

Research article

# Multiple Bone Metastatic Invasion with Clinical Implications due to Ductal Mammary Carcinoma – Case report and Short Literature Review

Nicoleta Daniela Calotă<sup>1</sup>, Carmen Oprea<sup>2,3,\*</sup>, Madalina Gabriela Iliescu<sup>2,\*</sup>, Alexandra Ecaterina Ciota<sup>2</sup>, Bogdan Obadă<sup>4</sup>, Diana Victoria Gidu<sup>1</sup>, Emma Gheorghe<sup>5</sup>, Răzvan Popescu<sup>6</sup>, Antoanela Oltean<sup>1</sup>, Elena Valentina Ionescu<sup>2</sup>

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- 1 Department of Kinetotherapy, Faculty of Physical Education and Sport, „Ovidius” University of Constanța, 1 Cpt. Aviator Alexandru Șerbănescu street, 900470, Constanța, România
- 2 Department of Rehabilitation, Faculty of Medicine, „Ovidius” University of Constanța, 1 University Alley, Campus – Corp B, 900470, Constanța, România
- 3 Department of Nursing, Faculty of Medicine, „Ovidius” University of Constanta, 1 University Alley, Campus – Corp B, 900470, Constanta
- 4 Department of Orthopedics, Faculty of Medicine, „Ovidius” University of Constanța, 1 University Alley, Campus – Corp B, 900470, Constanța, România
- 5 Department of Histology, Faculty of Medicine, „Ovidius” University of Constanța, 1 University Alley, Campus – Corp B, 900470, Constanța, România
- 6 Department of General Surgery, Faculty of Medicine, „Ovidius” University of Constanța, 1 University Alley, Campus – Corp B, 900470, Constanța, România

\* Correspondence: Carmen Oprea [carmen\\_oprea\\_cta@yahoo.com](mailto:carmen_oprea_cta@yahoo.com) ; Mădălina-Gabriela Iliescu [iliescu-madalina@gmail.com](mailto:iliescu-madalina@gmail.com)

**Abstract:** Multidisciplinary approach of clinical cases in rehabilitations units can be very complex and divers. Method: We present a case of a woman 30 years old, whose oncological history begins 9 years ago, when the diagnosis of invasive ductal mammary infiltrating canalicular carcinoma grade I was made and treated by tumorectomy (lumpectomy). The patient refused oncological treatment at that time and resorted to alternative medicine during a period of 7 years: diet without sugar and animal products; regular vitamin B17 treatments; almond kernel cure; high-dose intravenous vitamin C treatment for; intravenous ozone therapy; apitherapy with bee venom; oral administration of cannabis oil during the past four years until now; physical therapy. Results: The evolution is marked by the appearance of multiple bone metastatic lesions. The most worst clinical consequence was a hyperalgesic cervicobrachial neuralgia, due to multiple C6-T3 lytic lesions diagnosed 2 years ago and C7 compression (close to spinal cord injury), situation which had as medical approach two surgeries interventions, radiotherapy and chemotherapy. Conclusions: The rehabilitation program was adapted to every stage of clinical evolution and was marked by many complications. All the steps were made for functional improvement and for increase the quality of life.

**Keywords:** multimetastatic invasive ductal mammary carcinoma, cervical cord injury; physical therapy; alternative medicine

## 1. Introduction

Previous studies have largely focused on the oncological specific treatment for invasive ductal carcinoma, while little is known about this cancer evolution with alternative medicine approach. The variety of outcomes observed in clinical practice demonstrates that the biological behaviour of this disease can still be uncertain and often does not depend on the type of treatment offered to the patient, which indicates that the mechanisms involved in this process are not fully known [1]. Invasive ductal carcinoma (IDC), also

known as infiltrating ductal carcinoma, is cancer that began growing in a milk duct and has invaded the fibrous or fatty tissue of the breast outside of the duct. IDC is the most common form of breast cancer, representing 80% of all breast cancer diagnoses. Treatment for all types of IDC is determined by the exact type of cancer and staging. Depending on the size and spread of the tumour(s), most women will undergo a combination of any of the following treatments: lumpectomy, mastectomy, sentinel node biopsy, axillary node dissection, breast reconstruction, radiation, chemotherapy, hormonal therapy, biologic targeted therapy [1,2]. On the other side, medullary breast cancer (MBC) is an uncommon type of breast cancer, representing 1-7% of all cases, characterized by the occurrence of many histopathological features associated with a high grade of malignancy [3,4].

