Case Report
The Relationship between Multiple Myeloma with Renal Failure and Metastatic Calcification

Takanori Fukuta, Takayuki Tanaka, Yoshinori Hashimoto, and Hiromi Omura
Department of Hematology, Tottori Prefectural Central Hospital, Tottori, Japan
Correspondence should be addressed to Takanori Fukuta; takanori.fukuta@jfcr.or.jp
Received 14 April 2018; Accepted 27 May 2018; Published 20 June 2018
Academic Editor: Alessandro Gozzetti

Copyright © 2018 Takanori Fukuta et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

While cases of multiple myeloma (MM) with metastatic calcification have been reported, the mechanisms for this calcification have yet to be explained. We observed a case of MM in a patient with end-stage renal failure who developed vascular and pulmonary calcification. A 51-year-old male was diagnosed with Bence-Jones type MM and required maintenance hemodialysis. He was treated with bortezomib-dexamethasone, vincristine-doxorubicin-dexamethasone, the M2 protocol, and lenalidomide-dexamethasone (Rd) therapy. During the sixth cycle of Rd therapy, he complained of pain in both lower legs. Well-demarcated ulcers with severe pain had developed on the right lower leg, both exterior thighs, and penis. We found that the patient’s serum intact parathyroid hormone level was elevated, while it had previously been permissively controlled. Computed tomography scans showed widespread centrilobular opacities of the bilateral lungs and high-density lesions along small blood vessels in the trunk and all four extremities. Histological calcifications were identified in small blood vessels and the alveolar walls. The risk of metastatic calcification in MM appears to be associated with renal failure, but not with MM itself.

1. Introduction

Multiple myeloma (MM) is a clonal plasma cell proliferative disorder with symptoms related to bone marrow infiltration, impaired hematopoiesis, or end-organ damage, which ultimately leads to renal failure, bone lesions, and hypercalcemia.

Metastatic calcification is the deposition of calcium salts in systemic organs. Calcific uremic arteriolopathy (CUA), a type of metastatic calcification, is a rare condition characterized by cutaneous artery calcinosis, leading to skin ischemia and ulceration. The term “calciphylaxis” is also used to describe such lesions, but it was originally used to describe hypersensitivity [1].

Cases of MM with metastatic calcification have been previously reported, but the mechanism for this calcification is unclear. Here we describe a patient with MM and end-stage renal failure who developed vascular and pulmonary calcification, and we examine the relationship between MM and calcification.

2. Case Presentation

A 51-year-old male was referred to our hospital because of a three-month history of gradually progressing renal failure. During his first hospitalization, he complained of lumbar pain. On physical examination, he had conjunctival pallor and severe percussion tenderness of his back. No skin lesions or neurological deficits were seen. Laboratory test results were as follows: hemoglobin, 8.7 g/dL; creatinine, 7.01 mg/dL; total protein, 7.4 g/dL; albumin, 3.2 g/dL; calcium, 14.8 mg/dL; phosphate, 6.2 mg/dL; beta-2-microglobulin, 27.9 mg/L; IgG, 341 mg/dL; IgA, 21 mg/dL; IgM, 18 mg/dL; free kappa light chain, 99,900 mg/L; and free lambda light chain, 9.7 mg/L. Chest X-ray results were normal. Computed tomography (CT) showed vertebral compression fractures of Th8 and L1 and bilateral pleural effusions without calcified lesions. Urine immunoelectrophoresis showed a positive result for the Bence-Jones protein. Bone marrow aspiration revealed plasma cell proliferation (65% of total nucleated cells, Figure 1) with expression of CD38 and CD56, absence of CD19 and CD20, and an MIB-1 labeling index of 25%. Chromosomal analysis of the bone marrow by G-bandng showed a normal 46,XY karyotype, but fluorescence in situ hybridization revealed the abnormalities del(13q) and t(4;14). He was diagnosed with Bence-Jones protein type MM (stage III according to the International Staging System, and stage IIIB according to the Durie–Salmon classification system).
We began treatment with intravenous fluids and intra-muscular injections of calcitonin to treat the severe hypercalcemia. Simultaneously, he received bortezomib-dexamethasone (Bd) therapy (subcutaneous injection of 1.3 mg/(m^2·day) bortezomib plus 20 mg/day dexamethasone orally on days 1, 4, 8, and 11). Unexpectedly, he experienced severe acute heart failure on day 8, and temporarily required the support of a mechanical ventilator. Bd therapy was discontinued during the first treatment cycle. Because renal function had not improved, maintenance hemodialysis was initiated. Subsequently, we continued MM treatment with two cycles of vincristine-doxorubicindexamethasone (0.4 mg/body of vincristine and 9 mg/m^2 of doxorubicin on days 1 to 4; and 40 mg/body of dexamethasone on days 1 to 4, 9 to 12, and 17 to 20 of a 28-day cycle) and the M2 protocol (multiple chemotherapeutic agents, not including proteasome inhibitors), followed by lenalidomide-dexamethasone (Rd) therapy (5 mg/day lenalidomide on days 1 to 21 plus 20 mg/body dexamethasone on days 1, 8, 15, 22 of a 28-day cycle).

