



# Liver directed embolization therapy for long-term control of hypercalcemia of malignancy in metastatic breast cancer



H. LEE MOFFITT CANCER CENTER & RESEARCH INSTITUTE,  
AN NCI COMPREHENSIVE CANCER CENTER – Tampa, FL  
1-888-MOFFITT (1-888-663-3488) www.MOFFITT.org

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Sowmya Nanjappa MD, Carlos A. Pla Fernandez MD, Susmitha Apuri MD,  
Loreta Loftus MD, Bela Kis MD, PhD

## Introduction

Hypercalcemia of malignancy is a common complication of breast cancer, prostate cancer, lung cancers, and multiple myeloma, and it is most often due to osteolytic metastatic osseous lesions. Hypercalcemia secondary to ectopic secretion of parathyroid hormone related protein (PTHrP) most frequently occurs in squamous cell cancer but it is rare in breast cancer. Treatment of hypercalcemia of malignancy is usually symptomatic and involves intravenous hydration, bisphosphonates such as zoledronic acid that may provide temporary control of calcium levels. We report the first case of poorly differentiated breast carcinoma metastatic to lymph nodes and liver with paraneoplastic hypercalcemia that was effectively treated with the use of transarterial embolization (TAE) of hepatic metastatic lesions

## Case Report

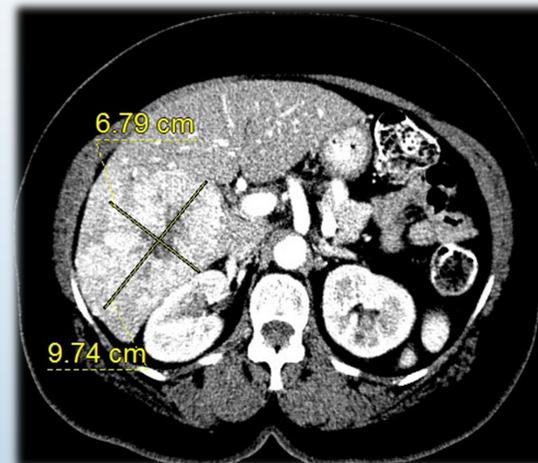
A 67-year-old woman presented with complaints of a palpable right axillary mass that was biopsied and showed poorly differentiated breast carcinoma with neuroendocrine differentiation. Axillary mass tissue was hormone receptor positive and HER-2/neu negative and initial staging CT scans identified suspicious liver lesions and liver biopsy revealed metastatic poorly differentiated carcinoma with neuroendocrine differentiation. She underwent a total of 6 cycles of cyclophosphamide/adriamycin treatment with good response and she was placed on letrozole indefinitely.

Four years after diagnosis, follow-up imaging studies demonstrated disease progression in the liver. She was treated with 3 cycles of carboplatin/taxol, with minimal response. Since she had liver predominant disease which was not responding to chemotherapy the patient was referred for transarterial liver directed therapy (Fig 1). She underwent radio embolization treatment using Y90 glass microspheres (TheraSphere; BTG International, London, England) to the right and left lobes of the liver followed by capecitabine chemotherapy.

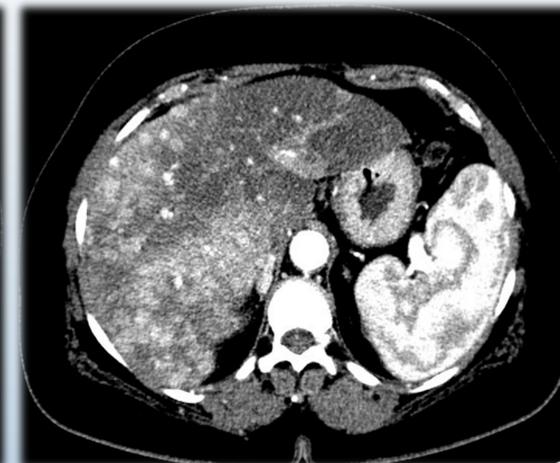
In subsequent clinic visits, months after the radioembolization treatment she presented with complaints of lethargy and generalized weakness. Serial labs demonstrated progressive hypercalcemia with serum calcium levels between 12-16 meq/ml. She was treated on multiple occasions with IV fluids and bisphosphonates (zoledronic acid), resulting in temporary improvement. Further evaluation showed elevated PTHrP with low intact PTH. Follow-up CT scan demonstrated multiple subcentimeter enhancing nodules in both lobes of the liver consistent with progression of metastatic disease (Fig 2). Her metastatic disease was still confined only to the liver and right axillary lymph nodes and there was no evidence of osseous metastasis. Therefore, repeat transarterial liver directed therapy was recommended to control her liver disease

