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FATTY DEGENERATION OF OSTEOCYTES OF THE FOURTH METATARSUS IN PATIENTS WITH IDIOPATHIC NECROSIS OF THE FEMORAL HEAD

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INDEXING WORDS

hip;osteonecrosis;hyperlipidemia;foot;metatarsus

SYNOPSIS

Bone biopsies from the femoral head and the fourth metatarsal head were obtained in 21 patients with idiopathic necrosis of the femoral head (INFH). Electron microscopy revealed fatty degeneration of osteocytes in 13 femoral heads and 11 metatarsal heads. Fifteen of the 21 patients (71.4%) had these osteocytic changes in either the femur and/or metatarsus. Serum chemistries in these 21 patients demonstrated hyperlipidemia in 12 (57%). Similar biopsies of the metatarsus in 13 control patients with rheumatoid arthritis disclosed no fatty degeneration of osteocytes except in one patient treated with steroids.

Clinical Relevance: The presence of fatty degeneration of osteocytes in normal appearing metatarsal bones of patients with INFH suggests that a systemic disturbance of fat metabolism affecting the epiphysis of long bones may be an important risk factor for this disease.

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INTRODUCTION

Although the etiology of idiopathic necrosis of the femoral head (INFH) is unknown, both systemic and local factors have been implicated in the pathogenesis of the disease. Our current theory suggests that a systemic disturbance of fat metabolism results in fatty degeneration of osteocytes and bone necrosis [4,6]. Hyperlipidemia and hyperlipoproteinemia have been reported in approximately half of total patients with INFH [2,3,7,8]. Histopathological examination of the femoral heads in these patients often demonstrate intracytoplasmic lipid droplets and fatty degeneration of the osteocytes, especially those in the subchondral area in the femoral heads of rabbits pretreated with either alcohol [5] or steroid compounds [4,6].

It remains controversial whether these lipid abnormalities are a possible cause of osteonecrosis or merely a reactive, morphological change to a vascular insult. The purpose of this study was to examine histologically the bone from normal appearing metatarsal heads of patients with INFH and compare the results with those of a control group of patients without INFH.

MATERIALS AND METHODS

Twenty-one patients with INFH underwent biopsy of both the involved femoral head and the ipsilateral fourth metatarsal head. There were 13 males and 8 females with an average age of 48.7 years (range of 24 to 70 years). Serum levels of cholesterol and triglycerides were drawn prior to surgery.

Thirteen females with rheumatoid arthritis had similar biopsies of their metatarsal heads at the time of resectional arthroplasty. None of these rheumatoid patients with average age of 46.5 years (range 34 to 73 years) had clinical symptoms or radiographic signs of INFH. Table 1 lists the sexs, ages, risk factors (steroid intake or alcohol abuse), associated diseases, and serum lipid profiles for all study and control patients.

All biopsy specimens were taken from the subchondral bone (Fig.1). The tissue was fixed in a mixture of 2.5% glutaraldehyde phosphate buffer and 10% buffered formalin for 24 to 48 hours at 4°C, and then decalcified for 2 to 3 weeks in

