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Original

Age-related changes in skull uptake on bone scintigraphy: a quantitative study

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Abstract

BACKGROUND: "Hot skull", or diffuse increased activity of bone seeking radiotracers, is frequently seen in the bone scans of some patients, especially elderly women. This finding has been attributed to enhanced bone metabolism in old age.

MATERIAL AND METHODS: We semi-quantitatively studied 342 normal bone scans (161 male and 181 female within the age range 12 to 82 years). We divided the patients into 7 age groups: 10–19, 20–29, 30–39, 40–49, 50–59, 60–69, and 70 and above. The geometric means of the anterior and posterior background corrected skull and mid-femoral ROI values were used for calculation of the skull to femoral ratio (SFR).

RESULTS: The skull to femoral ratio was significantly higher in female patients in the age groups 30-39 and above. In females, the five upper age groups (30–39, 40–49, 50–59, 60–69, and 70 and above) had significantly higher SFR than the lower age groups. In males, the two upper age groups (60–69, 70 and above) had significantly higher SFR than the lower age groups. The findings in males were not concordant with the previous studies addressing this issue, which could be explained by different bone mineral density in the Iranian population.

CONCLUSION: Our data showed that "hot skull" is not necessarily an abnormal finding, especially in elderly women. We suggest that every nuclear medicine department uses its own normal values and reference samples for quantitative evaluation, due to ethnic or socio-economical variations.

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Introduction

Bone scintigraphy is frequently performed to investigative many skeletal abnormalities (such as primary tumoural and metastatic involvement of the skeleton, infections of the bone and soft tissue, fractures and other traumatic lesions of the skeleton, etc.) in daily nuclear medicine practice. Interpretation of a skeletal scintigraphic study requires not only images of high quality, but careful scrutiny, bearing in mind the normal variants and evaluation in light of the particular clinical problem [1]. Age-related changes shown by whole-body bone scintigraphy with ^{99m}Tc-labeled phosphonates are well known, such as in growth plates, the sternum, and increased uptake diffusely in the skulls of postmenopausal women [1, 2].

A diffuse increased uptake in the calvarium (a "hot skull") was first attributed to extensive cytotoxic treatment in patients with breast cancer, but studies that are more recent have shown this to be specific neither to breast cancer nor cytotoxic treatment [2]. "Hot skull", or diffuse increased activity of bone seeking radiotracers, is a normal pattern in the bone scans of some patients, especially elderly women [2–6]. Metabolic disorders such as hyperparathyroidism and osteomalacia, as well as administration of chemotherapeutic drugs, can also cause increased skull uptake [7–12].

In this study we semi-quantitatively evaluated the skull uptake on the bone scans of patients without any apparent metabolic disease and/or known malignancy. To the extent of our knowledge, only two semi-quantitative studies have been performed regarding skull uptake on bone scans [3, 4], and male patients were included only in one of them [4].

Material and methods

Our study included 342 whole body bone scans (161 male and 181 female with an age range of 12 to 82 years). The exclusion criteria of our study are shown in Table 1.

All patients underwent whole-body bone scan 3 hours after intravenous injection of (phosphonomethyl)phosphonic acid-[^{99m}Tc] technetium ([^{99m}Tc]-MDP) using a dual head gamma camera

Table 1. Exclusion criteria of the study

Exclusion criteria
Metabolic bone disease
Any history of malignant disease
History of chemotherapeutic drug administration
Any surgery or trauma of the skull
History of cerebro-vascular accident
Any surgery or trauma of the femora
Asymmetric uptake of the femora

(E-CAM, Siemens, Erlangen, Germany) fitted with a low energy, high resolution collimator. The adult dose was 740 MBq, whereas in children the dose was adjusted for body weight. Regions of interest (ROIs) were drawn on the anterior and posterior views of both skull and mid-femoral areas, and the average count per pixel of each ROI was recorded. Background ROIs were placed on the soft tissue of the thigh (Figure 1 and 2). Geometric means of the anterior and posterior background corrected ROI values were used for calculation of skull to femoral ratio (SFR).

We divided the patients to 7 age groups: 10–19, 20–29, 30––39, 40–49, 50–59, 60–69, and 70 and above.

Statistical analysis was performed using SPSS software (version 11.5). The quantitative data were expressed as mean ± standard deviation (SD). Independent sample *t*-test was done for comparison of mean values between two independent groups. One-way ANOVA was used for comparison of mean values between age groups and Tukey's honestly significant difference test (Tukey HSD) was used for post Hoc analysis. P values less than 0.05 were considered statistically significant.

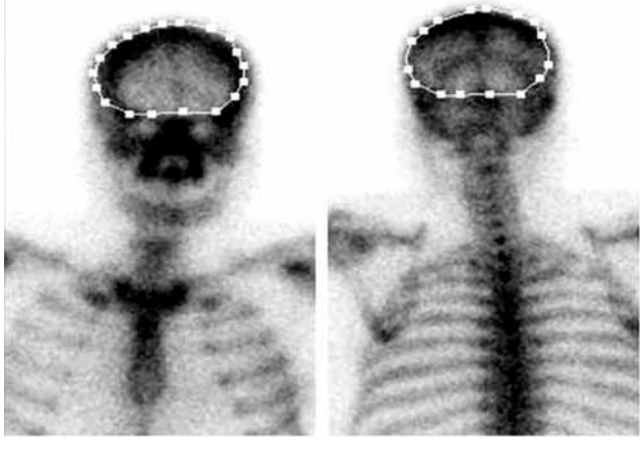

Figure 1. Example of ROI (region of interest) drawing on the skull.

