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SHORT REPORTS

Importance of early tumour exacerbation in patients treated with long acting analogues of gonadotrophin releasing hormone for advanced prostatic cancer

We describe the transient stimulatory effect—"tumour flare"—that occurred in patients with locally advanced or metastatic symptomatic prostatic cancer who were treated with either buserelin (D-ser (TBU)^6-LHRH ethylamide) or decapeptyl (D-(Trp)^6-LHRH), agonist analogues of gonadotrophin releasing hormone.

Patients, methods, and results

Forty six men aged 52-82 with symptomatic locally advanced or metastatic prostatic cancer were treated. Five patients received buserelin 200 μg thrice daily, 17 buserelin 200 μg five times daily, and eight buserelin 400 μg thrice daily intranasally, and five men were treated with monthly depot injections of buserelin calculated to release the compound at a mean rate of 150 μg daily. Eleven patients received depot injections of decapeptyl, which released the drug at a mean rate of 50, 100, or 200 μg daily over one month. Treatment was given for between one month and three years. All patients were assessed according to the criteria of the National Prostatic Cancer Project.

Objective improvement occurred in 26 of the 35 patients treated with buserelin and eight of the 11 patients treated with decapeptyl. Seventeen of 32 with bone pain at presentation and one without, however, had increased symptoms. Pain was generally first noted to have increased at 12 hours, became maximal at 36 hours, and eased by the end of the first treatment week. A patient with pelvic lymphadenopathy developed lymphoedema, which resolved after one week of treatment.

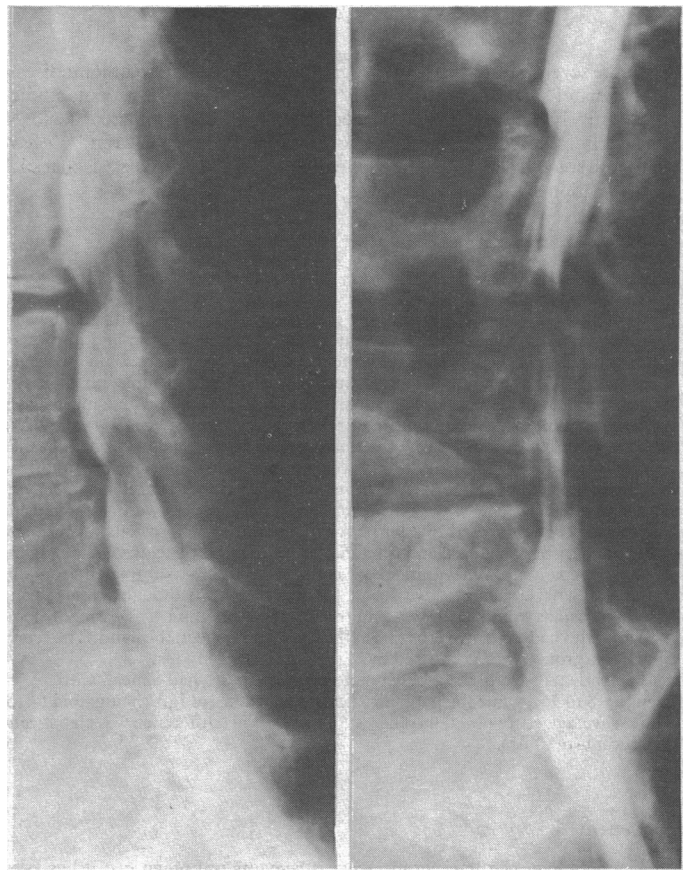
The 17 patients with increased bone pain experienced some additional problems. Four had increased lymphoedema, which was maximal at the end of the first treatment week and had resolved at one month. The serum creatinine concentration in one patient increased from 170 to 600 μmol/l (1·92 to 6·79 mg/100 ml) at the eighth treatment day and decreased at the end of the second treatment week.

The most serious case of tumour flare occurred in a patient presenting with bone pain and grade 4 weakness in the legs, who developed signs of compression of the cord with complete sphincter dysfunction and grade 3 weakness on the 13th treatment day. A pretreatment myelogram had shown indentation of the theca at lumbar disc spaces 1-4 while a myelogram on day 13 showed gross compression of the theca between the third and fifth lumbar vertebrae (figure). This patient had spinal radiotherapy and recovered full neurological function. Fourteen of the 19 patients with tumour flare responded to treatment.

Comment

Agonist analogues of gonadotrophin releasing hormone have provided an appreciable advance in the management of patients with advanced carcinoma of the prostate.[1-3] They are equivalent in efficacy to conventional treatment for prostatic cancer[4] but without its disadvantages. Because of the initial stimulatory effects of all agonists analogues, however, there may be a corresponding temporary increase in symptoms. Of the 46 men in this series, 19 had increased symptoms. In two of this group renal and neurological function was severely compromised.

Labrie *et al* suggested that combined treatment with an antiandrogen and agonist analogues may improve the response and its duration and avoid tumour flare.[5] We have described the incidence and potential importance of the initial stimulatory effects of agonist analogues. These observations do not minimise the contribution of the gonadotrophin releasing hormone



Changes in myelogram in patient with tumour flare in lumbar region. Left: Before treatment. Right: On day 13 of treatment.

agonists to the management of prostatic cancer but emphasise the importance of further investigation into their combined use with antiandrogens.

