

Resolution of Metastatic Calcification Revealed by Bone Scanning: Case Report

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We report here a case that shows the resolution of metastatic visceral calcification after correction of hypercalcemia. The resolution was visualized by serial whole body scans with the bone-scanning agent Tc-99m methylene diphosphonate.

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CASE REPORT

A 25-year-old woman developed low back pain in October 1975. In December nausea and vomiting supervened, and by January, when she was admitted to her local hospital, she had lost 20 pounds. The tentative diagnosis was pancreatitis or cholecystitis, but because of the development of "bizarre behavior" including hallucinations, she was transferred to a state mental hospital. There she was found to have hypercalcemia (14 mg %) and prerenal azotemia (BUN 45 mg %; creatinine 3.7 mg %). A previously palpated breast mass was biopsied and found to be carcinoma.

She was then transferred to our hospital, where her calcium was 17.7 mg %, BUN 59 mg %, and creatinine clearance 13 cc/min. Her chest film was normal but an abdominal film showed multiple lytic lesions of the pelvis and ribs. Serum parathormone level was normal. The initial bone scan, performed 3 hr after injection of 20 mCi of Tc-99m methylene diphosphonate, is shown in Fig. 1. Marked extraosseous activity was present in the lungs and stomach.

The hypercalcemia was treated with hydration, Mithramycin, Prednisone, and Furosemide, with a prompt response. The calcium level fell to 11.7 mg % within 7 days. Within 1 week the BUN and creatinine were down to 26 mg % and 1.3 mg %, respectively. She was then treated with Vincristine, 5-Fluorouracil, Adriamycin, Cyclophosphamide, and Prednisone for the metastatic carcinoma. Her calcium level was 8.7 mg % at discharge. Followup scans done 6 wk and 1 yr later (Fig. 2A and B) document the reversal of the uptake by nonosseous sites (i.e., lung and stomach).

DISCUSSION

Since the description of metastatic dyscrasia by Virchow in 1858 (1), the phenomenon of metastatic calcification has intrigued pathologists. Virchow stated that it was a result of oversaturation of the blood with calcium salts. He noted its appearance in the lungs and stomach. Later observers, noting the predilection of calcium to deposit in the kidneys as well as the lungs and stomach, postulated that this distribution occurs because these tissues are the three chief places in the body where acids are secreted. The secretion of acid should leave a more alkaline fluid where calcium salts should be more likely to precipitate. Hofmeister (2) showed the deposits as limited to the interglandular tissue about the upper part of glands of the fundus of the stomach (i.e., the location of the acid-secreting parietal cells). Wells (2) noted the prominence of calcium deposits in the endocardium of the left side of the heart, the coronary arteries and the pulmonary veins, but not in the pulmonary arteries and right side of the heart, and emphasized the difference in CO₂ content with the arterial circulation having a higher pH.

The localization of metastatic calcification was described and logically explained before the discovery of carbonic anhydrase. This enzyme's predominant location in red blood cells, gastric mucosa, and renal tubules in mammals gives credence to the concepts as described earlier and permits at least a

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FIG. 1. Initial scan (1/26/76), anterior view, showing uptake in lungs and stomach.

