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From the Orthopaedic Research Laboratories (Head: Göran C. H. Bauer) of the Department of Orthopaedic Surgery (Head: Sophus von Rosen) and the Department of Internal Medicine (Head: Jan Waldenström), Malmö General Hospital, University of Lund, Malmö, Sweden.

EXTERNAL COUNTING OF ^{85}Sr AND ^{47}Ca IN LOCALIZED BONE INFECTIONS

By

JOHN-FREDRIK DYMLING and BO WENDEBERG

INTRODUCTION

In 1959 *Bauer & Wendeberg* reported external counting over various localized bone lesions after administration of bone-seeking γ-emitting isotopes. Since that time several reports have been published dealing with isotope studies of skeletal metabolic response to fracture (*Wendeberg* 1961), tumour (*Gynning et al.* 1961, *Corey et al.* 1962, 1963, *Wendeberg & Yamamuro* 1965), coxarthrosis (*Danielsson, Dymling & Heripret* 1964) and infectious disease of the spine (*Lindberg & Felländer* 1965). This is a report on external counting of ^{85}Sr and ^{47}Ca over localized bone infections in the extremities.

METHODS

Carrier-free ^{47}Ca (half-life 4.9 days) or ^{85}Sr (half-life 65 days) were used. The isotope was given as a single, rapid, intravenous injection. External counting was performed usually 168 and 336 hours after injection over the diseased part of the skeleton, over the contralateral side and over the knees and thighs (*Bauer & Wendeberg* 1959). A 12° wide angle collimator placed in contact with the skin over the area to be counted was routinely used. When the opening of this collimator was considered to be too large, a cylindric collimator with an opening of 24 mm was used. This was especially the case in children. For specific purposes a 10 mm slot collimator was used.

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The maximal dose administered was 1μC per kilogram of body weight or 50 μC. The amount of radiation delivered to the skeleton by this dose was calculated to be less than the maximal permissible dose recommended by the International Comission on Radiological Protection (*Bauer & Wendeberg* 1959).

The results were expressed as *activity ratios* or *activity*.

Activity was expressed as per cent of a standard-solution of ^{85}Sr or ^{47}Ca in order to account for the physical decay. The ratio was taken between the diseased part of the skeleton and the contralateral side. Normally activity ratio is close to unity. *Danielsson, Dymling & Heripret* (1963) calculated the activity ratios between normal knees and found 1.00 ± 0.018 and between identical parts of the tibiae and found 1.03 ± 0.018.

MATERIAL

The clinical material consisted of 25 patients: 12 with active septic osteomyelitis; one with active septic coxitis; five with non-active septic osteomyelitis; three with active tuberculous osteomyelitis; one with active tuberculous coxitis; two with non-active tuberculous osteomyelitis; and one with non-active tuberculous gonitis.

The term osteomyelitis was defined to mean infectious disease involving bone caused by staphylococci, streptococci or tubercle bacilli. Infections caused by staphylococci and streptococci were called septic. The roentgenologic evaluation[1] was based on skeletal roentgenograms of the diseased part at the time of investigation and later in the course of the disease.

The diagnosis was established on the basis of clinical findings, findings at surgery, when performed, bacteriologic and roentgenologic findings. The time of observation after the study varied from 6 months to 7 years.

The cases of active septic osteomyelitis involved the calcaneus in three cases (C-87, C-96, D-83), the tibia in three cases (A-22, E-109, H-57), the femur in two cases (F-33, F-83), the humerus in two cases (A-31, B-15) and the ulna in one case (H-56). In one case there was involvement of the knee joint (B-39), and another case (H-55) was a coxitis caused by staphylococci. 15 studies were performed.

The five cases of non-active septic osteomyelitis involved the tibia in two cases (F-102, H-17) and the femur in three cases (F-72, G-35, H-56).

[1] The roentgenologic evaluation was kindly carried out by *Lars Andrén*, M.D., of the Department of Roentgenology, General Hospital, Malmö.

In three of these (F-72, F-102, G-35) the inflammatory activity in the infectious process was questionable at the time of tracer study, but continued observation during 2, 2 and 1½ years, respectively, established the diagnosis.

The four cases of active tuberculous infection involved the trochanteric region in two cases (B-6, B-94) and the ulna in one case (H-58). One case (H-52) was a tuberculous coxitis. The non-active tuberculous processes were localized in the trochanteric region in one case (H-23), in the hipjoint in one case (H-71) and in the kneejoint in one case (H-9). One study was performed in each of these cases. Pertinent data are found in Table 1.

