Early treatment of avascular necrosis in systemic lupus erythematosus

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SUMMARY Avascular necrosis (AVN) of the hips is associated with significant disability, and the majority of established cases require major surgery. In a retrospective analysis of 185 patients with systemic lupus erythematosus (SLE) 13 (7%) were found to have AVN. Of these, six had Raynaud’s phenomenon, all had been on corticosteroids, and one had digital vasculitis. The mean duration of corticosteroid therapy was two years (range four months to five years). Five patients developed AVN two to 10 years after discontinuing steroids. The mean duration of disease at the onset of AVN was 6.85 years (range 1–19 years), and the mean age at onset of AVN was 31 years. Ten patients had severe multisystem involvement. None of the patients abused alcohol. Surgery was performed on 11 hips. Three had total hip replacement for stages 3 and 4 and seven had core decompression for stages 1 and 2. AVN progressed in two (28%) of these patients. In another patient core decompression failed for technical reasons. She subsequently required total hip replacement. The early detection of AVN to avoid the need for major surgery is stressed.

Key words: corticosteroid, osteonecrosis, core decompression.

Avascular necrosis in systemic lupus erythematosus (SLE) was first described by Dubois in 1960. Since then numerous reports have appeared, the prevalence ranging from 2.8% to 11% in adults and up to 40% in children. Although there are isolated reports of AVN occurring in patients who have not received corticosteroid therapy, in most cases this complication has developed in patients who have received high dose corticosteroids at some stage of the disease. It has not been established whether it is a high daily dose or the total dose which increases the risk of AVN. The pathogenesis of AVN is not fully understood, and the fact that in some cases it develops many years after the cessation of therapy suggests that other factors, as yet unidentified, are involved.

Hungerford and Zizic noted a relationship between Raynaud’s phenomenon and AVN, but this has not been confirmed in other reports. A retrospective study was undertaken to determine the prevalence of AVN in patients attending a large lupus clinic and to determine the role of severity of disease, corticosteroid therapy, and Raynaud’s phenomenon in its genesis. The results of core decompression in the management of early cases are reported.

Patients and Methods

The records of 185 patients attending the Lupus Clinic at Groote Schuur Hospital during a 12 year period from March 1972 to March 1984 were studied retrospectively. The following data were recorded in those who developed AVN: overall severity of the disease, based on the nature and number of organs involved, the need for corticosteroid or immunosuppressive therapy, and the periods of activity; the
presence or absence of Raynaud's phenomenon and of vasculitis; the therapy administered, with particular reference to the total dose and duration of corticosteroid therapy; the onset of AVN in relation to corticosteroid therapy and to the duration of disease; the presence of diseases known to be associated with AVN such as diabetes mellitus, hyperlipidaemia, and pancreatitis; alcohol consumption.

Radiographs were staged according to criteria proposed by Arlet and Ficat for AVN. \(^{15}\) The number and nature of surgical procedures performed were recorded and the results of these procedures evaluated. The period of follow up after surgery was between four months and 12 years.

More recently, radiological involvement of one hip has been followed by a \(^{99}\)Tc bone scan to assess the contralateral hip. If this was positive intraosseous pressure studies, both resting and stress, were performed. Raised pressures were then treated by core decompression, as described by Hungerford and Zizic. \(^{11}\)

**Results**

AVN developed in 13 (7\%) of the 185 patients studied. All were women aged between 17 and 50 years (mean 31 years). Eleven were Cape coloured and two were South African Caucasian. Eleven of the 13 patients fulfilled the revised American Rheumatism Association criteria for the classification of SLE. \(^{16}\) Of the other two patients, one had a butterfly rash and a positive LE cell preparation, and the other had nephritis, pancytopenia, and psychosis.

In nine of these 13 patients (69\%) AVN developed before the age of 40 years. Of these, six were under 30 years of age. The duration of disease at onset of symptoms ranged from one to 19 years (mean 6-85 years). Raynaud's phenomenon was present in six (46\%), and one patient developed a vasculitic leg ulcer during the course of the illness.

Ten (77\%) patients were assessed as having severe SLE, two of whom died, one from cerebral involvement and the other from renal involvement.

All 13 patients had received corticosteroid therapy at some stage of the disease, and in five immunosuppressive agents were used in addition. The mean total dose of corticosteroid therapy was 15 g (range 3-2--47-0 g), and the mean duration of therapy was two years (range four months to four years).

The daily dose of corticosteroids did not exceed 60 mg. In 10 patients AVN developed within two years of initiating corticosteroid therapy, and in the remaining three patients (23\%) it developed between two and five years after corticosteroid treatment was started. Eight patients were receiving corticosteroid therapy at the time of diagnosis, with doses ranging from 2-5 mg to 10 mg daily. In the five patients who were not receiving corticosteroid therapy at the time the cessation of corticosteroids and the development of AVN ranged from two to 10 years (mean six years). None of the patients had active SLE at the time of developing AVN.

The commonest site involved was the femoral head (92\%), which was bilateral in 38\% of patients at presentation. The only other sites were the humeral head in two (15\%) and the talus and lunate in one patient. Surgery was confined to the hip and was performed in 11 of the 13 patients. One patient with stage 3 radiological change (1970) had an abduction osteotomy, while a further two had unilateral interposition arthroplasties. The only patient with stage 4 osteonecrosis had a total hip replacement. Core decompression was performed in the remaining patients with stage 1 and 2 radiological changes. Core decompression was performed in two patients with symptoms graded as stage 2 radiologically, and as a 'prophylactic' procedure in five patients who were asymptomatic, with no radiological changes but with a positive bone scan (opposite hip in unilateral disease). The period of follow up after surgery ranged from four months to 12 years (median 4-5 years).