About four months after starting Rd therapy, the patient suffered from myoclonus-like movement of the lower extremities. During the sixth cycle of Rd therapy, he complained of pain in both lower legs, but did not have skin lesions or tenderness. He had been taking loxoprofen, fentanyl (patch and buccal tablet), mecobalamin, ferrous fumarate, lansoprazole, amloidipine, furosemide, alfalcacidol, and darbepoetin alfa. It was unlikely that his pain was drug-induced.

The patient’s serum creatinine kinase level was elevated to 1,268 U/L. Diffusion-weighted and short tau inversion recovery magnetic resonance imaging revealed diffuse high signal intensity in the crural muscles (Figure 2(a)). A muscle biopsy was performed on the right tibial anterior muscles (Figure 3) and 40 mg/day prednisolone was prescribed by a neurologist because of suspected polymyositis/dermatomyositis. However, typical pathologic findings of polymyositis/dermatomyositis, like lymphocyte infiltration around muscle fibers, were absent and vessel calcification was noted. Prednisolone was ineffective against his symptoms. During steroid administration, well-demarcated ulcers developed on the right lower leg, both exterior thighs, and the penis. These ulcers gradually worsened (Figure 4) and the patient experienced severe pain, especially during dialysis or exercise. He could not continue dialysis because of this exacerbation of pain. Moreover, muscle atrophy of his lower limbs impaired his daily activities. The administration of 40 mg/day prednisolone was continued.

**Figure 1:** Morphology of the plasma cells in a bone marrow smear (May–Giemsa staining).

**Figure 2:** MRI/CT image of lower legs. (a) STIR (short tau inversion recovery) magnetic resonance image showing high-signal intensity areas in the lower leg muscles. These lesions had high DWI signals and normal ADC values. The muscle structure was intact. (b) Noncontrast enhanced computed tomography showing high density areas along the vessels.
for 42 days and was then stopped on the 84th day after tapering. The patient’s serum intact parathyroid hormone (PTH) level was 429 pg/mL, while previously it was permissively controlled within the range of 140–250 pg/mL. Before dialysis, his levels of serum albumin, calcium, and phosphate were 4.0 g/dL, 7.4 mg/dL, and 7.9 mg/dL, respectively. He was diagnosed with secondary hyperparathyroidism (HPT). We could not exclude a relationship between MM and HPT, although his free light chain ratio was decreasing.

CT showed widespread centrilobular opacities of both lungs (Figure 5(a)) and high-density lesions along small blood vessels in the trunk and extremities (Figure 2(b)), but the mediastinum, abdominal organs, and large vessels like the thoracic and abdominal aorta were intact. A pulmonary function test demonstrated restrictive impairment with reduced diffusion capacity: the predicted forced vital capacity was 48.6%, the forced expiratory volume of the first breath was 87.9%, and the predicted diffusing capacity of lung for carbon monoxide was 67.1%. 99mTc-hydroxymethylene diphosphonate scintigraphy revealed abnormal diffuse accumulation in both upper lung fields (Figure 6). Echography revealed no enlargement of the parathyroid glands.

Next, a transbronchial lung biopsy was performed, and microscopy confirmed the presence of calcifications of the alveolar walls (Figure 5(b)) and of a small vessel in the right anterior tibial muscle (Figure 3). However, pathological calcification was absent from the right exterior thigh ulcer. Healing of the skin biopsy wound was delayed.