Table 1

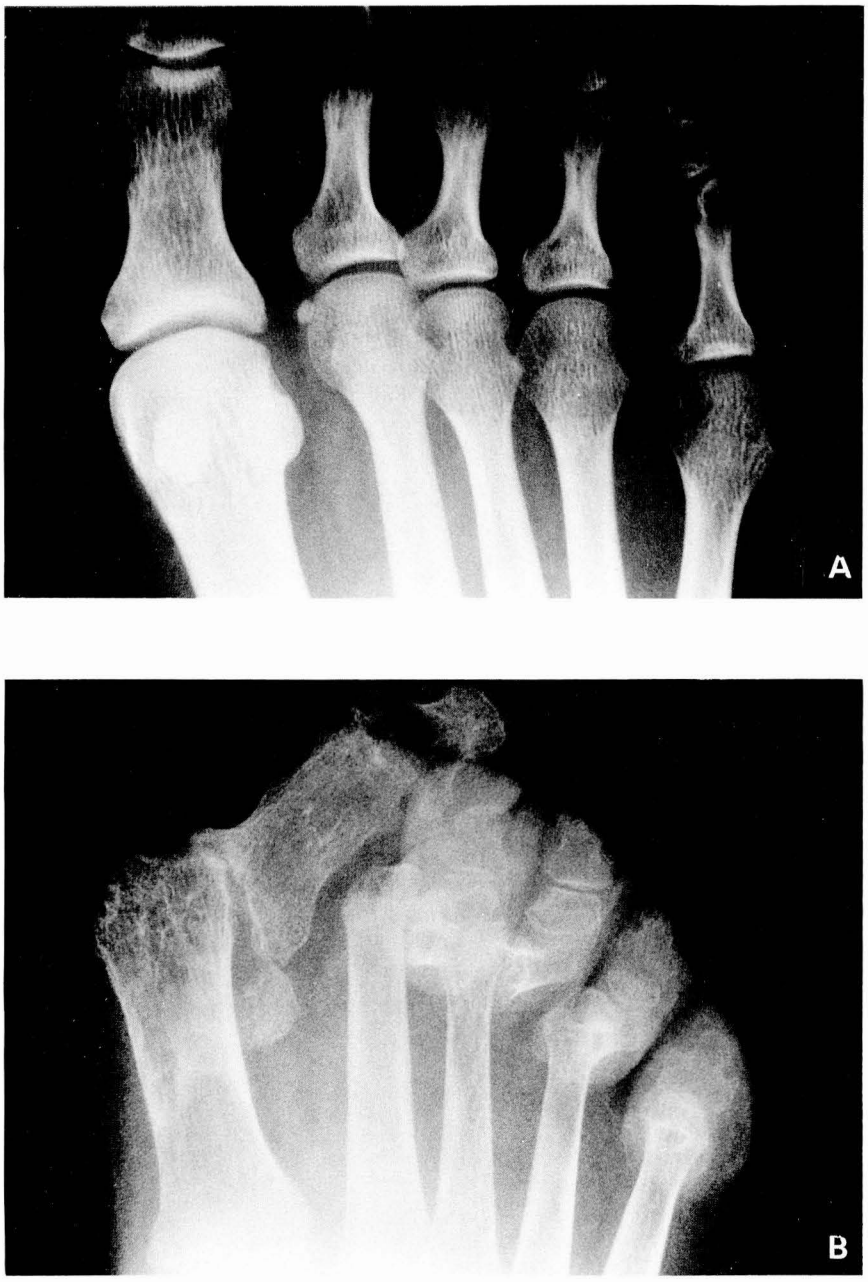
Case	Sex	Age at Surgery	Steroid(S)* Alcohol(A)	Complication	Serum Lipids** Cholesterol	Triglyceride	Histology*** Fatty degeneration of osteocytes Femoral head	IV metatarsal head
1	F	58	-		172	67	+ +	-
2	F	35	S	SLE (1)	197	109	+ +	+ +
3	F	67	S	DM (2)	**245**	**261**	-	-
4	F	70	-		199	71	-	-
5	F	68	S		155	68	-	-
6	F	46	S	SLE	211	61	-	-
7	F	37	S	SLE	**224**	**257**	+	-
8	F	51	S	SLE	215	**154**	+	+
9	M	54	-		167	96	+	+ +
10	M	51	S	PSS (3)	**231**	109	+	+ +
11	M	65	A	Liver cirrhosis	**252**	**142**	-	+
12	M	35	S	DM	166	**222**	-	+
13	M	38	-		209	**160**	+ +	+ +
14	M	70	-		153	79	+	-
15	M	32	A	Liver cirrhosis	178	129	-	-
16	M	24	S	Liver cirrhosis	191	**156**	+	+
17	M	39	-		209	**203**	-	-
18	M	38	A		207	**165**	+	-
19	M	38	-		129	**256**	+ + +	+ +
20	M	40	A	Liver cirrhosis	159	**141**	+	+
21	M	29	S	Nephrotic synd	163	81	+	+
22	F	60	-	RA (4)	**251**	136	not done	-
23	F	53	-	RA	216	110	not done	-
24	F	72	-	RA	170	60	not done	-
25	F	34	-	RA	160	55	not done	-
26	F	67	-	RA	172	70	not done	-
27	F	73	-	RA	157	55	not done	-
28	F	59	-	RA	232	104	not done	-
29	F	72	-	RA	194	72	not done	-
30	F	62	-	RA	204	122	not done	-
31	F	49	S	RA	**241**	**179**	not done	-
32	F	44	-	RA	131	95	not done	-
33	F	43	S	RA	147	76	not done	+
34	F	46	S	RA	180	124	not done	-

(1)SLE : Systemic lupus erythematosus
(2) DM : Dermatomyositis
(3) PSS Progressive systemic sclero
(4) RA Rheumatoid arthritis