Surgery was successful in all the patients who had arthroplasties, except for mild pain in one patient who had a hemiprostheses inserted. Of the two patients who were asymptomatic at the time of core decompression (radiological stage 2), one had ongoing symptoms postoperatively and has subsequently developed stage 4 radiological change. Of the five asymptomatic patients who had core decom-

<table>
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<th>Table 1</th>
<th>Surgical treatment carried out for avascular necrosis in 11 hips of patients with SLE</th>
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<td>Stage</td>
<td>Procedure</td>
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<tr>
<td>1</td>
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<td>3</td>
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<tr>
<td>3</td>
<td>Osteotomy</td>
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<td>3</td>
<td>Bicentric hemiarthroplasty</td>
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<td>4</td>
<td>Bipolar total hip replacement</td>
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Asymptomatic (1) Recurrence of pain (1) Asymptomatic (1) Asymptomatic (1) Deterioration (1) Asymptomatic (3) Deterioration (1) Asymptomatic (1) Deterioration and total hip replacement (1)
pression, one progressed to stage 3 radiologically, and in one patient, in whom the procedure failed for technical reasons, the lesion progressed to stage 4 and a total hip replacement was done (Table 1).

The accompanying histogram (Fig. 1) has been constructed using the age at onset of AVN as the primary key in ascending order. There is no apparent relation between the age at onset or the duration of disease. Nor is there any relation between these parameters and the total dose or duration of steroid therapy.

**Discussion**

AVN is a serious and not infrequent complication of SLE. The observations in early studies of a high prevalence of AVN in young patients with SLE, and of the strong association of AVN with corticosteroid therapy have been confirmed in several subsequent series. The mechanisms whereby corticosteroids produce AVN are unknown. It has not been established whether it is the size of the daily dose, the total dose, the duration of therapy with corticosteroids, or all three which predispose to AVN.

Rabbits treated with cortisone developed changes of AVN in the humeral heads as early as three weeks after administration. There are also several reports of AVN developing in patients with Cushing's syndrome, in patients with pemphigus who have been on prolonged corticosteroid therapy (a non-vasculitic disease), and in renal transplant patients.

The localisation of the lesion to the subchondral area of bone suggests a number of possible pathogenetic mechanisms. These have recently been reviewed. It is well established that corticosteroids produce a disturbance of lipid metabolism. Solomon has proposed that this results in an enlargement of the adipose cells, thus occluding the intraosseous veins and causing an increase of intraosseous pressure. Crues, however, postulates that AVN results from intravascular occlusion of small arterioles by fat droplets and notes the similarity of the lesion with those encountered in caisson disease, Gaucher's disease, and sickle cell anaemia. He also observes that the hypoxia consequent upon arterial embolism results in lymphocyte hyper- trophy. Hungerford has implicated vasculitis as an additional factor, but the exact pathogenesis of steroid induced AVN remains speculative.

AVN has been reported in association with cytotoxic agents and non-steroidal anti-inflammatory drugs (NSAIDs) used alone. All the patients in our study had received corticosteroids, and it is therefore not possible to comment on the role of the former agents in the pathogenesis of AVN.

Ethanol abuse was not a factor in this study nor were any of the patients clinically hypothyroid.

Our findings are in agreement with those of most other studies as regards the prevalence of AVN and the predilection for younger patients and support the view that corticosteroids have a pathogenetic role in the development of the disease. From our data it is not possible to determine whether it is the size of the daily dose or the total dose of corticosteroids that places the patients at risk. Why AVN develops months or years after cessation of corticosteroid therapy in some patients cannot be explained, nor can the reason why all patients with SLE on high doses of corticosteroids do not develop AVN.

There have been reports of patients with SLE...
developing AVN without having received corticosteroids. Patients with SLE who receive steroids generally have more severe disease, and it is possible that disease severity itself may be a pathogenetic factor.

A clearer understanding of the pathogenesis and earlier diagnosis has modified the treatment of AVN. Early disease is treated by metaphysical decompression with core biopsy. Abduction and rotation osteotomies are still used for certain cases of stage 2 and 3 AVN. The later stages of the disease are treated by bipolar hemiarthroplasty or total hip replacement. Stage 4 disease reflects a failure of early detection.

Until recently, treatment of AVN has been aimed at measures which reduce pain and discomfort. This was generally achieved by reduction of weight bearing loads and the use of analgesics and NSAIDs. Hungerford has shown clearly that core decompression prevents progression to stages 3 and 4, while conservative measures are invariably associated with a subsequent need for major surgery in the form of arthroplasty. There is, therefore, no longer a place for conservative management of AVN.

Our results of core decompression are disappointing compared with those of other series, but the numbers are too small at this stage to be meaningful. The failure rate for stage 1 disease was 25%, progression having occurred within six months of decompression. In stage 2 disease the failure rate was 50%, and it is probable that cancellous bone or vascularised pedicle grafting of the femoral head will prove the most effective therapy for this stage.

It is suggested that a significant number of patients with clinically and radiologically undetectable AVN have a significant increase of intraosseous pressure. A prospective study with a technetium bone scan is in progress to evaluate the prevalence of asymptomatic AVN. Patients will have scans and pelvic radiology at six month intervals. Intraosseous venous pressure studies and core decompression will be offered to patients who develop positive scans even in the absence of symptoms, as good results have been claimed in early cases.

It is hoped that with early detection of AVN core decompression will be developed to the point where major surgery can be avoided.

References