

Evaluation of diffusely high uptake by the calvaria in bone scintigraphy

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The present study was undertaken to evaluate the finding of diffusely high uptake by the calvaria in a series of 994 consecutive whole body scans in regard to the incidence and degree, and to discuss the mechanism. A total of 86 patients had positive scans (73 women and 13 men) and there were 71 malignant (27 breast, 16 lung, and 28 other malignancies), and 15 benign disease cases (5 degenerative bone, 3 blood, and 7 miscellaneous diseases). Positive rate of the finding was 8.7% in total, 14.9% in women, and 2.6% in men. The difference between women and men was significant ($P < 0.001$). The finding was significantly correlative with the ages of patients. Also the finding is shown to be predominant in women ranging 50-59 years of age. On the other hand, the same finding as was made by Creutzig and his coworker was confirmed in malignant cases under high-dose anticancer drug therapy. On the basis of these results, the finding may be not only a side effect of intensive cytotoxic medication on the skeleton, but also a physiological event relative to bone change with age and postmenopausal osteoporosis.

Key words: Bone scintigraphy, Calvarial uptake, Sickie sign, Postmenopausal osteoporosis

INTRODUCTION

DIFFUSELY HIGH UPTAKE of skeletal agents in the calvaria has been noticed in patients with primary or secondary hyperparathyroidism^{1,2} or other bone diseases.³ The finding was also present in patients with breast cancer under cytotoxic therapy, and called "sickle sign."⁴

The authors have encountered the finding in many aged patients with various diseases besides the above-mentioned or with malignant neoplasm not treated with anticancer drugs. The present study was undertaken to evaluate the finding in regard to the incidence and degree, and to discuss the mechanism.

MATERIALS AND METHODS

A series of 994 consecutive whole body scans were performed during the review period (February 1983-June 1985). The study population included 489 women and 505 men, ranging from 0 to 91 years of age,

and consisted of 170 and 724 cases with benign and malignant diseases, respectively (Table 1).

Whole body scan of the skeleton in posterior view was taken about three hours after intravenous injection of Tc-99m-methylene diphosphonate (0.3 mCi/kg of body weight), using a scinticamera equipped with a low-energy, high-resolution collimator with a scan speed of 40 or 50 cm/min, following or followed by routine multifformat imaging of the axial skeleton in both anterior and posterior views.

The finding of diffusely high uptake by the calvaria was judged and graded optically by comparing the image density of the calvaria with that of the cervical and lumbar vertebral columns, scoring one to three points: 1, the calvaria equal to the cervix; 2, higher than the cervix but lower than the lumbar; 3, equal to or higher than the lumbar (Fig. 1).

Three patients with hyperparathyroidism and 24 patients with malignant neoplasm, in which multiple hot areas were revealed in the skeleton except in the articular region on bone imaging, were eliminated from the positive cases.

In a number of the cases X-ray skull images were taken, and the serum levels of alkaline phosphatase, calcium and phosphate were measured to determine any relation to the finding.

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Table 1 Number of subjects

Range of age (years)	Men			Women			Total
	Benign	Malig.	Total	Benign	Malig.	Total	
0-9	3	7	10	2	4	6	16
10-19	7	16	23	5	13	18	41
20-29	3	11	14	5	14	19	33
30-39	11	7	18	8	39	47	65
40-49	16	43	59	16	72	88	147
50-59	21	87	108	12	84	96	204
60-69	9	148	157	22	112	134	291
70-	12	104	116	18	63	81	197
Total	82	423	505	88	401	489	994

