

## Research letter

## Osteonecrosis of the femoral head in men following short-course corticosteroid therapy: a report of 15 cases

Michael D. McKee, James P. Waddell, Patricia A. Kudo, Emil H. Schemitsch, Robin R. Richards

Osteonecrosis has long been recognized as a complication of systemic steroid use and was initially believed to occur only in patients who received high doses (equivalent to more than 4000 mg of prednisone) for extended periods (3 months or longer).<sup>1-6</sup> Previous sporadic case reports have described patients in whom osteonecrosis developed following relatively brief courses (7 days) of low-dose, orally administered steroid medication.<sup>7-11</sup> The exact mechanism by which these medications cause osteonecrosis remains elusive.<sup>1,3,5,7,12,13</sup> Current research has focused on the development of a hypercoagulable state, with subsequent impaired fibrinolysis and venous thrombosis in bone.<sup>14,15</sup>

At a tertiary care, university-affiliated orthopedic unit specializing in the treatment of osteonecrosis of the femoral head, we reviewed the charts of patients who pre-

sented from 1986 to 1996 with osteonecrosis of the femoral head who had received a single short-course of corticosteroid medication within the 3 years before presentation (Table 1). We identified 15 patients who met the inclusion criteria. An exhaustive examination for other potential risk factors revealed only 3 patients with such factors; none of these risk factors was felt to be sufficient, in isolation, to cause osteonecrosis.<sup>13-21</sup>

All 15 patients were male. Their mean age was 32.2 (range 20-41) years. The mean steroid dose in equivalent milligrams of prednisone was 850 (range 290-3300) mg. The mean duration of drug therapy was 20.5 (range 7-39) days. The mean time from administration of steroids to the development of hip symptoms was 16.6 (range 6-33) months. There was significant diagnostic delay in the ma-

**Table 1: Characteristics of 15 patients with osteonecrosis of the femoral head following short-course corticosteroid therapy**

Case	Age, yr	Indication for steroid therapy*	Duration of therapy, d	Dose, mg†	Other medical conditions	Time from therapy to hip pain, mo
1	38	Pneumonia	20	550	None	7
2	35	Brain abscess	6	435	Recurrent otitis media	8
3	33	Aneurysm	26	3300	Alcoholism	16
4	34	Bells palsy	36	Unknown	None	31
5	30	Asthma	39	1050	Asthma	6
6	36	Arthralgia	20	620	Type 2 diabetes mellitus	28
7	34	Migraine	20	700	Migraine	12
8	26	Poison ivy	21	660	None	8
9	32	Poison ivy	14	560	None	11
10	35	Poison ivy	7	290	Alcoholism	23
11	21	Mononucleosis	14	620	None	12
12	20	Optic neuritis	28	840	Hip dislocation	33
13	36	Pneumonia	14	700	None	9
14	32	Optic neuritis	28	900	None	16
15	41	Bee sting	14	700	None	29

\*Prednisone was prescribed in 13 cases and dexamethasone in 2.

†Doses are listed in equivalent milligrams of prednisone.

majority of cases, such that symptoms had often been present for many months or years before referral. All of these patients subsequently required surgical intervention.

A potential criticism of our study is that the osteonecrosis seen in our patients may have been either idiopathic or associated with some other (as yet unknown) precipitating factor. Although this is possible, we think that the number of cases in this series provides a strong link between steroid administration and the subsequent development of osteonecrosis in these patients. We do not, however, attempt to define the incidence of this complication, because the total patient population who received steroid medication from which our patients were identified remains unknown.

Osteonecrosis of the femoral head is a condition with a poor natural history that can be crippling, especially in young active patients. Our series does not provide conclusive proof that there is a cause-effect relation between short-course steroid therapy and osteonecrosis. However, the number of patients seen with this condition in our unit is strong presumptive evidence that some association exists. When weighing the risks and benefits of the use of steroid medication, especially in self-limited diseases or those for which steroids are of dubious benefit, clinicians should be aware of this potential problem. Patients should be informed of the potential risk of osteonecrosis following the use of steroid medication. Complaints of hip pain in people who have previously been prescribed steroids should produce a high index of suspicion for underlying osteonecrosis of the femoral head. Although early treatment before collapse of the femoral head occurs is beneficial,<sup>22</sup> prevention of this complication is preferable.

This article has been peer reviewed.

Dr. McKee is Assistant Professor in the Division of Orthopaedics, Department of Surgery, Dr. Waddell is Professor of Orthopaedics, Dr. Kudo is Research Assistant, Division of Orthopaedics, Dr. Schemitsch is Associate Professor, Division of Orthopaedics, Department of Surgery, and Dr. Richards is Associate Professor, Division of Orthopaedics, St. Michael's Hospital, University of Toronto, Toronto, Ont.

Competing interests: None declared.

