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Abnormal Focal Jaw Uptake of 153 Sm-Ethylene-Diamine-Tetra-Methylene-Phosphonate (EDTMP) – What is the Reason?

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Abstract

Abnormal focal tracer uptake in the jaw during conventional bone scintigraphy is a quite frequent finding usually not related to malignant disease. In patients undergoing radionuclide therapy with lanthanoids or rhenium, the appearance is also quite frequent. It's origin so far has not been studied in a large number of patients. Objective, to evaluate the underlying reason of abnormal focal tracer uptake in the jaw in patients who underwent 153Sm-EDTMP therapy for painful metastatic lesions. Methods, out of 138 patients, 82 revealed a positive result, 60 males and 22 females (mean age: 63.9 ± 13.9years; range 19-90 years), with metastatic bone pain were examined. Their lesions were judged by a dentist clinically and radiologically. Results, the most frequent reason of increased focal uptake in the group of mainly prostate and breast cancer patients was inflammation in 13 (24.5%) and 9 (41%) patients, respectively. In the patients below 70 years of age, inflammation was the most frequent reason with (32.7%) while in the older ones of 70 years, it was mechanically irritated by a prosthesis with (50%). In 4 of the patients, the increased uptake of 153Sm-EDTMP was due to metastatic disease as shown by PET/CT and/or MRI. Conclusion, although the number of secondary lesions in the jaw is small (4.8%), the underlying reason in conventional bone scintigraphy as well as in post-therapeutic scintigraphy should be always evaluated.

Keywords: ^{153}Sm-EDTMP; Abnormal focal jaw uptake; Bone scintigraphy; Ortho-pantomo-graphy

Abbreviations: EDTMP: Ethylene-Diamine-Tetramethylene-Phosphonate

Introduction

Patients with a history of malignancy are periodically tested with technetium–99m methylene diphosphonate bone scans for the early detection and monitoring of metastases [1]. Bone scintigraphy reflects the metabolic activity within a bone lesion or at its margins, it may already be positive if there is approximately a 10% increase in the osteoblastic activity above normal [2]. Focally increased tracer uptake in the jaw in these patients is a common finding. The most frequent causes of focally increased 99mTc-MDP uptake are related to prior surgical manipulations in the implant (tooth extraction, root canal surgery), fracture and malignancy [3].

Less common causes of enhanced jaw uptake, like ossifying fibroma, odontoma residual osteitis, osteomyelitis, enchondroma, osteoma (Gardner's syndrome) actinomycosis and lymphoma should also be considered for differential diagnosis [4]. Long-term bisphosphonate therapy can also result in jaw osteonecrosis which has an estimated incidence of up to 15% for 3years [5]. 99mTc-MDP 3-phase bone scan has been shown as the most sensitive imaging method for the detection of jaw osteonecrosis at an early stage [6]. Since oral malignancies represent approximately 5% of all neoplasms in the body only, the jaw region is an unlikely site for metastatic bone lesions [7].

Currently, there are a variety of radioactive isotopes used as an alternative treatment modality for metastatic bone pain palliation, they are retained in the areas of rapid osteoblastic activity by a factor of up to about 10 times versus healthy bone [8].

Due to its much lower radiation toxicity and high concentration at sites of increased bone turnover equally to that of 99mTc diphosphonates, 153Sm is the radioisotope with the widest clinical experience in these days for bone pain palliation [9].

No systematic study on the nature of jaw uptake of any of the bone pain palliation agents including rhenium is currently available. Therefore, it was the aim of the study to describe the underlying reason for this abnormal scintigraphic finding. In case of an abnormal focal tracer uptake in the jaw which was recommended to be judged by a dentist who examined all the positive cases clinically and radiologically. The retrospectively collected results were analyzed.

Materials and Methods

This was a retrospective clinical study on 138 patients who underwent 153Sm EDTMP for therapy of painful metastatic bone lesions.

Treatment design

153Sm-EDTMP administration was performed according to the Vienna protocol developed at the Department of Nuclear Medicine [10]. The protocol was defined as follows: 30 mCi (1.1 GBq) 153Sm-EDTMP are repeatedly administered intravenously on an outpatient basis, the first dose till the 5th one being performed every 3 months, 6th dose till the 10th one being performed every 6 months, 11th dose till 15th one being performed every 9 months, thereafter at 12 months intervals. Red and white blood cell as well as platelet count was performed (3 and 6 weeks and immediately before the next treatment respectively). The treatment

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interval was reduced by 3 months in case of any indicator of disease progression assessed by radiography, MRI, scintigraphy, tumor marker increases and/or increasing bone pains. Whole body bone Scintigraphy was performed usually on the next day, anyway, about 20 hours after radionuclide application to achieve complete blood clearance, using large field of view double headed γ-camera, LEHR-collimation, energy window 20%, 103 Kev, acquisition mode continuously 15 cm/min, early images (<4 hours) showed significantly lower quality. The study included patients had been treated at Department of Nuclear Medicine, Medical University of Vienna, Austria.