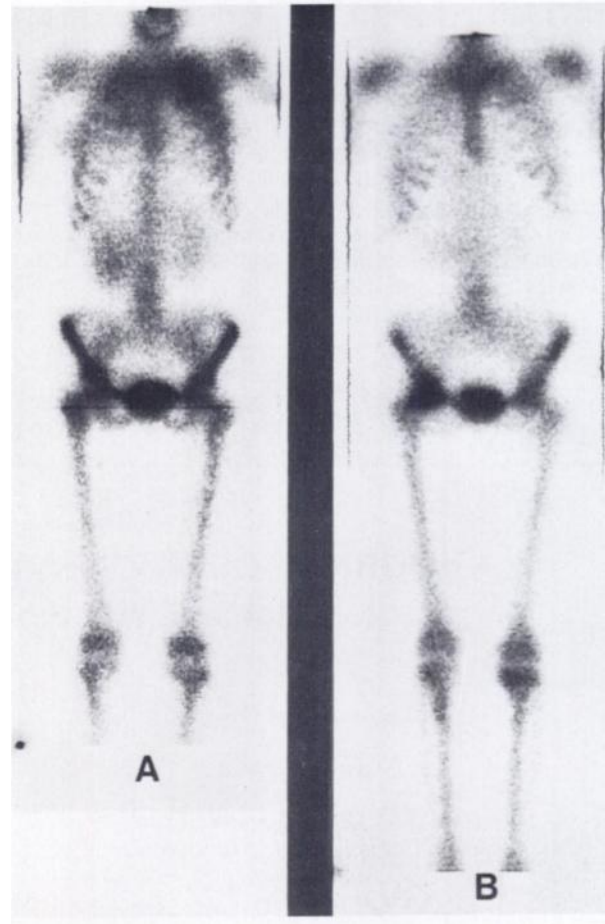


FIG. 2. Subsequent scans, A (3/5/76) and B (1/7/77), showing resolution of increased uptake in lungs and stomach. Note that metastasis in right pelvis is more prominent.

schematic understanding of the reason for the alkalinity of the lungs, stomach, and kidneys.

There have been several reports showing metastatic calcifications with bone scanning agents, initially with strontium and more recently with Tc-99m-labeled phosphates and phosphonates (4,5), but serial scans documenting resolution of the soft-tissue activity have not been reported. It is generally, though not universally, felt that the mechanism of localization of these compounds is by chemisorption onto the surface of hydroxyapatite crystals (6,7). This is in agreement with the observations of Alfrey, who has shown that the visceral calcium deposit in hypercalcemia is initially brushite [$\text{Ca HPO}_4 \cdot 2\text{H}_2\text{O}$], which is subsequently transformed to hydroxyapatite [$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$] (8,9). Arterial and tumoral calcium deposits in uremic patients are also composed of hydroxyapatite. The visceral calcifications in uremia are not, for they have a whitlockite structure. This point was emphasized by Conger (10), who found hydroxyapatite absorbed 98% of Tc-99m diphosphonate from a bath, whereas the amorphous

calcium phosphate (with thermonuclear properties of whitlockite crystal structure), as found in visceral calcifications in uremia, absorbed only 24% (10).

It should not be surprising that the metastatic calcium deposits of hypercalcemia should resolve, since they are hydroxyapatite. Alfrey (11) has demonstrated radiologically the disappearance of gross tumoral calcifications of chronic uremia after transplantation, with phosphate supplementation, or (rarely) parathyroidectomy. It is felt that the case reported here shows the dissolution of the hydroxyapatite in metastatic visceral foci after correction of hypercalcemia.

REFERENCES

1. VIRCHOW R: *Cellular Pathology*. New York, Robert M. DeWitt, 1860, pp 249-254
2. WELLS HG: Metastatic calcification. *Arch Int Med* 15: 574-580, 1915
3. MAREN TH: Carbonic anhydrase: Chemistry, physiology, and inhibition. In *Physiological Reviews*, vol 47, Baltimore, Waverly Press, 1967, pp 595-781
4. GRANES GM, SAUSER DD, JANSEN C, et al: Radionu-

clide detection of diffuse interstitial pulmonary calcification. *JAMA* 230: 992-995, 1974

5. RICHARD AG: Metastatic calcification detected through scanning with ^{99m}Tc polyphosphate. *J Nucl Med* 15: 1057-1060, 1974

6. FRANCIS MD: The inhibition of calcium hydroxyapatite crystal growth by polyphosphonates and polyphosphates. *Calcif Tiss Res* 3: 151-162, 1969

7. KRANE SM, GLINCHER MJ: Transphosphorylation from nucleoside di- and triphosphates by apatite crystals. *J Biol Chem* 237: 2991-2998, 1962

8. ALFREY AC, SOLOMON CC: Bone pyrophosphate in

uremia and its association with extrasosseous calcification. *J Clin Invest* 57: 700-705, 1976

9. ALFREY AC, SOLOMONS CC, CIRICILLO J, et al: Extrasosseous calcification evidence for abnormal pyrophosphate metabolism in uremia. *J Clin Invest* 57: 692-699, 1976

10. CONGER JD, ALFREY AC: Letter to the editor. Reply. *Ann Int Med* 84: 224-225, 1976

11. ALFREY AC, JENKINS D, CROTH CG, et al: Resolution of hyperparathyroidism renal osteodystrophy and metastatic calcification after renal homotrasplantation. *New Engl J Med* 279: 1349-1356, 1968

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