LEADING ARTICLE

ISCHAEMIC NECROSIS OF BONE

S C Ng

SINGAPORE MED J 1991; Vol 32: 386-387

Ischaemic necrosis of bone is the process whereby a segment of bone is damaged and finally dies as a result of compromised blood supply. This name is preferable to avascular necrosis as the bone is only truly avascular in the end stage of the disease. Other names used to describe this condition include aseptic necrosis (to emphasize the lack of infection), osteonecrosis and osteochondritis dessicans (mainly for smaller bones).

Dubois first described ischaemic necrosis in patients with Systemic Lupus Erythematosus (SLE) in 1960[1]. Since then it is recognised as an important complication occurring in about 4 to 11% of SLE patients[2]. A local series of 56 consecutive SLE patients revealed 12 patients with radiographic evidence of ischaemic necrosis of the femoral head ie 21%[3]. Ischaemic necrosis of the bone is therefore an important problem in SLE patients in Singapore. In fact, as this study looked only at the hips and used plain X-rays to screen for the condition, the actual problem of ischaemic necrosis of all grades in all bones may even be greater. In general, involvement of multiple sites are common; with the femoral head, tibial plateau and humeral head being most often involved[2]. In one study, using bone marrow pressure measurement, an invasive but sensitive technique to study ischaemic necrosis, 81% of the patients had multiple bones involved. Of these, 81% had bilateral hip involvement. Humeral head involvement was also seen[4].

Treatment with glucocorticoids has often been blamed as the major predisposing factor to the development of ischaemic necrosis in SLE[5]. However, it is not clear as to which aspect of therapy is associated with higher risk. Many show that the total steroid dose is important; others show that it is the maximal steroid dose given for a particular period; as well as mode of administration (daily vs alternate day dosing). The local study did not show a significant difference between the duration of steroid therapy, the mean prednisolone dose per day, the total cumulative dose and the maximum dose given in the group of SLE patients with ischaemic necrosis verses the group without ischaemic necrosis[3].

Many mechanisms whereby glucocorticoids cause ischaemic necrosis has been suggested. Glucocorticoids cause lipocyte hypertrophy which may lead to compression of circulation and sinusoidal ischaemia[6]. Fat embolism to the femoral head subchrondral arterioles and capillaries is another possible mechanism[7]. Patients who develop Cushingnoid facies appear to be more prone to the development of ischaemic necrosis[3, 8]. Perhaps the redistribution of fat centrally has indeed compressed the femoral vessels. In the local study, 67% of those SLE patients who developed ischaemic necrosis had Cushingnoid facies whereas only 27% of those who did not have radiographic changes were Cushingnoid.

Ischaemic necrosis has been reported to occur in SLE patients not given steroids, but this is rare. Possible mechanisms for the SLE process causing ischaemic necrosis include vasculitis[9], Raynaud's phenomenon[10] and thrombosis related to the anti-phospholipid syndrome[11].

It may not be just steroids but rather several factors that act synergistically to produce ischaemic necrosis. For example, Raynaud's phenomenon appears to make SLE patients more prone to ischaemic necrosis and a lower mean dose of steroids may be required to produce this complication[8].

Ischaemic necrosis is often painful. One study shows that 85% of the patients are symptomatic[12]. Pain on motion and even at rest, with limitation in joint motion have been known to precede radiographic changes by several months to years.

Interestingly, our local study found pain to be an insensitive index of ischaemic necrosis as 8 of the 12 patients with ischaemic necrosis were asymptomatic[3].

X-rays are used in the diagnosis and staging of ischaemic necrosis. An easy scheme based on the criteria of Arlet and Ficat is as follows[8]:

Stage I	X-rays are normal, at most minimal osteopaenia
Stage II	Patchy osteoporosis and osteosclerosis often in a wedge-shaped area
Stage III	Crescent sign, translucent subcortical band appearing as a fine line under and parallel to the articular cortex
Stage IV	Subchondral collapse with flattening of articular surface of discrete discontinuity and subsequent destruction of the joint.

Clearly the use of X-rays alone will miss all the patients with Stage I disease. Other non-invasive imaging techniques have been tried. This includes isotope bone scanning with pertechnetate or sulphur colloid but there is a high incidence of false positive and false negative results[13]. CT scan is available and recently, Magnetic Resonance Imaging has been shown to be very useful in detecting early femoral head ischaemic necrosis[14]. Of course although the newer techniques are more sensitive, it involves more radiation and is much more expensive. Once there is compromised blood flow, the process of ischaemic necrosis starts and usually progresses. The rate of progression is unpredictable. Some believe that if steroids can be stopped, the process can be halted. Hence it is very important to be able to diagnose ischaemic necrosis early and steroids stopped if possible.

Management starts with increased awareness of the problem, early diagnosis and conservative treatment. The results of the local study suggest that X-rays of the hips is an inexpensive, simple and useful screening test for diagnosis of asymptomatic ischaemic necrosis. Perhaps this should be routinely

Department of Medicine
Alexandra Hospital
Alexandra Road
Singapore 0314

S C Ng, MBBS, M Med (Int Med), AM
Senior Registrar

done for patients who develop Cushingnoid facies while on glucocorticoids. For patients who have normal hip X-rays but complain of hip pain and in those in whom ischaemic bone necrosis is suspected, Magnetic Resonance Imaging is a far more sensitive yet non-invasive test.