Breast cancer has several outcomes in spite of the treatment used, and the presence of the axillary metastases is a strong indicator of poor prognosis [5]. A meta-analysis involving 11 studies [6] concluded that tumour size greater than 2 cm and angiolymphatic invasion indisputably increase the probability of axillary lymph node involvement [1]. Ductal carcinoma *in situ* (DCIS) of the breast is an early localized stage of the carcinoma in the process of the multistep breast carcinogenesis. If left untreated, a significant proportion of these tumours will evolve into invasive cancer. Optimal management of DCIS remains controversial, the goal of treatment being to control local disease and prevent subsequent development of invasive cancer. Following breast-conservation therapy, about 50% of the tumours recur as invasive cancer [7].

Data exist that suggest that not all cases of histologically detectable DCIS will progress to aggravated cancer forms [8, 9]. Also, it cannot be distinguished which DCIS will progress to an invasive breast cancer and which will remain latent and for how long [7].

There are several studies that report the outcome of patients with tumour recurrence after primary tumour treatment or excision. Solin *et al* [10] presented 42 recurrences in patients with DCIS who received breast-conservation therapy: 23 had invasive carcinoma and 19 had DCIS; Zangouri *et al* [11] concluded after a study that despite the poor and aggressive pathological features of MBC, its clinical outcome is more favourable compared to IDC; Price *et al* [12] reported 60 patients who had 26 recurrences after treatment, two of them presenting distant metastases. Solin *et al* [13] followed for 15 years patients after initial treatment using breast conservation therapy and the 5-year actuarial rate of freedom from distant metastases was 86%.

Distant metastases in the absence of local recurrence is rare, with an incidence of less than 1% and can also be associated with contralateral breast cancer [13, 14]. Evidence shows that a substantially greater rate of distant metastases exists among women with local recurrence than among those without local recurrence after breast-conservation therapy [7].

The occurrence of vertebral metastases is far from rare. The majority of patients with advanced breast cancer have evidence of skeletal metastases by the time of death [15]. Bone metastases may remain asymptomatic, but pain is common (the most frequent site of the first distant relapse) and hypercalcemia, pathological fractures and leuco-erythroblastic anaemia may occur. When the case, spinal cord compression is treated by surgical decompression if the signs are rapidly progressing [16].

Bone metastases also lead to nerve compression. In breast cancer, osteolytic metastases are most common, but mixed and osteoblastic metastases occur in significant number of patients. Stimulation of osteoblasts can paradoxically increase osteoclast function, as bone-synthesizing osteoblasts are the main regulators of bone-destroying osteoclasts. Co-expression of osteolytic and osteoblastic factors can thus produce mixed metastases or increased osteolysis [17].

Bone metastasis significantly affects both quality of life and survival of the breast cancer patient. The presence of metastatic lesions in bone disrupts the normal bone microenvironment and upsets the fine balance between the key components. The changes in

the bone microenvironment then create a vicious cycle that further promotes bone destruction and tumour progression [18]. The unique pathophysiology of bone pain involves spinal cord astrocytosis, enhanced neuronal activity through c-Fos expression and sensitization of the central dorsal horn of the spinal cord mediated by dynorphin, a pro-hyperalgesia peptide [19].

Spinal cord compression is a potentially devastating complication which occurs in up to 8% of patients with metastatic breast cancer [20]. A multidisciplinary team approach with experienced surgeons, radiation oncologists, medical oncologists, palliative care physicians, cancer nurses and coordinators is often necessary [21]. Optimal management consists of high dose corticosteroids, magnetic resonance imaging to confirm diagnosis, prompt surgical decompression and radiotherapy [22].

## 1. Results

The evolution is marked by the appearance of a cervicobrachial neuralgia three years ago, initially improved by physical therapy sessions, which included postures, stretching, respiratory gymnastic, free active and active resistance exercises, to re-ax and tone the scapular girdle, but accentuated again after Yumeiho massage maneuvers, moment when cervicodorsal magnetic resonance imaging - MRI was performed Figure 1, following which multiple metastatic lesions in bones, lung, pleura, mediastinum, aortic cross, arterial left emergencies and multilevel lymph nodes lesions were identified. There is also a tumor mass in the left breast, with a large left axillary lymphadenopathy with big compression and invasion of left brachial plexus. which explained the clinical neuralgic symptoms. The MRI multiplanar sequences shows very various metastatic lesions in skeleton, at vertebral level the most important was at C7 level, with compression to spinal cord, which explained major neurologic and statical problems. Also vertebral the metastasis were at C6, T1 at the somatic and pediculi of the vertebrae and at the vertebral bodies of T3 and T5. Other bone lesions were identified at: posterior part first left rib, left scapulae, multiple left and right ribs. pAt that time, the patient underwent intravenous corticotherapy and, after it, a laminectomy without osteosynthesis for the bone fragility cause. Due to intense pain, morphine patches were then used and then a morphine pump plus Oxinorm –Oro 10 mg tablets.