The patient was ultimately diagnosed with muscle and skin ischemia from CUA. He was treated with cinacalcet, and his intact PTH levels fell to a normal range. He underwent four
additional cycles of Rd therapy, but ulcer infections occurred repeatedly in both thighs, occasionally progressing to sepsis. He has since been monitored closely for MM, without treatment, for four months. Meanwhile, the ulcers have achieved epithelialization after topical treatment, but his serum free light chain ratio level increased from 290 to 1532. He is currently undergoing Pd therapy (2mg/day pomalidomide on days 1 to 21, plus 4mg/day dexamethasone on days 1, 8, 15, and 22 of a 28-day cycle) without any adverse events. Since severe heart failure occurred during the combined regimen with bortezomib, we have avoided administering proteasome inhibitors. His disease is stable according to the International Myeloma Working Group criteria.

3. Discussion

In this case, metastatic calcification occurred in an MM patient with end-stage renal failure and secondary HPT. Melosalgia triggered the diagnosis of CUA. Histological calcifications were observed in small blood vessels and the alveolar walls. Cutaneous ulcers were found symmetrically in our patient, on both lower limbs and the penis, which were accompanied by strong pain exacerbated by dialysis and exertion. This symptom is consistent with ischemia: dialysis reduces the circulating plasma volume, while exertion increases oxygen demand. Clinicians should avoid biopsy for the definite diagnosis of suspected CUA based on clinical presentations, because such lesions may exhibit delayed wound healing. CUA causes a high mortality rate due to sepsis from wound infection [2]. The myoclonus-like movement of the lower extremities of our patient might have been another consequence of ischemia.

The mineral and bone metabolism of patients with renal failure should be controlled to improve prognosis. Recently, the term “chronic kidney disease-mineral and bone disorder” has been used for the condition traditionally called renal osteodystrophy. Complex abnormalities of calcium, phosphate, and PTH are all part of chronic kidney disease-mineral and bone disorder.

Where the relationship between MM and HPT is unclear. Hussain et al. described 30 cases of MM with primary HPT and reported that this condition is more common in females, its effects are observed in various types of MM immunoglobulin chains, and it does not coincide with the appearance of HPT. Unfortunately, the frequency of renal failure in these patients is not currently available [3]. Our hypothesis is that the main risk factor for HPT is not MM, but renal failure. Secondary HPT is common within dialysis populations. For example, Hedgeman et al. reported that the prevalence of secondary HPT within dialysis populations ranges from about 30 to 50% [4].

### Table 1: Data for patients with multiple myeloma plus lung or vessel calcifications.

| Age | Sex | Immunoglobulin chain | Cr (mg/dL) | Corrected Ca (mg/dL) | P (mg/dL) | Intact PTH (pg/mL) | Lung lesions* | Pathological vessel calcifications | Reference |
|-----|-----|-----------------------|------------|----------------------|-----------|-------------------|--------------|-------------------------------|-----------|
| 45  | M   | Lambda                | 2.6        | 12.3                 | NA        | NA                | +            |                      | [9]       |
| 57  | F   | IgA lambda            | 7.44       | 7.5                  | 11.9      | 149               | +            |                      | [10]      |
| 52  | F   | IgG kappa             | 1.66       | 13.8                 | NA        | NA                | +            |                      | [12]      |
| 44  | M   | Nonsecretory          | Elevated   | Elevated             | NA        | NA                | +            |                      | [13]      |
| 42  | M   | IgG lambda            | Normal     | Normal               | Normal    | Normal            | +            |                      | [14]      |
| 60  | F   | Kappa                 | 5          | 18                   | 11.4      | NA                | +            |                      | [15]      |
| 52  | M   | Kappa                 | 2.56       | 20                   | 5.82      | NA                | +            |                      | [16]      |
| 54  | F   | Nonsecretory          | 4.9        | 16.4                 | 7.7       | Normal            | +            |                      | [17]      |
| 49  | M   | NA                    | 7          | 12.8                 | NA        | NA                | +            |                      | [18]      |
| 51  | F   | IgG kappa             | 15.3       | 12.5                 | 6.6       | NA                | +            |                      | [19]      |
| 66  | F   | IgA lambda            | 2.75       | 12.8                 | NA        | NA                | +            |                      | [20]      |
| 66  | F   | IgA lambda            | 1.92       | 18.0                 | NA        | NA                | +            |                      | [20]      |
| 47  | M   | NA                    | Elevated   | Elevated             | NA        | NA                | +            |                      | [21]      |
| 70  | M   | IgG                   | 4          | 17.5                 | 5.2       | NA                | +            |                      | [22]      |
| 62  | M   | IgG                   | 8.6        | 12                   | NA        | NA                | +            |                      | [22]      |
| 57  | M   | IgA kappa             | 7.3        | 16.7                 | 5.7       | NA                | +            |                      | [23]      |
| 51  | F   | IgG                   | 2.01       | 14.1                 | NA        | NA                | +            |                      | [24]      |
| 55  | M   | IgA lambda            | 3.1        | 14.6                 | 3.4       | NA                | +            |                      | [25]      |
| 53  | M   | Lambda                | 3          | 14.4                 | 4.9       | <100              | +            |                      | [26]      |
| 56  | M   | IgA lambda            | 3.3        | 17.5                 | NA        | NA                | +            |                      | [27]      |
| 63  | M   | NA                    | NA         | 16.4                 | NA        | NA                | +            |                      | [28]      |
| 74  | F   | IgG lambda            | NA         | Normal               | Normal    | Normal            | Normal       |                      | [29]      |
| 55  | M   | NA                    | Elevated   | NA                   | NA        | +                 |              |                      | [30]      |
| 37  | M   | NA                    | 4.9        | 13.1                 | 7.2       | NA                | +            |                      | [31]      |
| 73  | F   | IgG kappa             | 3.5        | 15.3                 | 5.8       | NA                | +            |                      | [32]      |
| 65  | M   | IgG kappa             | 1.8        | 14.7                 | 4.4       | NA                | +            |                      | [33]      |
| 67  | M   | IgA lambda            | 4.9        | 12.5                 | Normal    | NA                | +            |                      | [34]      |
| 51  | M   | Kappa                 | 7.01       | 15.6                 | 6.2       | 429               | +            | +                  | Our case |