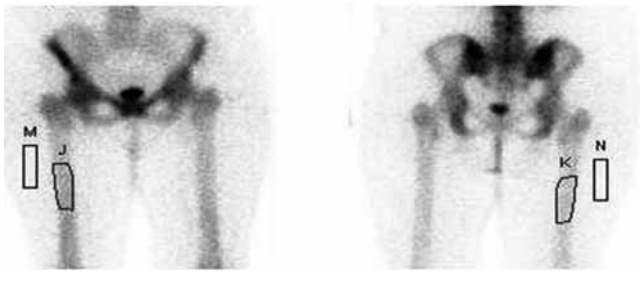

Figure 2. Example of ROI (region of interest) drawing on the skull on the mid-femoral and background areas.

Table 2. Means and standard deviations of skull to femoral ratio (SFR) in different age groups of male patients

Age group	Number of patients	Mean SFR	SD
10–19	28	1.8667	0.3675
20–29	40	2.0571	0.4337
30–39	16	2.1378	0.1443
40–49	24	2.4371	0.2065
50–59	21	2.7494	0.1925
60–69	20	3.2172	0.0510
70 and above	12	3.6391	0.3474
Total	161	2.4410	0.62385

SD — standard deviation

Table 3. Means and standard deviations of skull to femoral ratio (SFR) in different age groups of female patients

Age group	Number of patients	Mean SFR	SD
10–19	26	2.1520	0.14775
20–29	38	2.4063	0.34295
30–39	26	2.8114	0.36355
40–49	26	3.1790	0.29500
50–59	22	3.5945	0.44044
60–69	15	3.7842	0.09382
70 and above	24	4.1957	0.64163
Total	181	3.0189	0.80302

SD — standard deviation

Results

Tables 2 and 3 show the means and standard deviations of SFR in different age groups for males and females.

The value of SFR for all patients as a whole was 3.0189 ± ± 0.80302 for females and 2.4410 ± 0.62385 for males.

Both genders showed a gradual increase in SFR (From 2.1520 ± 0.14775 to 4.1957 ± 0.64163 in females and 1.8667 ± 0.3675 to 3.6391 ± 0.3474 in males). SFR was significantly higher in female patients in the age groups of 30–39 and above. Lower age groups did not show any significant difference in this regard.

In males, the age group 60–69 had a significantly higher SFR than the lower age groups (p-value < 0.05). The age group of 70 and above also showed the same finding.

In females, the five upper age groups (30–39, 40–49, 50–59, 60–69, and 70 and above) had significantly higher SFR than the lower age groups.

Discussion

Diffusely high uptake in the skull on bone scintigraphy has been reported in conditions such as metabolic disorders (hyperparathyroidism, osteomalacia, etc) and administration of chemotherapeutic

drugs for the treatment of malignant disorders [7–12]. However, "hot skull" is significantly age and sex dependent and can be considered a normal variant in bone scintigraphy [2–4].

Kigami et al. [2] reported that changes of bone tracer distribution pattern with aging were significantly different in men and women. Uptake by the head increased with age in women. They found that in men no such tendency was clearly observed. In women over 50 years of age, significantly higher uptakes were observed in the head while male patients demonstrated no such significant differences [2]. The frequency of "hot skull" was shown to be higher in post-menopausal women in previous studies. This finding was attributed to the post-menopausal changes in bone metabolism in females [2–4]. Males did not experience such a metabolic change and did not show such a trend in skull uptake. Enhanced systemic bone metabolism could be the cause of increased skull uptake in this age group, since the skull is less affected by the osteoporosis process (compared to the rest of the skeleton, especially the axial skeleton) and gradually appears to be hot as patients age [3, 13].

Our study also supports the above-mentioned findings; however, the age of "hot skull" appearance in the female group was lower in our study, and men also showed "hot skull" in the age groups over 60. These findings might be due to the different bone mineral density in the Iranian population compared to the previously mentioned studies [14–17]. Larijani et al. reported a high frequency of osteoporosis in the Iranian male population and suggested using a separate reference sample for diagnosis of osteoporosis in our country due to the different values of bone mineral density [14]. Salehi et al., in a recently published study, reported a high prevalence of low bone mineral density in the young Iranian population, which could explain the lower age of "hot skull" appearance in our study compared to the previously published studies regarding this issue [16]. This high prevalence of low bone mineral density in the young population of our country is most likely due to cultural and socio-economic factors. Factors such as low calcium diet, little exercise, and vitamin D deficiency can contribute to this fact.

Conclusions

We conclude that "hot skull" in bone scans is not necessarily an abnormal finding, especially in elderly women, and is probably related to enhanced systemic bone metabolism in old age. Due to racial and socio-economic variations between different patient populations, we suggest that every nuclear medicine department uses its own normal values and reference samples for quantitative evaluation. These differences have to be considered when reporting bone scans. Using the normal values and references from other institutions (especially when located in countries with different cultural and socio-economic background) can cause interpretation mistakes and should be avoided if possible.

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