Dental lesions characteristics

82 patients (out of a total of 138) who showed abnormal tracer uptake in the jaw area were examined by a dentist in this study. Afterwards an orthopantomography (Acrograph ZeusRF, 60KV, 10mA) a serial X-ray technique giving a panoramic view of the teeth and the jaw was performed to verify dental lesions. When one or more dental lesions like, (extraction, implant, bisphosphonate therapy, tumor, inflammation, mechanical irritation due to prosthesis, unknown) was found, patients underwent conventional dental X-ray in this region for exact assessment and measurement. Also in four patients, further investigations like, PET/CT and/or MRI were done to exclude metastatic lesions. Type of X-ray was Image X from DeGötzen. A sensor from Trophy (80ms, 8mA, 70KV) was used as digital data processing system. The measurement occurred with tools from Trophy Windows 5.0, the X-ray did not give any hint regarding the origin of the dental lesion, however, an exact measuring of the dental lesions was performed.

This study was approved by the Ethics Commission at the Medical University of Vienna and the Vienna General Hospital (AKH), each patient was explained the details of the procedure, benefits and side effects of therapy and the follow-up protocol and all patients provided written informed consent.

Statistical analysis

Date entry and data analysis were done using SPSS version 16 (Statistical Package for Social Science). The data of the patients were retrospectively collected. Continous variables were summarized as means and standard deviations, while categorical variables were summerized as numbers and percentage. Chi square test was used to test for significance. For all P-values <0.05 were selected as significant.

Results

During reviewing of the all 138 153Sm-EDTMP post-therapeutic whole-body bone scintigraphy images, we noticed 82 patients with abnormal focal tracer uptake at the jaw region, 60 males and 22 females (mean age: 63.8 ± 1.4years; range 19-90 years), 53 patients (64.7%) were

Personal Characteristics		
Age (years)		
Mean ± SD	63.9 ± 13.9	--
Range	19 – 90 years	--
Sex	**n**	**%**
Male	60	73.2
Female	22	26.8
Type of cancer	**n**	**%**
Prostate cancer	53	64.7
Breast cancer	22	26.8
lung+ other primaries	7	8.5
*Descriptive test		

Table 1: Demographic characteristics.

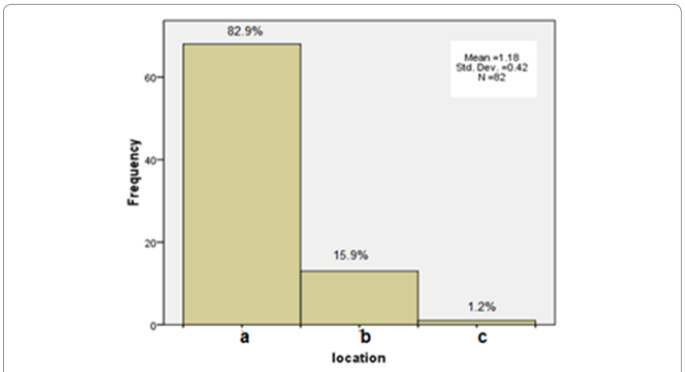

Figure 1: Number of the dental lesions (A) mono-lesion (B) bi-lesions (C) triple lesions.

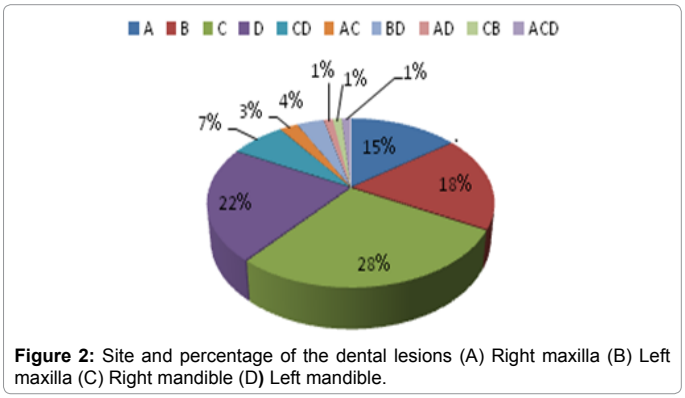

Figure 2: Site and percentage of the dental lesions (A) Right maxilla (B) Left maxilla (C) Right mandible (D) Left mandible.

prostate, 22 (26.8%) were breast and only 7 patients (8.5%) were other primaries (Table 1).