*The blank spaces for “lung lesions on CXR/CT/scintigram or histology finding” and “pathological vessel calcifications” mean that these findings were not described. M: male; F: female; NA: not available. *Not corrected; **findings on CXR/CT/scintigram or histology.
Interestingly, our patient developed metastatic pulmonary calcification, depositions of calcium in the pulmonary parenchyma, and pathologically identified calcifications of the alveolar walls, but not of lung small vessels. CT images showed a relatively strong deposition of calcium in the upper lung zone, which is typical of metastatic pulmonary calcification. It has been reported that the ventilation-perfusion ratio of the lung apex is higher than that of the base; therefore, the partial pressure of carbon dioxide in the artery is low and its pH is high. This environment appears to facilitate tissue calcification [5]. These lung lesions often do not cause respiratory failure and they are difficult to detect by chest radiography [5]. Kaltreider et al. found just 13 cases of interstitial pulmonary calcification in a series of 7,221 autopsies [6]. In contrast, metastatic pulmonary calcification was observed in 60% (9/15) [7] to 75% (42/56) [8] of chronic dialysis patients in an autopsy series. Chronic dialysis thus appears to carry a high risk of lung calcification.

To clarify the relationship between MM and metastatic calcification, PubMed was searched using the terms “multiple myeloma,” and “metastatic calcification,” and we then added other appropriate articles published between 1980 and 2015. Table 1 shows data from 29 MM patients with metastatic calcification or CUA. Twenty-four of the patients (92%, excluding three with unclear renal function) presented renal insufficiency, and 26 (90%) developed hypercalcemia. Calcification of both the lungs and vessels were confirmed in eight patients (28%). PTH values were available in few cases. The type of immunoglobulin light and heavy chains observed were not uniform. These previous reports indicate that myeloma does not seem to have a primary role in metastatic calcification. We hypothesize that renal failure, not only in patients requiring dialysis, is a fundamental cause of calcinosis in MM patients.

