Research letter

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

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Steonecrosis 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).¹⁻⁶ Previous sporadic case reports have described patients in whom osteonecrosis developed following relatively brief courses (7 days) of lowdose, orally administered steroid medication.⁷⁻¹¹ The exact mechanism by which these medications cause osteonecrosis remains elusive.^{1,3,5,7,12,13} Current research has focused on the development of a hypercoaguable state, with subsequent impaired fibrinolysis and venous thrombosis in bone.^{14,15}

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 presented 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.¹³⁻²¹

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-

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

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

*Prednisone was prescribed in 13 cases and dexamethasone in 2. †Doses are listed in equivalent milligrams of prednisone.

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jority 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,²² prevention of this complication is preferable.

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References

- 1. Haajanen J, Saarinen O, Laasonen L, Kuhlback B, Edgren J, Slatis 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.
- Sutton RD. Aseptic necrosis of bone: a complicaton of corticosteroid therapy. In: Meyler L, Peck HM, editors. Symposium on drug induced disease. New York: Excerpta Medica Foundation; 1968. p. 171-6.

- 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.
- Fisher DE, Bickerl WH. Corticosteroid induced avascular necrosis: a clinical study of seventy-seventy patients. J Bone Joint Surg Am 1971;53:859-73
- Heiman WG, Freiberge 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. 7 Neurosurg 1984;61:983-5.
- Good AE. Bilateral aseptic necrosis of femur following a 16-day course of corticotropin. 7AMA 1974;228:497.
- 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 ther-apy. 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. Glueck CJ, Freiberg R, Glueck HI, Henderson C, Welch M, Tracy T, et al.
- 14. Hypofibrinolysis: a common, major cause of osteonecrosis. Am 7 Hematol 1994; 45:156-66
- Glueck CJ, Freiberg R, Glueck HI, Tracy T, Stroop D, Wang Y. Idiopathic os-15. teonecrosis, 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. Hougaard K, Thomsen PB. Traumatic posterior dislocation of the hip: prog-
- nostic 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 osteo-
- necrosis 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.
- 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.

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