We thank Anne Buxton, who helped to compile the data.

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Predominant wrist disease in rheumatoid arthritis associated with high concentration of IgA rheumatoid factor

Both the severity of radiological progression and the pattern of joint disease in rheumatoid arthritis are extremely variable. In a series of patients studied prospectively those with high concentrations of IgA rheumatoid factor in their serum showed a predominance of erosions affecting the wrist.[1] We have therefore studied a larger number of patients to test the hypothesis that such an association exists.

Patients, methods, and results

We studied 46 patients with definite or classical rheumatoid arthritis. Twenty three had raised values of IgA rheumatoid factor in their serum and in the rest these values were normal. Nineteen patients in the first group and 21 in the second had raised IgM rheumatoid factor concentrations. The group with high IgA rheumatoid factor values consisted of six men and 17 women with a mean age of 56·5 years (range 34-78) and a mean duration of disease of 8·7 years (range 2-24), and the group with normal IgA rheumatoid factor values comprised eight men and 15 women with a mean age of 54·6 years (range 35-74) and a mean duration of disease of 7·6 years (range 2-25). Rheumatoid factor was measured by an enzyme linked immunosorbent assay.[2] Radiographs of hand and wrist were assessed using the defect score described by Sharpe *et al*,[3] the scores for erosions in wrist and hand (metacarpophalangeal and proximal and distal interphalangeal joints) being recorded separately. The number of hand erosions was subtracted from the number of wrist erosions to give a score for each patient. Although a ratio of hand to wrist erosions would have been a more satisfactory method of assessment, some patients who had extensive erosions in the wrist had none in the hand. The scores in the two groups were compared by Wilcoxon's rank sum test.

The patients with high IgA rheumatoid factor values had a mean score of 7·1 (range −8 to 36), while the patients with normal values of IgA rheumatoid factor had an average score of −0·4 (range −32 to 18). This difference was statistically significant ($p<0·05$).

Comment

The aetiology of rheumatoid arthritis remains unknown but it has been suggested that the disease may represent several disorders with different immunogenetic backgrounds and environmental trigger factors. This possible heterogeneity makes the search for aetiological factors very difficult. It therefore seems reasonable to look for subgroups of disease and that studying these separately may help elucidate the problem. IgA rheumatoid factor has already been associated with a poor prognosis in rheumatoid arthritis.[1] Finding an association with a particular radiological pattern lends further support to the view that patients with rheumatoid arthritis and high values of IgA rheumatoid factor may represent a subgroup of the disease. This association has been shown despite our patients having established disease, for which several had received "specific" or disease modifying agents (gold salts, penicillamine, steroids) which lower IgA rheumatoid factor values (unpublished observations). Burns and Calin have reported a different radiological pattern in patients with seronegative rheumatoid arthritis. (Some patients who are conventionally seronegative have high values of IgA rheumatoid factor in their serum.) They interpreted their findings as suggesting that seronegative rheumatoid arthritis has a different pathological mechanism from seropositive rheumatoid arthritis.[4] Other studies categorising the radiological progression of rheumatoid arthritis have noted an association between rheumatoid factor titre and severity of erosive disease but have not commented on the pattern of joint erosion.[3,5]

Though it is unclear why IgA rheumatoid factor should be a marker for a disease subset of rheumatoid arthritis, we believe that IgA rheumatoid factor deserves closer examination in patients with rheumatoid arthritis.

We acknowledge the help of Dr Ingvar Teitsson, who performed the rheumatoid factor assays.

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The neglected hospital wheelchair

Hospital wheelchairs are in constant use and have to withstand considerable wear. We observed that many were in a poor state of repair and that patients had sustained injuries owing to faulty wheelchairs. A previous study identified some faults in hospital wheelchairs,[1] but the prevalence and implications of such faults have not been assessed. We examined this problem.

Methods and results

We inspected all the transit and self propelled wheelchairs in a geriatric hospital (215 beds) and all those in the medical wing of a teaching hospital (204 beds). The type of tyre (pneumatic or solid) was recorded, and the backrest, seat, armrests, and footrest plates were examined for defects. The pneumatic tyres were inspected for wear and state of inflation. They were recorded as worn if the central part of the tread was indistinct, soft if there was insufficient air to support a person sitting in the wheelchair and excessive bulging of the tyre occurred, and deflated if there was clearly no air in the inner tube. The deflated tyres were pumped up, their valves tested, and the tyres later re-examined to determine if a puncture was present. Steering and brakes were tested with a person sitting in the wheelchair. Each brake was applied separately and recorded as defective if the wheelchair could still be moved easily.

To evaluate injuries to patients caused by defective wheelchairs we prospectively investigated for two months all accidents on our geriatric unit in which wheelchairs played a part and that required the completion of a hospital accident report.

There were 93 wheelchairs in the geriatric hospital and 30 in the medical wing. Only 21 and seven, respectively, were free from faults. The table gives details of the faults found. Wheelchair arms were termed dangerous when their foam covering had been torn away, exposing the sharp ends of the bolts inside. Spikes on the footrest plates were sharp vertical projections that remained on the