The risk of metastatic calcification in MM appears to have a strong relationship with renal failure, but not with MM itself. Metastatic calcification, such as CUA and metastatic pulmonary calcification, is rare complication in MM patients, even in those with renal failure. However, clinicians should be aware of this condition, because it can induce organ injury or lethal outcomes.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

References

[1] H. Selye, G. Gabbiani, and R. Strebel, “Sensitization to calciphylaxis by endogenous parathyroid hormone,” Endocrinology, vol. 71, no. 4, pp. 554–558, 1962.
[2] S. M. Roe, L. D. Graham, W. B. Brock, and D. E. Barker, “Calciphylaxis: early recognition and management,” American Surgeon, vol. 60, no. 2, pp. 81–86, 1994.
[3] N. Hussain, M. Khan, A. Natarajan et al., “A case of multiple myeloma coexisting with primary hyperparathyroidism and review of the literature,” Case Reports in Oncological Medicine, vol. 2013, Article ID 420565, 8 pages, 2013.
[4] E. Hedgeman, L. Lipworth, K. Lowe et al., “International burden of chronic kidney disease and secondary hyperparathyroidism: a systematic review of the literature and available data,” International Journal of Nephrology and Renovascular Disease, vol. 2015, Article ID 184321, 15 pages, 2015.
[5] E. D. Chan, D. V. Morales, C. H. Welsh, M. T. McDermott, and M. I. Schwarz, “Calcium deposition with or without bone formation in the lung,” American Journal of Respiratory and Critical Care Medicine, vol. 165, no. 12, pp. 1654–1669, 2002.
[6] H. B. Kaltreider, G. L. Baum, G. Bogaty, M. D. McCoy, and M. Tucker, “So-called “metastatic” calcification of the lung,” American Journal of Medicine, vol. 46, no. 2, pp. 188–196, 1969.
[7] J. D. Conger, W. S. Hammond, A. C. Alfrey et al., “Pulmonary calcification in chronic dialysis patients. Clinical and pathologic studies,” Annals of Internal Medicine, vol. 83, no. 3, pp. 330–336, 1975.
[8] D. C. Kuzela, W. E. Huffer, J. D. Conger, S. D. Winter, and W. S. Hammond, “Soft tissue calcification in chronic dialysis patients,” American Journal of Pathology, vol. 86, no. 2, pp. 403–424, 1977.
[9] S. R. Surani, S. Surani, A. Khimani, and J. Varon, “Metastatic pulmonary calcification in multiple myeloma in a 45-year-old man,” Case Reports in Pulmonology, vol. 2013, Article ID 341872, 3 pages, 2013.
[10] K. Ueki, S. Yamada, A. Tsuchimoto et al., “Rapid progression of vascular and soft tissue calcification while being managed for severe and persistent hypocalcemia induced by denosumab treatment in a patient with multiple myeloma and chronic kidney disease,” Internal Medicine, vol. 54, no. 20, pp. 2637–2642, 2015.
[11] C. K. Weber, J. M. Friedrich, E. Merkle et al., “Reversible metastatic pulmonary calcification in a patient with multiple myeloma,” Annals of Hematology, vol. 72, no. 5, pp. 329–332, 1996.
[12] S. Cagirgan, N. Soyer, F. Vural et al., “Metastatic pulmonary calcinosis and leukocytoclastic vasculitis in a patient with multiple myeloma,” Turkish Journal of Haematology, vol. 29, no. 4, pp. 397–400, 2012.
[13] H. Kempter, G. Hagner, A. N. Savaser, H. Huben, and C. Minguillon, “Metastatic pulmonary calcification in a patient with nonsecretory multiple myeloma,” Respiration, vol. 49, no. 1, pp. 77–80, 1986.
[14] R. F. Raper and L. S. Ibels, “Osteosclerotic myeloma complicated by diffuse arteritis, vascular calcification and extensive cutaneous necrosis,” Nephron, vol. 39, no. 4, pp. 389–392, 1985.
[15] C. Crippa, S. Ferrari, M. Drera et al., “Pulmonary calciphylaxis and metastatic calcification with acute respiratory failure in multiple myeloma,” Journal of Clinical Oncology, vol. 28, no. 9, pp. e133–e135, 2010.
[16] E. Sullivan and C. Hoyle, “Calciphylaxis, occurring 10 weeks after hypercalcemia, in a patient with multiple myeloma,” British Journal of Haematology, vol. 155, no. 2, p. 136, 2011.
[17] A. J. Chaves Alvarez, A. Herrera Saval, J. Marquez Enriquez, and F. Camacho Martinez, “Metastatic calcinosis cutis in multiple myeloma,” British Journal of Dermatology, vol. 142, no. 4, pp. 820–822, 2000.
[18] E. Marchiori, N. L. Muller, A. S. Souza et al., “Unusual manifestations of metastatic pulmonary calcification: high-resolution CT and pathological findings,” Journal of Thoracic Imaging, vol. 20, no. 2, pp. 66–70, 2005.
[19] R. H. Poe, C. Kamath, M. A. Bauer et al., “Acute respiratory distress syndrome with pulmonary calcification in two patients
with B cell malignancies,” *Respiration*, vol. 56, no. 1-2, pp. 127–133, 1989.