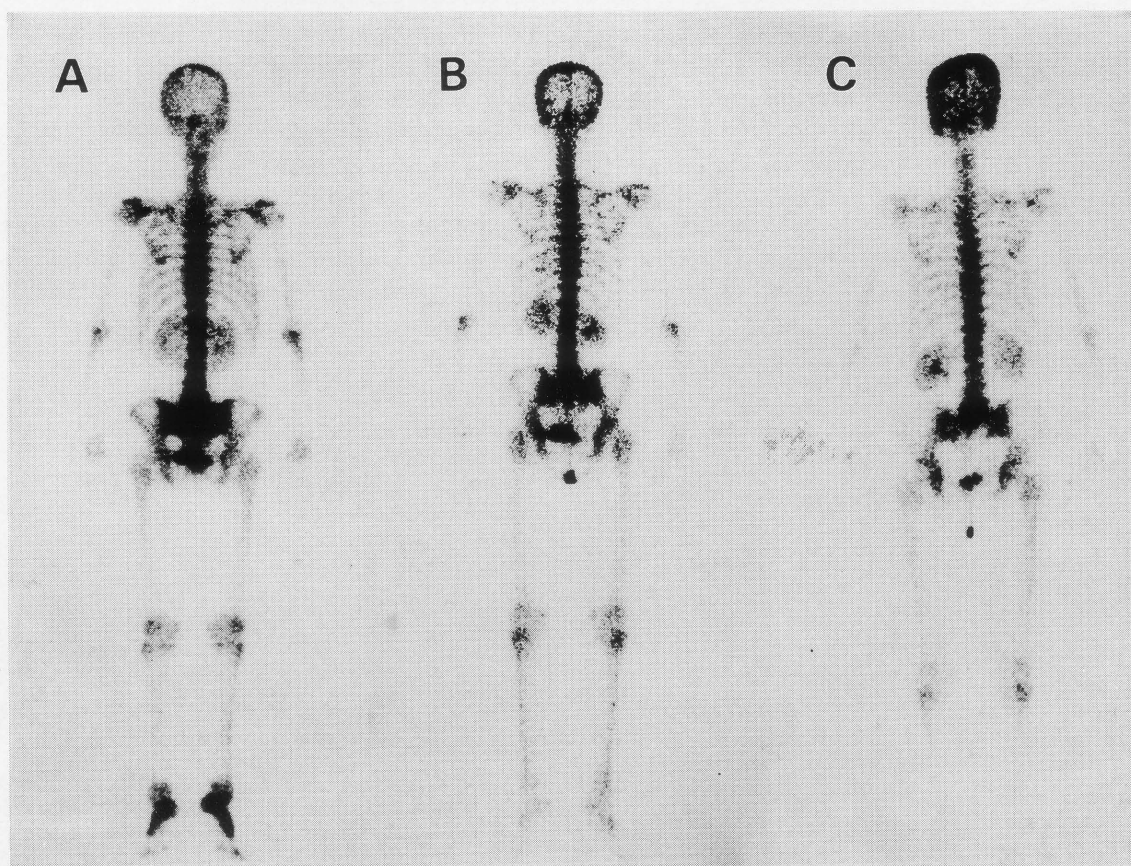


Fig. 1 Whole body images of the skeleton, demonstrating three grades of calvarial uptake. A: equal to cervical uptake, B: higher than cervical but lower than lumbar uptake, C: equal to or higher than lumbar uptake.

Chi-square and Student's *t*-test were used for determining the respective statistical differences of positive rate and degree of the finding among sex, age, and disease groups of the subjects. The level of significance was selected as 0.05.

RESULTS

A total of 86 patients had positive scans (73 women and 13 men) and there were 71 malignant (27 breast,

16 lung, and 28 other malignancies), and 15 benign disease cases (5 degenerative bone, 3 blood, and 7 miscellaneous diseases). The finding was absent in female cases aged less than 32 years and male cases aged less than 50, except for the case of a 20-year-old man with perosteal sarcoma under high-dose chemotherapy.