**: normal range
Cholesterol: 150-230mg/dl
Triglyceride: 30-140mg/dl

***: Histologic grading
"+++" : severe (over 80% of osteocytes is Sudan positive)
"++" : moderate (80-50%)
"+" : slight (50-10%)
"-" : none (blow 10%)

* : History of steroid intake(S)
History of alcohol abuse(A)



[Fig.1] Roentgenograms of the forefoot from case #20 with INFH (A) and from case #23 with RA (B). The biopsy specimens of the fourth metatarsal heads from both cases were histologically examined.

ethylenediaminetetraacetic acid solution. Portions of the specimens were then processed separately for light and electron microscopy. For light microscopy, the specimens were either sectioned and stained with hematoxylin and eosin, or sectioned by a cryostat technique after freezing and stained with Sudan IV. For electron microscopy, the specimens were sectioned into small pieces and post-fixed in 2% buffered osmium tetroxide for 2 hours. The sections were then dehydrated in alcohol and embedded in Epon 812. Ultrathin sections were stained with uranyl acetate and lead citrate, and examined under 3000 to 10,000 magnification using the H-300 electron microscope (Hitachi Co., Tokyo, Japan).

RESULTS

Serum cholesterol and/or triglyceride levels were elevated in 12 of the 21 INFH patients. Only 2 of the 13 control patients showed abnormally elevation of lipid levels.

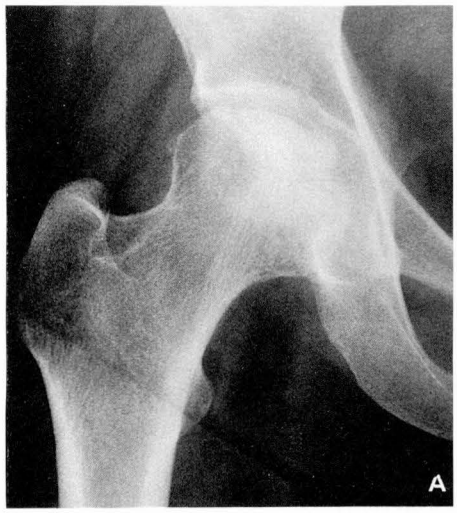
Lipid deposits stained with Sudan IV were observed in osteocytic lacunae at the border between necrotic and unaffected areas of the biopsy specimens in 13 of the 21 femoral heads (Fig.2). Electron microscopy confirmed that these lipid droplets were located eccentrically within the cytoplasm of the osteocytes. The size of these deposits varied but often occupied nearly the entire volume of the cell.

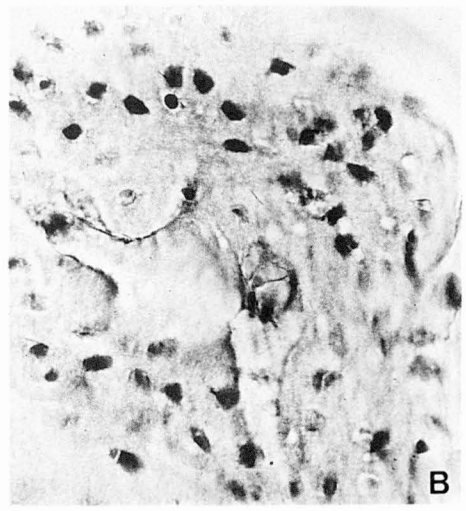
Similar intracytoplasmic lipid deposits were noted in 11 of the 21 metatarsal biopsies in the INFH patients (Fig.3). The ultrastructure of the droplets was indistinguishable from that of lipid droplets in the osteocytes of necrotic femoral heads.

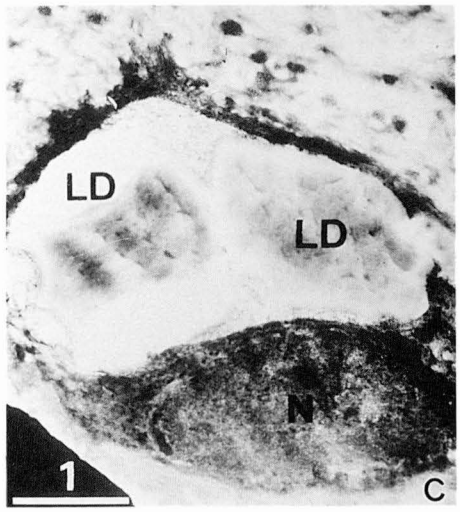
Lipid deposits within the osteocytic lacunae were detected by light microscopy or electron microscopy in only one of the 13 metatarsal biopsies in the rheumatoid patients. This patient was on chronic steroid medication(case #33).