Contributors: Dr. McKee was the principal investigator and contributed to the writing of the article. Dr. Waddell was the senior author and provided clinical observations and data. Dr. Kudo contacted, assessed and followed up patients and contributed to the writing of the article. Dr. Schemitsch assisted with the statistical analysis and contributed to the writing of the article. Dr. Richards contributed to the writing of the article and provided clinical care. Drs. Schemitsch and Richards also provided insight from the literature.

## References

1. Haajanen J, Saarinen O, Laasonen L, Kuhlback B, Edgren J, Slati P. Steroid treatment and aseptic necrosis of the femoral head in renal transplant recipients. *Transplant Proc* 1984;16(5):1316-9.
2. McCluskey J, Gutteridge DH. Avascular necrosis of bone after high doses of dexamethasone during neurosurgery. *BMJ* 1982;284:333-4.
3. Sutton RD. Aseptic necrosis of bone: a complication of corticosteroid therapy. In: Meyler L, Peck HM, editors. *Symposium on drug induced disease*. New York: Excerpta Medica Foundation; 1968. p. 171-6.

4. Ficat RP, Arlet J. Cortisone associated necrosis of bone. In: Hungerford D, editor. *Ischemia and necrosis of bone*. Baltimore: Williams and Wilkins; 1980. p. 136-40.
5. Fisher DE, Bickerl WH. Corticosteroid induced avascular necrosis: a clinical study of seventy-seventy patients. *J Bone Joint Surg Am* 1971;53:859-73.
6. Heiman WG, Freiberg RH. Avascular necrosis of the femoral head and humeral heads after high dose corticosteroid therapy. *N Engl J Med* 1960; 263:672-5.
7. Fast A, Alon M, Weiss S, Zer-Aviv FR. Avascular necrosis of bone following short-term dexamethasone therapy for brain edema. *J Neurosurg* 1984;61:983-5.
8. Good AE. Bilateral aseptic necrosis of femur following a 16-day course of corticosteroid. *JAMA* 1974;228:497.
9. O'Brien TJ, Mack GR. Multifocal osteonecrosis after short term high-dose corticosteroid therapy. *Clin Orthop* 1990;279:176-9.
10. Taylor LJ. Multifocal avascular necrosis after short-term high-dose steroid therapy. A report of three cases. *J Bone Joint Surg Br* 1984;66:431-3.
11. Sambrook PN, Hassall JE, York JR. Osteonecrosis after high dosage, short-term corticosteroid therapy. *J Rheumatol* 1984;11:514-6.
12. Precious D, Armstrong J, Morrison A, Field C. The incidence of total hip replacement in orthognathic surgery patients receiving short-term steroid therapy. *J Oral Maxillofac Surg* 1992;50:956-7.
13. Anderton JM, Helm R. Multiple joint osteonecrosis following short-term steroid therapy. *J Bone Joint Surg Am* 1982;64:139-41.
14. Glueck CJ, Freiberg R, Glueck HI, Henderson C, Welch M, Tracy T, et al. Hypofibrinolysis: a common, major cause of osteonecrosis. *Am J Hematol* 1994; 45:156-66.
15. Glueck CJ, Freiberg R, Glueck HI, Tracy T, Stroop D, Wang Y. Idiopathic osteonecrosis, hypofibrinolysis, high plasminogen activator inhibitor, high lipoprotein(a), and therapy with Stanozolol. *Am J Hematol* 1995;48:213-20.
16. Humphreys S, Spencer JD, Tighe JR, Cumming RR. The femoral head in osteonecrosis. *J Bone Joint Surg Br* 1989;71:205-8.
17. Jacobs B. Alcoholism-induced bone necrosis. *NY State J Med* 1992;92(8):334-8.
18. Houggaard K, Thomsen PB. Traumatic posterior dislocation of the hip: prognostic factors influencing the incidence of avascular necrosis of the femoral head. *Arch Orthop Trauma Surg* 1986;106:32-5.
19. Urbaniak JR, Coogan PG, Gunneson EB, Nunley JA. Treatment of osteonecrosis of the femoral head with free vascularized fibular grafting. *J Bone Joint Surg Am* 1995;77:681-94.
20. Hastings DE, MacNab I. Spontaneous avascular necrosis of the femoral head. A clinical and pathological review. *Can J Surg* 1965;8:68-83.
21. Sutton RD, Benedek TG, Edwards GA. Aseptic bone necrosis and corticosteroid therapy. *Arch Intern Med* 1963;263:672-5.
22. Louie BE, McKee MD, Richards RR, Mahoney JL, Waddell JP, Beaton DE, et al. Treatment of osteonecrosis of the femoral head by free vascularized fibular grafting: an analysis of surgical outcome and patient health status. *Can J Surg* 1999;42(4):274-83.

Reprint request to: Dr. Michael D. McKee, Ste. 800, 55 Queen St. E, Toronto ON M5C 1R6; fax 416 359-1601; mckee@the-wire.com



Your window on today's health news

[www.cma.ca/cmaj](http://www.cma.ca/cmaj)