RESULTS

The activity ratios 14 days after injection were plotted against the duration of clinical symptoms in the active cases (Fig. 1). The activity ratios were found to increase above normal after an initial lag period of approximately 14 days.

The activity ratios 14 days after injection were better separated than those 7 days after injection (Fig. 2). The cases that were injected during the lag period have been indicated with open circles in Fig. 2. If the cases are excluded, the activity ratios in active bone infections were above 2.2 and in non-active bone infections below 1.5.

The results of the roentgenologic examination at the time of study

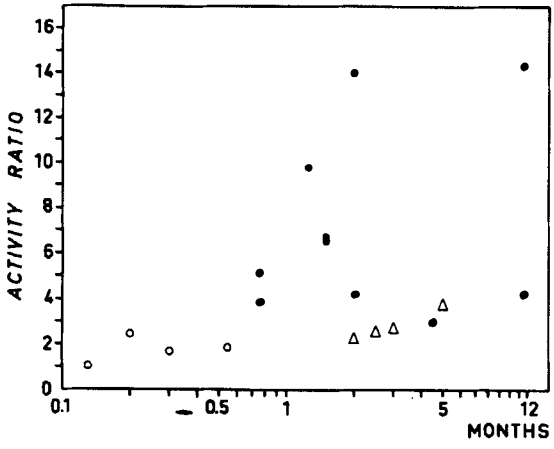

Fig. 1.
Activity ratios 14 days after injection of ^{47}Ca or ^{85}Sr. Circles indicate septic infections and triangles tuberculous infections.

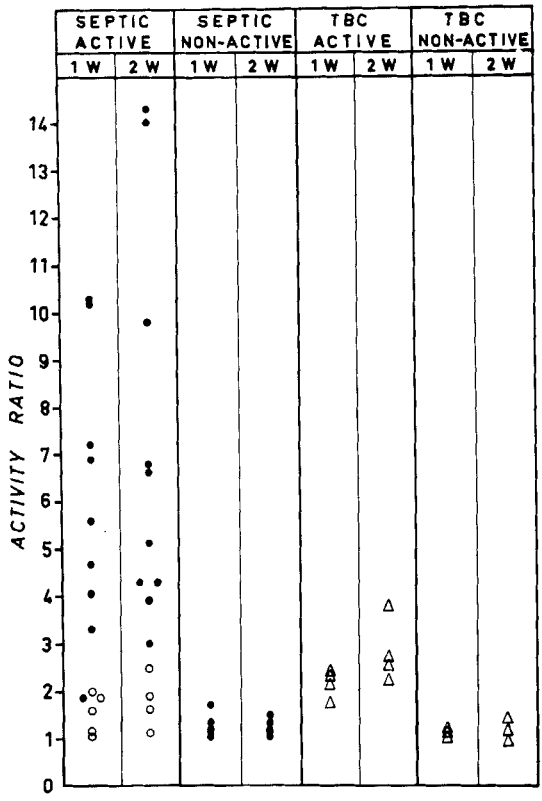

Fig. 2.
Activity ratios 7 and 14 days after injection of ^{47}Ca or ^{85}Sr.

varied (Table 1), but in the following cases no definite signs of active bone infection could be found: A-22, B-39, C-87, C-96, D-83, E-109, F-83, H-57 in the septic group and B-94 in the tuberculous group. Later in the course of the disease all acute cases developed roentgenologic evidence of bone involvement and the recurrent cases showed changes in the skeletal roentgenograms.

CASE HISTORY

Case F-83 is illustrative and will be reviewed: The patient was a 42 year old engineer, admitted to the orthopaedic clinic in May 1962 with a complaint of intermittant, predominantly nocturnal pain in the area of his right knee; of five years duration. He had no known focus of infection, however, in 1957 he had acute cystitis, at which time he was cystoscoped. Clinical investigation and skeletal roentgenograms showed no evidence of intra- or extra-articular disease. E.S.R. was 4 mm/hr. Femoral angiography was normal. Isotope study demonstrated a localized