The abnormal focal tracer uptake of the jaw were assessed according to the number, location, reason & incidence of occurrence, influence of type of cancer and patients age on the nature and distribution of the dental lesions.

The abnormal focal tracer uptake of the jaw was divided according to their numbers into 3 sites (Figure 1). 68 patients (82.9%) had only abnormal focal jaw tracer uptake in one site (mandible or maxilla), 13 patients (15.9%) had bilateral focal lesions in the jaw and only one patient (1.2%) had triple lesions at the jaw as shown in (Figures 2 and 3).

While according to their locations (Figure 2), the right mandible turned out to be the most common site of abnormal increased tracer uptake in the jaw (28%) followed by the left one (22%), the left maxilla (18%) and the right maxilla (15%).

The areas of focally increased tracer uptake in the jaw after being judged clinically and radiologically by the dentist were identified according to their incidence and dental origin as shown in Table 2. Inflammation (soft tissue origin) carried the highest incidence (28%) among the other morphological and pathological dental lesions followed by mechanical irritation of the jaw caused by prosthesis (18.2%), while the incidence of the tumor (bone origin) is very low (4.8%).

Out of 82 patients with abnormal focal tracer uptake in the jaw, 75 patients were prostate and breast cancer (91.5%), we excluded 7 patients (8.5%) with other primaries in this analysis due to their limited number, their lesions distributed as the following;(e=1, i=2, b=1, f=1 and u=2), dental lesions were distributed in prostate and breast cancer patients as shown in Table 3. Breast cancer patients expressed a high incidence of inflammation (41%) as compared to prostate cancer patients (24.5%)

followed by mechanical irritation caused by prosthesis which showed high incidence among prostate cancer (22.6%) than breast cancer (13.6%), 5 (9.4%) patients only of prostate cancer has abnormal focal tracer uptake in the jaw with unknown etiology. Only 4 (7.5%) of prostate cancer patients expressed tumor in the jaw region, so statistical analysis for them was not done. There was no significant difference in the distribution of the abnormal tracer uptake in the jaw between prostate and breast cancer patients in the most of morphological and pathological dental lesions except for inflammation and mechanical irritation caused by prosthesis which showed significance (P-value =0.019 and 0.03 respectively) as showed in Table 3.

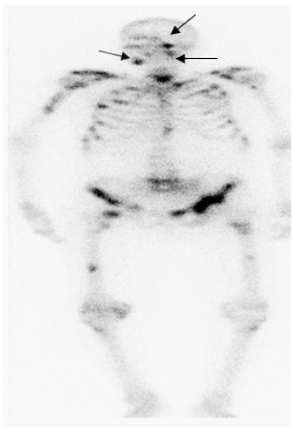

Figure 3: Male patient, 63-years-old, prostate cancer, received only a single dose of 153Sm-EDTMP therapy, his bone scintigraphy revealed abnormal focal tracer uptake at multiple areas of the skeleton involved right humerus, shoulders, ribs, clavicles, mid & lower axial skeleton, pelvic region and femori. There were two focal lesions involving the left side of the jaw (mandible & maxilla) and one focal lesion at the lower right mandible {arrows} which were examined by a dentist, PET/CT revealed metastases.

Focally enhanced tracer uptake in the Jaw	n.	%	Origin
Extraction (E)	13	15.8	Bone
Implant (I)	8	9.9	Bone
Bisphosphonate Treatment (B)	12	14.6	Bone
Tumors (T)	4	4.8	Bone
Inflammation (F)	23	28	Soft Tissue
Prosthesis (M)	15	18.4	Soft Tissue
Unknown (U)	7	8.5	?
Total	82	100	-
?unknown origin			

Table 2: Prevalence of the prospective dental lesions in the oral cavity.

Focal increased tracer uptake of the jaw	Prostate		Breast		P-value
	N.s	%	N.	%	
Extraction (E)	8s	15.2	4	18.2	0.058
Implant (I)	3	5.6	3	13.6	0.882
Bisphosphonate Treatment (B)	8	15.2	3	13.6	0.248
Tumors (T)	4	7.5	0	0	-
Inflammation (F)	13	24.5	9	41	0.019*
Prosthesis (M)	12	22.6	3	13.6	0.03*
Unknown (U)	5	9.4	0	0	-
Total (75)s	53	100	22	100	
Chi square test - No statistical test was done. *Statistical significant difference (P<0.05)					

Table 3: The distribution of the focal increased tracer uptake of the jaw in prostate and breast cancer patients.