DISCUSSION

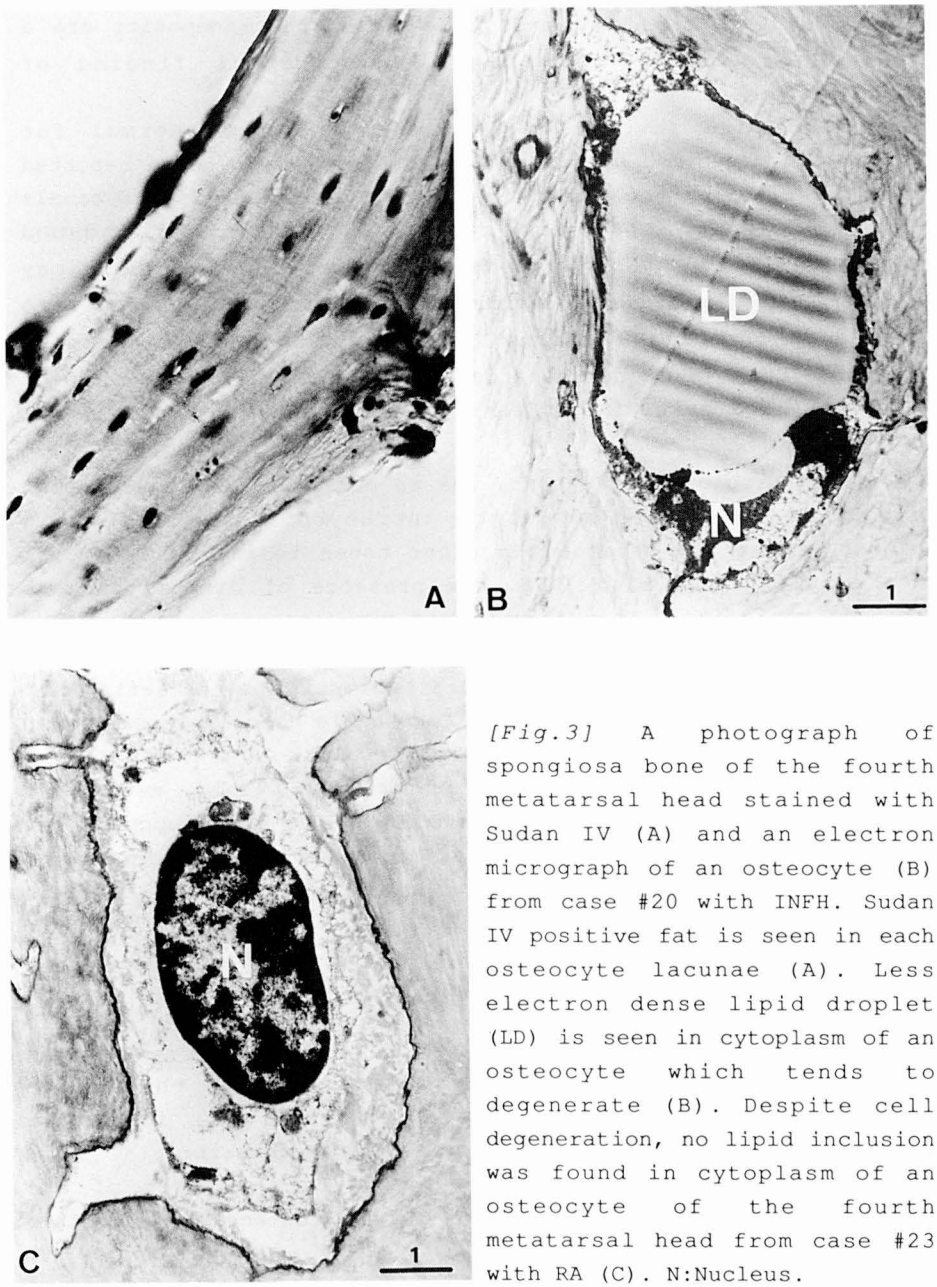
The precise role of abnormal lipid metabolism in the genesis of osteonecrosis is unclear. Hyperlipidemia is frequent in patients with alcoholic liver disease and patients on chronic steroid medication. Abnormal lipid deposits can be detected







[Fig.2] Case #19. 38 year-olds male, alcoholism. X-ray picture shows osteonecrosis of the right femoral head (Fig2-A). Core decompression was done and subchondral bone was biopsied. By the Sudan IV staining scarlet and/or reddish granules were found in osteocyte lacunae both from the femoral head (Fig2-B) and the fourth metatarsal head. An electron micrograph demonstrates lipid droplet in osteocyte lacunae of the femoral head.