Septic Active

Code No	A–22	A–22	A–31	B–15
Age (years)	6	6	29	66
Sex	M	M	M	M
Occupation	–	–	Factoryforeman	Factoryworker
Weight (kg)				80
Diagnosis	Osteomyelitis tibia dx acuta	Idem	Osteomyelitis humeri dx recidivans	Osteomyelitis humeri dx acuta
Roentgenogram at time of isotope study	0	0	Large osteolytic focus with surrounding sclerosis and small sequestration	Osteolytic focus with periosteal reaction
Duration of symptoms d=days w=weeks	4 d	22 d	50 w	6 w
Isotope	^{85}Sr	^{85}Sr	^{85}Sr	^{85}Sr
Dose μC	7	11	35	45
Ratio 24 h	–	–	2.48 (72 h)	4.8 (72 h)
168 h	1.15	4.69 (120 h)	10.3 (192 h)	–
336 h	1.10	3.92 (480 h)	14.3	6.76 (360 h)

Septic Active

Code No	E–109	F–33	F–83
Age (years)	6	39	42
Sex	M	M	M
Occupation	–	Seaman	Engineer
Weight (kg)		65	80
Diagnosis	Osteomyelitis tibiae sin acuta	Osteomyelitis femor dx acuta	Osteomyelitis femor dx
Roentgenogram at time of isotope study	0	Osteolytic focus with periosteal reaction	Insignificant slight increase in thickness of cortex
Duration of symptoms d=days w=weeks	6 d	6 w	18 w
Isotope	^{85}Sr	^{85}Sr	^{85}Sr
Dose μC	20	50	45
Ratio 24 h	–	–	–
168 h	1.88	6.9	1.86
336 h	2.48	6.6	3.00

B-39	C-87	C-96	D-83
58	14	14	10
M	M	F	F
Officeworker	–	–	–
49		58	44
Osteomyelitis femor dx cum gonitis recidivans	Osteomyelitis calcan. dx acuta	Osteomyelitis calcan. dx acuta	Osteomyelitis calcan. dx acuta
Old osteomyelitis in lower femur with reactive changes in bone. Deformed joint in valgus position	0	0	0
5 w	1 d	9 d	16 d
^{85}Sr	^{85}Sr	^{85}Sr	^{85}Sr
50	20	20	15
–	–	–	–
7.20 (192 h)	1.09 (120 h)	1.62	1.41 (96 h)
9.80	–	1.63 (188 h)	1.87

F-83	H-55	H-56	H-57
42	19	44	41
M	M	M	M
	Soldier	Engineer	Furrier
77	77	76	76
	Coxitis dx acuta	Osteomyelitis ulnae dx recidivans	Osteomyelitis tibiae dx recidivans
Idem	Periacetabular osteopenia and reduced cartilage	2 large osteolytic foci	Irregular structure with sclerosis and thickening of tibia
50 w	8 w	8 w	3 w
^{85}Sr	^{85}Sr	^{85}Sr	^{85}Sr
75	50	50	50
–	–	–	–
3.33	4.07	10.2	5.63
4.30	4.29	14.0	5.10

Septic Non-Active

Code No	F–72	F–102	G–35	H–17	H–56
Age (years)	65	40	48	36	44
Sex	M	F	M	M	M
Occupation	Factoryworker	Housewife	Officeworker	Factoryworker	Engineer
Weight (kg)	60	70	66	69	76
Diagnosis	St. p. osteomyelitis troch. sin et coxitis	St. p. osteomyelitis tibiae dx	St. p. osteomyelitis femor dx	St. p. osteomyelitis tibiae sin	St. p. osteomyelitis femor sin
Roentgenogram at time of isotope study	Deformed caput and usuration of trochanter with small fragments	Irregular sclerosis	Irregular bone structure and antero-medial curvature	Irregular bone structure with thickening of tibia	Irregular bone structure with sclerosis
Duration of symptoms d=days w=weeks					
Isotope	^{85}Sr	^{85}Sr	^{85}Sr	^{85}Sr	^{85}Sr
Dose μC	50	50	50	50	50
Ratio 24 h	–	–	–	–	–
168 h	1.19	1.13	1.35	1.73	1.02
336 h	1.20	1.11	1.30	1.51	1.10