Positive rate of the finding (Table 2) was 8.7% in total, 14.9% in women, and 2.6% in men. The difference between women and men was significant

($P < 0.001$) in both benign and malignant disease groups. The rate was the highest in women of the age group ranging 50–59 years, followed by the group ranging 60–69. And, the correlation between the

rate and the age range was significant ($P < 0.01$) in women. On the other hand, there were no significant differences among the rates in the benign disease, breast cancer, and lung cancer groups. However,

Table 2 Number and rate of positive cases

Range of age (years)	Men			Women			Total
	Benign	Malig.	Total	Benign	Malig.	Total	
0–19	0	0	0	0	0	0	0
20–29	0	1 (9.1%)	1 (7.1%)	0	0	0	1 (3.0%)
30–39	0	0	0	0	2 (5.1%)	2* (4.3%)	2 (3.1%)
40–49	0	0	0	1 (6.3%)	12 (16.7%)	13* (14.8%)	13 (8.4%)
50–59	0	5 (5.7%)	5 (4.6%)	1 (8.3%)	22 (26.2%)	23* (24.0%)	28 (13.7%)
60–69	1 (11.1%)	4 (2.7%)	5 (3.2%)	7 (31.8%)	18 (16.1%)	25* (18.7%)	30 (10.3%)
70–	0	2 (1.9%)	2 (1.7%)	5 (27.8%)	5 (7.9%)	10* (12.3%)	12 (6.1%)
Total	1§ (1.2%)	12† (2.8%)	13‡ (2.6%)	14§ (15.9%)	59† (14.7%)	73‡ (14.9%)	86 (8.7%)

* $p < 0.01$ from Chi-square test correlation between the rate and the age of women group.

§; †; ‡ $p < 0.001$ from Chi-square test comparison between the rates of men and women.