In patients who have been diagnosed to have ischaemic bone necrosis it is important to critically review the use of glucocorticoids. This should be stopped as soon as possible. Those with very mild disease may be quickly tapered off, those who need a little steroids may be given hydroxychloroquine which is very useful for mild lupus. Those who are more sick may need steroid sparing cytotoxic drugs like azathioprine or cyclophosphamide. It will be best to discontinue the glucocorticoids completely but sometimes the patient does require some steroids to control the symptoms of the disease. These patients who continue to take steroids are certainly at risk for involvement of the other bones. They have to be told of this risk. It is indeed a fine balance between allowing untreated inflammation or risking the toxic side effects of any of the alternate drugs that we use to treat SLE. The patient has to be told all this.

Treatment of the affected hips begins with non-weight bearing crutches for several months followed by partial weight bearing. Non-steroidal anti-inflammatory drugs (NSAID's) like Indomethacin 50 mg qds has been found to be useful. Often, high doses like this are required and we have to beware of the problem of NSAID induced nephropathy. Patients particularly at risk for NSAID nephropathy are those with renal impairment and hypertension, problems often seen in SLE patients requiring high dose steroids, the same patients at high risk for ischaemic necrosis of the bone.

The orthopaedic surgeon should be consulted early. Conservative surgical treatment has been attempted in early ischaemic necrosis of the femoral head. This involves core decompression, a process whereby a core of bone is removed from the ischaemic head to reduce the intraosseous pressure. Results from a controlled study was very impressive and was best for Stage I disease[15]. Other procedures include osteotomy to alter joint mechanics and reduce weight on the ischaemic femoral head. Cortical bone grafts have been used to provide support for the subcortical bone. But when the joint is very badly damaged resulting in very painful disability total hip replacement has been done. Results have been good in the short term. However total hip replacement is often delayed for as long as possible as the patients are much younger than the others requiring surgery. There is also an increased risk of post-operative complications. These includes infections, deep venous thrombosis, poor healing and loosening of the prosthesis due to associated steroids induced osteoporosis.

In this issue of the Singapore Medical Journal, C K Low et al[17] report that total hip replacement can be done fairly safely in SLE patients with painful disabling ischaemic necrosis of the hips. Follow up result at about four years was good. This is reassuring. We now look forward to more reports to tell us what to do in earlier cases, before the development of painful disability, like whether core decompression can be done successfully here.

References

1) Dubois EL, Cozen L : Avascular (aseptic) bone necrosis associated with SLE JAMA 1960; 174 : 966-71.
2) Dubois EL, Wallace DJ .eds: Clinical and laboratory manifestations of SLE in Dubois' Lupus Erythematosus. 3rd Edition. Lea & Febiger : Philadelphia 1987 : 317 - 449
3) Ng SC, Wang WY, Sundrum F et al : Avascular Necrosis of the hips in SLE patients in Singapore - abstract presented at the 2nd International Conference on SLE, Singapore, 1989
4) Zizic TM, Hungerford DS, Stevens MB : Ischaemic Necrosis in SLE - The early diagnosis of Ischaemic Necrosis. Medicine 1980; 59 : 134-42.
5) Weiner ES, Abeles M : Aseptic necrosis and glucocorticoids in SLE : A re-evaluation. J Rheumatol 1989; 16 : 604 - 8
6) Wang G, Swee DE, Reger SI et al : Fat cell changes as a mechanism of avascular necrosis of the femoral head in cortisone treated rabbits. J Bone Surg 1977; 59 : 729 - 35
7) Jones JP, Engelman EP, Stemback HL et al : Fat embolism as a possible mechanism producing avascular necrosis (abstract) Arthritis Rheum 1965; 8:448.
8) Zizic TM : Osteonecrosis in Primer on the Rheumatic Diseases, 9th Edition Schumacher HR. ed. Arthritis Foundation: Atlanta Georgia 1988 : 253 - 7.
9) Siemsen JK, Brook J, Meister L : Lupus Erythematosus and Avascular Necrosis : A clinical Study of three cases and Review of the literature. Arthritis Rheum 1962; 5 : 492 - 501.
10) Klipper AR, Stevens MB, Zizic TM et al : Ischaemic Necrosis of Bone in SLE. Medicine 1976; 55 : 251- 7.
11) Asherson RA, Junger P, Liote F et al : Ischaemic Necrosis of Bone Associated with the Lupus Anticoagulant and Antibodies to Cardiolipin. Proceedings of the XVIth International Congress of Rheumatology, Sydney, Australia, May 1983 : 373
12) Zizic TM, Marcoux C, Hungerford DS et al : The early diagnosis of Ischaemic Necrosis of the Bone. Arthritis Rheum 1986; 29 : 1177 - 86
13) D Ambrosia R, Riggins R, Stadalnik R et al : 99mTc Diphosphonate scintigraphy validated with Tetracycline labelling. Clin Orthop 1976; 121 : 143 - 8.
14) Kalunian KC, Hahn BH, Bassett L : Magnetic Resonance Imaging Identifies Early femoral Head ischaemic necrosis in Patients receiving systemic glucocorticoid therapy. J Rheumatol 1989; 16 : 959 - 63
15) Hungerford DS, Zizic TM : Ischaemic Bone Necrosis in Systemic Lupus Erythematosus : The treatment of Ischaemic Bone Necrosis of the Bone. Medicine 1980; 59 : 143 - 8
16) Prupas HM, Patzakis M, Quismorio FP : Total Hip Arthroplasty for Avascular Necrosis of the Femur in SLE. Clin Orthop 1981; 161 : 186 - 90.
17) Low CK, Lai CH, Low YP : Results of Total Hip Replacement in Systemic Lupus Erythematosus. Singapore Med J 1991 : 32: 391-2