Tbc Active

Code No	B–6	B–34	H–52	H–58
Age (years)	56	41	52	29
Sex	M	F	M	M
Occupation	Factoryworker	Housewife	Factoryworker	Truckdriver
Weight (kg)	50	57	61	80
Diagnosis	Osteomyelitis tbc troch. sin recidiv	Osteomyelitis tbc troch. dx recidiv	Coxitis tbc dx recidiv	Osteomyelitis tbc ulnae sin
Roentgenogram at time of isotope study	Irregular structure with progressive bone and joint destruction and sequestration	Irregular structure with large postoperative defect. No signs of activity	Progressive changes	Cystic changes with sequestration
Duration of symptoms d=days w=weeks	12 w	8 w	20 w	10 w
Isotope	^{47}Ca	^{85}Sr	^{85}Sr	^{85}Sr
Dose μC	50	50	50	35
Ratio 24 h	–	–	–	–
168 h	2.35	2.15	1.76	2.38
336 h	2.75	2.24	3.83 H/K–5.45 right H/K–1.71 left	2.57

Tbc Non-Active

Code No	H–9	H–23	H–71
Age (years)	31	63	42
Sex	M	F	M
Occupation	Factoryworker	Spinster	Technician
Weight (kg)	61	77	57
Diagnosis	St. p. gonitis tbc dx	St. p. osteomyelitis troch. sin	St. p. coxitis tbc dx op.
Roentgenogram at time of isotope study	Irregular joint with large usurations and reduced cartilage	Irregular structure with small defect in cortex	Resorption around cup. Sclerotic acetabulum
Duration of symptoms d=days w=weeks			
Isotope	^{85}Sr	^{85}Sr	^{85}Sr
Dose μC	50	50	40
Ratio 24 h	–	–	–
168 h	1.15	1.22	1.06
336 h	1.42	1.18	0.96

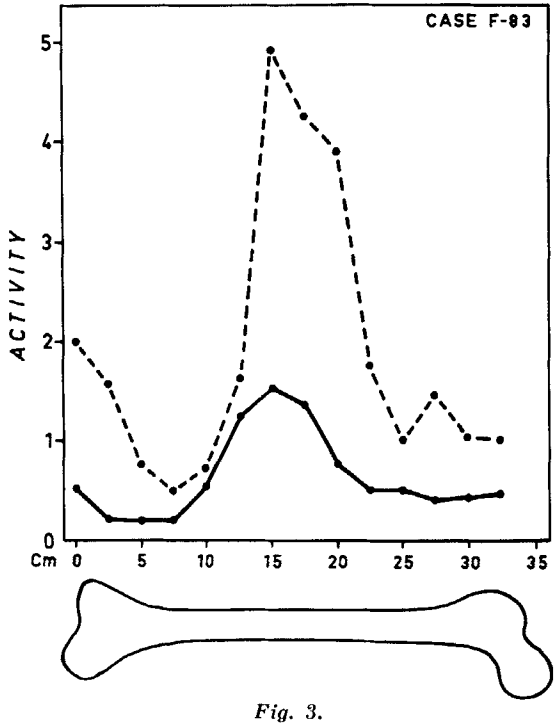

Fig. 3.
Activity at various locations over the right femur in case F-83. External counting was performed at 2.5 cm intervals with a 10 mm wide slot collimator. The continuous line shows the activity obtained in May 1962 and the broken line the activity found in October 1962.

area of increased ^{85}Sr uptake 15 cm proximal to the superior border of the patella (Fig. 3).

The patient was discharged and after a short symptom free period during the summer the pain returned. Repeat roentgenograms in October 1962, including tomography, was normal except for an area of slight cortical thickening of the medial aspect of the femoral shaft. Repeat isotope study was principally identical to the first (Fig. 3).

Operative exploration of the medial aspect of the femoral shaft revealed an area of periosteal hyperemia and softening of the underlaying bone tissue corresponding to the peak of increased ^{85}Sr uptake. Biopsy of this area showed histologic signs of chronic osteomyelitis. Penicilline was administered. Postoperatively the patient has remained almost completely symptom free.

DISCUSSION

The increased uptake of bone-seeking isotopes found with external counting over localized bone disease is interpreted as a sign of increased

skeletal metabolism or more specifically, locally increased accretion rate. The easiest way to express this increase is to calculate the ^{85}Sr or ^{47}Ca activity ratio between the diseased part of the skeleton and the contralateral side. This requires access to a contralateral side which is possible except for the axial skeleton. External counting over the spine may be expressed in different ways (*Gynning et al.* 1961, *Bauer & Scoccianti* 1961, *Lindberg & Felländer* 1965). Furthermore the contralateral side should be normal. If the contralateral side is affected by some disease process some other point of reference must be found. This is exemplified by case H-52. In this case the right hip was hit by infection and the left by arthrosis. This was manifested in an increased hip over knee ratio on both sides (cf. *Danielsson, Dymling & Heripret* 1963). The hip/hip activity ratio of 3.8 should consequently have been even higher, had the left hip been normal. Normally the activity ratio is close to unity. In cases of old non-active osteomyelitis this is not the case. This may be due to postinfectious remodelling of the bone and differences of bone mass seen by the detector.