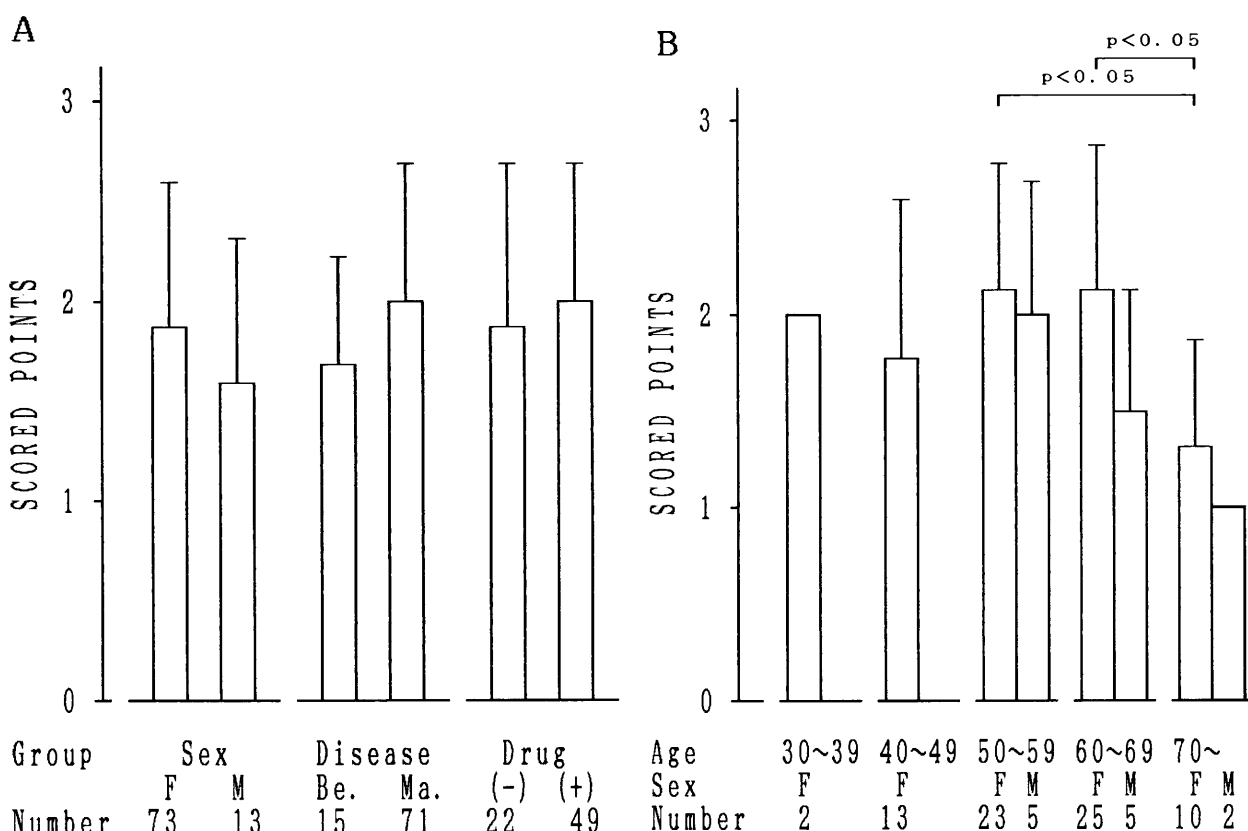


Fig. 2 Comparison among scored points (mean \pm 1 SD) of positive cases. A: Comparison between female (F) and male (M), between benign (Be.) and malignant (Ma.) disease, and between malignant subgroups treated with (+) and without (–) anticancer drugs. B: Comparison among female (F) and male (M) age groups.

the rate in the malignant disease subgroup treated with anticancer drugs was significantly ($P < 0.01$) higher than that in the subgroup not treated. In women the rate in the breast cancer group was also significantly ($P < 0.01$) higher than that in the malignant disease group excluding breast cancer.

Scored points of the degree were $1.9 (\text{mean}) \pm 0.7$ (S.D.) in women and 1.6 ± 0.7 in men. There was no significant difference between these two groups nor between the benign and malignant disease groups and between the malignant disease subgroups treated with or without anticancer drugs (Fig. 2A). However, the score of women of the age group over 70 years, which measured 1.4 ± 0.5 , was significantly ($P < 0.05$) lower than those of the groups ranging 50–59 and 60–69 years (Fig. 2B).

Many patients with a high score finding had an endosteal or subperiosteal demineralization of the skull on X-ray image and some increase in the serum level of alkaline phosphatase. However, there was no significant correlation between the score and the serum level of alkaline phosphatase, calcium, or phosphate.

DISCUSSION AND CONCLUSION

The present study suggests that the finding of diffusely high uptake by the calvaria on bone scintigraphy is significantly correlative with both sex and age of patients. And, the finding is shown to be predominant in women ranging 50–59 years of age. On the other hand, the same finding as had been found by Creutzig and his coworker⁴ was confirmed in malignant cases under high-dose anticancer drug therapy.

On the basis of these results, the finding may be not only a side effect of intensive cytotoxic medication on the skeleton, but also a physiological event relative to bone change with age and postmenopausal osteoporosis.

It is well documented that the bone change in aged females is due to an increase in serum parathyroid hormone level,^{5,6} a decrease in serum calcitonin⁷ and estrogen level,⁸ or/and a decrease in calcium intake.⁹ Although bone change with age is caused by heterogeneous mechanisms, progressive osteopenia in some patients with postmenopausal or senile osteoporosis may be conditioned by an osteoclastosis, elevations in circulating parathyroid hormone, and a relative increase in poorly mineralized osteoid tissue.¹⁰ These conditions may cause bone scans with findings resembling a typical calvarial uptake in hyperparathyroidism.

On the other hand, Tc-99m-methylene diphosphonate accumulation rates were small in osteoporosis and greater in hyperparathyroidism.¹¹ Also, bone scans usually reveal an inverse linear correla-

tion between the patient's age and the image quality, suggesting a decrease in the mineral mass or exposed crystal surface area of the aged patient's cancellous bone.¹² However, in diffuse osteoporosis the mineral loss of the skeleton is significantly greater in the axial cancellous bone than in the peripheral cortical bone,¹³ and the vertebrae and pelvis are the most commonly affected by osteoporosis. The relatively decreased uptake by the vertebrae should enhance the finding of the calvaria. And, it should be due to a further extension of osteoporotic change up to the calvaria that the scored points of the finding were significantly lower in the age group of women over 70 years than in the groups ranging 50–59 and 60–69 years.

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