Focal increased tracer uptake of the jaw	≤ 70 y (N=56)		>70 y (N=24)		P-value
	N.	%	N.	%	
Extraction (E)	10	17.2	3	12.5	0.052
Implant (I)	8	13.8	0	0	0.04*
Bisphosphonate Treatment (B)	7	12.1	5	21	0.564
Tumors (T)	4	6.9	0	0	-
Inflammation (F)	19	32.7	4	16.5	0.002*
Prosthesis (M)	3	5.2	12	50	0.02*
Unknown (U)	7	12.1	0	0	-
Total	58	100	24	100	-
Chi square test - No statistical test was done. *Statistical significant difference (P<0.05)					

Table 4: Influence of age on the nature of focal tracer uptake in the jaw.

The distribution of the dental lesions among patients below and above 70 years was showed in Table 4. Inflammation was the main cause of abnormal tracer uptake in the jaw (32.7%) among the younger age (≤ 70 y), while the main cause of abnormal tracer uptake in the jaw among the oldest patients was the mechanical irritation caused by prosthesis (50%). Statistically, there was no influence of the patients age on the nature of the morphological and pathological dental lesions except for inflammation and implant as well as the mechanical irritation of the jaw by the prosthesis which showed a significant difference among the patients age (P-value=0.002, 0.04 and 0.02 respectively).

Discussion

There are several studies supporting the added value of bone scintigraphy in detecting the pathophysiological changes of the jaw region [11]. They may show similar results as we have but this is the first study performed with different radiotracer,153Sm-EDTMP. Lyons, et al. [12] reported that dental extraction may cause positive scintigrams up to 8 months with normalization thereafter unless complications arise. Arias et al. [13] found that abnormal jaw scintigrams may be due to other reasons than oncological diseases such as dental prosthesis and implants resulting in hot spots on the scintigram. Recently, Jamdade, et al. [14] stressed the value of correlating radiographic and scintigraphic imaging in defining the extent and nature of histologically proven benign lesions of the jaw in order to decide on the surgical margins especially on the ill-defined lesions in 20 patients were investigated pre-operatively by panoramic radiography and bone scintigraphy. The radiographic extent was correct in 15 cases and was underestimated in five, while scintigraphic extent was correct in 18 cases and was overestimated in two.

Ramachandran et al. [15] suggested that the distribution and sensitivity of 153Sm EDTMP was similar to that of 99mTc-MDP bone scanning resulting in identical images. In this study, we described the underlying reason for abnormal focal tracer uptake in the jaw in 82 (out of a total of 138) patients who underwent 153Sm-EDTMP therapy of painful metastatic bone lesions. In those patients revealed focally increased tracer uptake in the jaw, a dental examination recommended by the nuclear medicine physician. According to the results of the clinical dental investigation on the oral cavity, the dental lesions were judged as the following (post-extraction status of more than 3 months, normal tissue, inflammation, infection (acute or chronic) or any combination, implant, bisphosphonate therapy, tumor, mechanical ittitation due to prosthesis, unknown). The right mandible turned out to be the most common site of increased tracer uptake in the jaw (28%) followed by the left one (22%), the left maxilla (18%) and the right maxilla (15%)

(Figure 2). There was no significant difference in the distribution of the abnormal tracer uptake in the jaw between prostate and breast cancer patients in the most of morphological and pathological dental lesions except for inflammation and mechanical irritation caused by prosthesis which showed significance (P-value =0.019 and 0.03 respectively). The most frequent reason for focally increased uptake in the jaw among this group of patients (prostate and breast cancer) was inflammation as judged by the dentist (24.5% vs 41%, respectively) (Table 3).

We found a highly significant influence of age in patients above and below 70 years of age whose the focally increased tracer uptake in the jaw was due to inflammation (P value=0.002), implant (P value=0.04) and mechanical irritation due to prosthesis (P value =0.02). In the patients below 70 years, the most frequent reason of increased tracer uptake in the jaw was inflammation (32.7%), while in those older than 70 years, mechanical irritation due to prosthesis as underlying reason was the leading cause (50%) (Table 4).

In 4 patients above 70 years of age, the increased uptake of 153Sm-EDTMP was due to metastatic disease, further investigation like PET/CT and/or MRI was done respectively to exclude malignancy.

Increased focal uptake in the jaw is a rather frequent but underestimated incidental finding. The predominating reason for it being inflammation in younger people and misfitting of dental prosthesis in older patients, both required medical intervention. Even in rare cases, malignant tissue might be discovered, therefore follow up search in each of this patient is strongly recommended.

Conclusion

Our results indicate that the evaluation of abnormally increased tracer uptake in the jaw region always should be done. A clinical dental investigation and morphological imaging tool are required to judge all abnormal morphological and metabolical changes in the jaw and in jaw area to exclude secondary malignancy.

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