The patient underwent two transarterial bland embolization of the right hepatic lobe and one treatment of the left hepatic lobe using 100 micron Embosphere embolization microspheres (CeloNova Biosciences, Inc., San Antonio, TX) within a six-month period. Her serum calcium level decreased to 10.6 meq/ml after the first two interventions and to 9.8 mEq/mL after the left lobe embolization. Serum calcium has been monitored in subsequent clinic visits and remained in the normal range for 11 months without further interventions, with the lowest level was 8.7 mEq/mL. No complications or side effects were noted. Chemotherapy with exemestan and everolimus were able to be continued since her hypercalcemia was adequately controlled and she did not require further hospitalizations for symptomatic hypercalcemia.

## Figures



**Figure 1**  
Contrast-enhanced axial CT image obtained at arterial phase demonstrates a large enhancing mass with central necrosis in the right lobe of the liver



**Figure 2**  
Contrast-enhanced axial CT image obtained at arterial phase demonstrates multiple subcentimeter enhancing nodules in the liver, predominantly in the right lobe

## CT scan after 21 months of treatment



**Figure 3**  
Contrast-enhanced axial CT image obtained at arterial phase demonstrates multiple multiple tiny calcified nodules in the liver which represent dystrophic calcifications of necrotic tumor nodules. There was no enhancing lesion seen in the liver indicating complete radiographic response to embolization and subsequent chemotherapy treatments

## Discussion

Hypercalcemia of malignancy affects up to 44.1% of patients and it is most common in the advanced stages of malignancy. Four distinct causes of hypercalcemia have been described; osteolytic hypercalcemia accounts for ~80% of cases, humoral hypercalcemia due to PTHrP accounts for ~20% of cases, 1,25 (OH) secreting lymphomas and ectopic hyperparathyroidism account for ~2% of remaining cases. In metastatic breast cancer, hypercalcemia is most frequently caused by osteolytic lesions. However, it has been shown that secretion of PTHrP is associated with local bone resorption in patient with metastatic breast cancer even with normal serum levels of PTHrP.

Regardless of etiology, no standard therapies exist for treatment of hypercalcemia of malignancy that result in long term control of serum calcium levels. There have been published case reports of effective control of paraneoplastic hypercalcemia with transcatheter arterial chemoembolization in patients with hepatocellular carcinoma (HCC) and colorectal cancer metastatic to liver without bone metastasis or increase in PTHrP.

In fact, liver directed transarterial embolization had been established as the primary therapy for hypercalcemia of malignancy related to humoral mediators secreted by HCC. Despite evidence of effective treatment of metastatic HCC with direct embolization, there is scarce evidence in metastatic breast cancer.

## Conclusion

- Hypercalcemia of malignancy is a common paraneoplastic manifestation of certain types of cancer.
- There are currently no standard therapies for the treatment of hypercalcemia of malignancy secondary to paraneoplastic syndromes that result in long-term control of serum calcium levels.
- Cases of transcatheter arterial chemoembolization in patients with hepatocellular carcinoma and colorectal cancer metastatic to liver have been published.
- Our patient is the first case of refractory hypercalcemia secondary to paraneoplastic syndrome in a patient with metastatic breast cancer to the liver that was effectively treated with transarterial embolization of the liver metastasis.