiple pulmonary emboli. She received a 1 week course of intravenous heparin followed by 3 months of warfarin.

In December, 1981 she was found to be 8 weeks pregnant. Self-administered subcutaneous heparin 5,000 units twice daily was commenced. In April 1982, after 19 weeks of treatment, mid-dorsal back pain and tenderness developed. A chest radiograph taken 3 weeks later demonstrated a thoracic scoliosis but no abnormal bony nor pulmonary lesions. Simple analgesics were given.

She was delivered of a full term infant on 3rd July, 1982. The baby had Hirschsprung's disease necessi-

tating a colostomy. As the mother wished to breast-feed, subcutaneous heparin was continued.

On 9th August she was experiencing severe back pain and could not walk un-aided. Standing height had diminished by three and a half inches. There was marked lumbar and dorsal kyphosis. Heparin-induced osteoporosis with vertebral collapse was suspected and the heparin was discontinued. Radiographs of the dorsolumbar spine and pelvis revealed generalized severe osteoporosis, with multiple biconcave wedged vertebral bodies. The metacarpal index was normal.

Dietary assessment suggested an adequate calcium intake. Blood tests showed a haemoglobin of 11.9 g/dl, total leucocyte count of 7.9×10^9 cells/l and erythrocyte sedimentation rate of 9 mm/hr. Serum concentrations of calcium, phosphate, alkaline phosphatase, hepatic enzymes, albumen, immunoglobulins and 25-hydroxy-cholecalciferol, thyroid function, parathyroid hormone, 24-hr urinary calcium and cortisol excretions were normal. No paraprotein nor Bence Jones protein was detected.

The pain rapidly abated after stopping the heparin. After 4 weeks in a plaster jacket, an iliac crest bone biopsy was taken. Histology revealed moderate osteoporosis with excess osteoid, characteristic of bone remodelling.

Discussion

There are no previous reports in the English literature of heparin-induced osteoporosis from a dose as low as 10,000 units daily, in the absence of other osteopenic agents, such as adrenal corticosteroids. In addition to the low dose, the duration of treatment (36 weeks) in our case was also relatively short. The treatment period in other cases ranges from 9 weeks in a 20-year-old pregnant patient (Aarskog, Aksnes and Lehmann, 1980) to 5 years in a 53-year-old man with ischaemic heart disease (Griffith *et al.*, 1965). Susceptibility to the skeletal effects of heparin varies between individuals.

The mechanism by which heparin causes osteo-

porosis is unknown. As heparin is a potent inhibitor of a variety of enzymatic reactions, it may exert its effect via enzyme systems involved with bone and mineral metabolism (Avioli, 1975) such as collagen synthesis and maturation, vitamin D activation, and parathyroid induced increases in skeletal cyclic adenosine monophosphate.

The apparent sensitivity in our patient may be due to her pregnant state. During pregnancy and lactation there is an increased demand on the mother for calcium. It is thought that the maternal skeleton is protected from decalcification by a rise in production of calcitonin throughout this period (Stevenson, Hillyard and MacIntyre, 1979). Individuals, who have low levels of calcitonin during pregnancy, may be predisposed to skeletal demineralization. In such a patient, heparin administration may further aggravate the mineral loss. Thus overt heparin osteoporosis may appear in a pregnant patient, where the dose of heparin used is much less than the doses incriminated in non-pregnant cases.

Heparin osteoporosis is rare, but its effects in a

young mother may be devastating. Until the risk factors are established, heparin should be used with caution in pregnancy and discontinued if osteoporosis is suspected.

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