[Fig.3] A photograph of spongiosa bone of the fourth metatarsal head stained with Sudan IV (A) and an electron micrograph of an osteocyte (B) from case #20 with INFH. Sudan IV positive fat is seen in each osteocyte lacunae (A). Less electron dense lipid droplet (LD) is seen in cytoplasm of an osteocyte which tends to degenerate (B). Despite cell degeneration, no lipid inclusion was found in cytoplasm of an osteocyte of the fourth metatarsal head from case #23 with RA (C). N:Nucleus.

commonly in osteocytic lacunae of specimens from necrotic femoral heads but rarely in specimens of normal or osteoarthritic femoral heads [5]. It remains controversial whether these deposits are a cause, an effect, or merely an incidental finding of osteonecrosis.

There are several mechanisms by which abnormal fat metabolism may cause bone necrosis. Fisher, et al. have reported that fat emboli are observed in the haversian vessels and canals of the femoral heads of rabbits with steroid induced hyperlipidemia [1]. Wang hypothesized that bone necrosis may result from the elevated intramedullary pressure secondary to increased numbers of marrow fat cells [9]. We have recently reported that fatty degeneration of osteocytes in the femoral head may be a prime factor in the development of osteonecrosis [2,4,6].

The purpose of this study was to determine if the abnormal deposition of large amount of intracytoplasmic lipids in osteocytes can be detected in other bones besides the femoral heads in patients with INFH. The presence of diffuse osseous changes would imply that these lipid deposits are not caused by osteonecrosis but may actually be involved in the pathogenesis of the disease. Eleven of 21 metatarsal biopsies in patients with INFH demonstrated lipid deposits. Comparable changes were evident in only one of 13 control patients.

We concluded that a disturbance of lipid metabolism leading to intracytoplasmic deposition of fat in osteocytes may be a significant risk factor for the development of osteonecrosis. The specific role of the lipid in cellular death has yet to be determined.

SUMMARY

(1) Bone biopsies from the femoral heads and the fourth metatarsal head were obtained in the patients with idiopathic necrosis of the femoral head and with rheumatoid arthritis.
(2) 71.4% of the patient with idiopathic necrosis of the femoral head revealed fatty degeneration of osteocytes in either the femur and/or metatarsus.
(3) 57% of those patients demonstrated hyperlipidemia.

(4) Metatarsal biopsies obtained from the patients with rheumatoid arthiritis disclosed no fatty degeneration of osteocytes except in one patient treated with steroids.

ACKNOWLEDGEMENT

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REFERENCES

1. Fisher,D.E.and Bickel,W.H. J.Bone and Joint Surg.,1971. 53A. 859/873. Corticosteroid Induced Avascular Necrosis.
2. Hirohata,K. and Kawai, K. Orthop. Traum. Surg.(in Japanese) 1983.26.1009/1017. A Role of Fat Metabolism in the Pathogenesis of Idiopathic Necrosis of the Femoral Head.
3. Hirohata,K. Pauwels. F. Memorial Symposium on the Occasion of his 100th Birthday, Aachen, May 31.1984. A Causative Factor of Idiopathic Aseptic Osteonecrosis of the Femoral Head from the Biological Aspect.
4. Hirohata,K. Transaction of 18th SICOT. 1990. Current trends lecture. Behavior of osteocytes in the pathology of osteonecrosis of the hip. Clinical and experimental study.
5. Kawai,K.et al. Rinsho Seikeigeka. 1985.20.751/758 Alcoho-Induced Osteocytes Changes of the Femoral Head in Rabbits.
6. Kawai,K. et al. J.Bone and Joint Surg. 1985. 67A. 755/763. Steroid-Induced Accumulation of Lipid in the Osteocytes of the Rabbit Femoral Head.
7. Puhl.W. et al. Z. Orthop. 1978. 116. 81/92. Metabolische Storungen bei der idiopathoschen Huftkopfnekrose Erwachsener.
8. Sugioka,Y.et al. Proceeding of the second Report by the Study Group of Japanese Ministry of Health and Welfare. 1978. 69/74. Serum Lipoprotein in Idiopathic Aseptic Necrosis of the Femoral Head.
9. Wang,G.J. et al. J.Bone and Joint Surg. 1977.59A.729/735. Fat-cell Changes as a Mechanism of Avascular Necrosis of the Femoral Head in Cortisone-Treated Rabbits.