[20] H. Nilsson-Ehle, C. Holmdahl, M. Suurkula, and J. Westin, “Bone scintigraphy in the diagnosis of skeletal involvement and metastatic calcification in multiple myeloma,” *Acta Medica Scandinavica*, vol. 211, no. 6, pp. 427–432, 1982.

[21] G. L. Arbona, S. Antonmattei, M. R. Tetalman, and J. D. Scheu, “Tc-99m-diphosphonate distribution in a patient with hypercalcemia and metastatic calcifications,” *Clinical Nuclear Medicine*, vol. 5, no. 9, p. 422, 1980.

[22] M. Salvatori, V. Valenza, A. Ursitti, and G. Menichella, “Bone scan demonstration of metastatic calcification in multiple myeloma,” *Rays*, vol. 12, no. 1, pp. 63–66, 1987.

[23] P. Morassi, G. Paladini, G. Mazzanti et al., “Bone scintigraphy in the diagnosis of pulmonary calcification in multiple myeloma,” *European Journal of Nuclear Medicine and Molecular Imaging*, vol. 11, no. 8, pp. 327–329, 1985.

[24] J. L. Coolens, P. Devos, and M. De Roo, “Diffuse pulmonary uptake of 99mTc bone-imaging agents: case report and survey,” *European Journal of Nuclear Medicine and Molecular Imaging*, vol. 11, no. 1, pp. 36–42, 1985.

[25] F. Cardellach, J. Rabasseda, A. Pujol et al., “Detection of metastatic calcification in lungs and stomach with radionuclide in multiple myeloma,” *Thorax*, vol. 37, no. 7, pp. 552–553, 1982.

[26] Y. Hirose, J. Tachibana, S. Sugai et al., “Metastatic calcification in the stomach demonstrated by a bone scan in Bence Jones lambda myeloma,” *Japanese Journal of Medicine*, vol. 26, no. 1, pp. 72–75, 1987.

[27] M. Ito, C.-T. Hsu, S. Shikuwa et al., “Multiple myeloma in alcoholic liver cirrhosis,” *Tohoku Journal of Experimental Medicine*, vol. 157, no. 1, pp. 39–44, 1989.

[28] J. H. Liou, L. C. Cho, and Y. H. Hsu, “Paraneoplastic hypercalcemia with metastatic calcification—clinicopathologic studies,” *Kaohsiung Journal of Medical Sciences*, vol. 22, no. 2, pp. 85–88, 2006.

[29] N. Kerk, V. Meyer, and T. Goerge, “Calciphylaxis induced by acquired protein S deficiency in a patient with multiple myeloma - effective treatment with low-molecular-weight heparin,” *Journal der Deutschen Dermatologischen Gesellschaft*, vol. 10, no. 7, pp. 518-519, 2012.

[30] T. Kanoh, H. Uchino, I. Yamamoto, and K. Torizuka, “Soft-tissue uptake of technetium-99m MDP in multiple myeloma,” *Clinical Nuclear Medicine*, vol. 11, no. 12, pp. 878-879, 1986.

[31] M. Livingood and S. A. Newman, “An unusual presentation of perforating metastatic calcinosis cutis,” *SkinMed*, vol. 11, no. 5, pp. 314-315, 2013.

[32] B. A. Eagel, S. A. Stier, and C. Wakem, “Non-osseous bone scan abnormalities in multiple myeloma associated with hypercalcemia,” *Clinical Nuclear Medicine*, vol. 13, no. 12, pp. 869–873, 1988.

[33] M. M. Cooper, “Metastatic calcification: an unusual cause of lower intestinal hemorrhage,” *New York State Journal of Medicine*, vol. 88, no. 7, pp. 389-390, 1988.

[34] S. Wynchank, A. J. Brendel, F. Leccia et al., “Transient intense gastric fixation of 99mTc-MDP,” *European Journal of Nuclear Medicine and Molecular Imaging*, vol. 8, no. 10, pp. 458–460, 1983.