Increased activity ratios were not found immediately the symptoms appeared. This means that the metabolic response of the bone as a tissue is delayed. It is probable that this delay is related to the metabolic turn-over rate of the affected bone. If this is the case the lag period should vary from bone to bone since the turn-over rate varies from bone to bone (*Frost, Villanueva & Roth* 1960). These possible differences cannot be evaluated in this series. However, when the tracer study was started two weeks or more after the symptoms appeared, increased activity ratios were obtained in all cases.

The optimal time for external counting cannot be exactly assessed but in general external counting performed 14 days after injection is superior to external counting performed 7 days after injection. The rationale of this is, that at 14 days after injection little activity is found in the soft tissues and the exchangeable fraction of bone (*Wendeberg* 1961), and consequently the local accretion is of greater importance. The experience in our laboratory is that external counting performed 14 days after injection gives reliable informations and is easily arranged both for the patients and the laboratory.

In the acute cases it was found that external counting gave evidence of local bone disease at a time when the roentgenograms were still normal. This is in accordance with findings in similar studies of bone tumours. In chronic cases the question if the infectious process is active or not, is notoriously difficult to answer on the basis of roent-

genograms. In these cases external counting gave reliable results as far as prolonged clinical observation and repeated roentgenograms are capable of distinguishing this entity. In no case in our series were there roentgenologic or clinical signs of activity and normal external counting. In no case of non-active osteomyelitis was the activity ratio above 1.5. In the active cases the ratio 14 days after administration of the isotope was always above 2.2. It is concluded that an activity ratio of 2.0 is a reasonably reliable arbitrary border-line with the detector geometry used here. If the clinical findings suggest active bone infection and the symptoms have lasted more than a fortnight before injection of the isotope, an activity ratio above 2.0 strongly supports the clinical diagnosis even if the roentgenograms are normal or do not show any signs of activity.

The case history illustrated that external counting can give evidence of localized bone disease when roentgenograms are questionable or even negative. The tracer data gave the surgeon an exact localization of the disease process; an exploration would not have been undertaken without these data.

SUMMARY

External counting after injection of ^{47}Ca or ^{85}Sr has been performed in 17 cases of active and 8 cases of non-active bone or joint infections. Increased uptake of bone-seeking radioisotopes were regularly found in areas of active bone infection, when the symptoms had lasted for approximately 14 days. Active and non-active bone infections could be completely separated by this method.

External counting gave reliable information earlier than roentgenologic investigation in acute cases, and was particularly useful as a compliment to roentgenograms in evaluating recurrence of the infectious process in chronic cases.

RESUME

Il a été procédé un comptage externe après injection de ^{47}Ca ou de ^{85}Sr dans 17 cas d'infections osseuses ou articulaires actives et dans 8 cas non-actives. On a régulièrement trouvé un nombre accru de radioisotopes recherchant les os dans les régions d'une infection osseuse active, lorsque les symptômes avaient duré approximativement 15 jours. Les infections osseuses actives et non-actives ont pu être entièrement séparées au moyen de cette méthode.

Le comptage externe a donné des informations sures plus tôt que les

examens radiographiques dans les cas aigus et il a été particulièrement utile comme un complément aux radiogrammes pour évaluer, dans les cas chroniques, les chances de récurrence du processus infectieux.

ZUSAMMENFASSUNG

Externe Zählung nach Injektion von ^{47}Ca oder ^{85}Sr wurde in 17 Fällen von aktiven und in 8 Fällen von nichtactiven Knochen- oder Gelenksinfektionen ausgeführt. Gesteigerte Aufnahme von knochenaufsuchenden Radiumisotopen wurden regelmässig in Gebieten aktiver Knocheninfektion gefunden, wenn die Symptome ungefähr 14 Tage bestanden hatten. Aktive und nicht-aktive Knocheninfektionen konnten auf diese Weise vollständig voneinander getrennt werden.

Externe Zählung gab in akuten Fällen frühzeitiger verlässliche Auskunft als röntgenologische Untersuchung und war besonders wertvoll als eine Ergänzung der Röntgenuntersuchung bei der Beurteilung von Rezidiven des infektiösen Prozesses in chronischen Fällen.

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