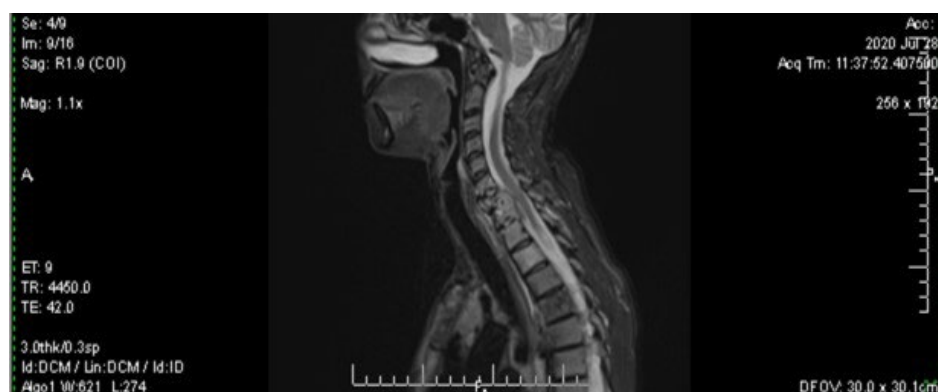




Figure 1. Cervicodorsal MRI two years ago

Two years ago, the patient was consulted in other sevice, where she was offered an etiological assessment with a biopsy, but she refused. Clinical presentation at that time: very difficult bilateral hyperalgesic cervicobrachial neuralgia, due to cervical-dorsal vertebral and brachial plexum metastatic lesions with root compression, a second primary tumor other than a breast tumor occurring after lumpectomy (local excision), breast tumour recurrence in the same sector, near the original lesion. One year ago, the patient had a second surgery , as a result of which osteosynthesis material was placed on the area where the laminectomy was initially performed in Romania Figure 2. Following the intervention, the compressive pain was significantly improved. The patient underwent a thoraco-lumbar orthosis Figure 3 and underwent physical therapy again, to increase the postural muscles tone and improve respiration.



Figure 2. The incision



Figure 3. Orthosis

In the early fall last year, hyperalgesic cervical-brachial neuralgia returned, at which point the patient accepted 10 sessions of radiation therapy (which resulted in temporary damage to the larynx), which again resulted in pain relief but in the short to medium term. Currently, the patient accepted chemotherapy and undergoing complex various oncological treatments.

## 2. Discussion

Alternative medicine along with physical therapy has been applied to a case of invasive ductal mammary infiltrating canelular carcinoma grade I for 7 years. Unfortunately, this only gained some time for the patient, the disease evolving anyway. The most common cause of spinal cord compression in people with cancer is metastasis to the spine. Any type of cancer can spread to the spine, but it is more common with the following

cancers: breast cancer, lung cancer, prostate cancer, kidney cancer, lymphoma, multiple myeloma [23].

Coleman and Rubens [16] stated that 13 of their studied subjects developed spinal cord compression with a median survival of 3 months (range 0-26 months) after this complication. Surgery is used to remove as much of the tumour as possible. It is also used to stabilize the spine and relieve pressure within the spine [24].

A case of a 43-year-old female patient with breast cancer for 8 years and metastasis in thoracic spinal intramedullary area which had been partially excised and then given adjuvant radiotherapy and chemotherapy is the opposite type of medical approach than that of our case report (eight years ago, at the onset, she received chemotherapy and radiotherapy). She was admitted to the hospital with complaints of weakness in both legs. On her neurological examination, she had paraparesis (left lower extremity: 2/5, right lower extremity: 3/5) and urinary incontinence. Spinal MRI revealed a gadolinium enhancing intramedullary lesion. Pathologic examination of the lesion was consistent with breast carcinoma metastasis. The patient has been taken into radiotherapy. Microsurgical resection was necessary for preservation or amelioration of neurological state and also for increased life expectancy and quality [25]. Alternative medicine and oncological treatment seem to lead to the same point in the course of the evolution of a breast cancer.

Bone metastasis from breast cancer is a common condition and is associated with incurable disease, significant complications, morbidity and reduced quality of life [26-29]. Treatment of bone metastases is palliative and is aimed at reducing SREs, preserving mobility and improving quality of life [21], both physically and in the area of emotions and mental activity [25, 26]. The bone fragility for which the patient was operated with laminectomy without osostosynthesis could also have been accentuated by possible osteoporotic damage, given the intravenous corticosteroid treatment performed, a pathology that may lead to a further decrease in the patient's quality of life [30].

### 3. Materials and Methods

We present a case of a woman 30 years old, whose oncological history begins 9 years ago, when the diagnosis of invasive ductal mammary infiltrating canalicular carcinoma grade I was made and treated by tumorectomy (lumpectomy). The patient refused oncological treatment at that time and resorted to alternative medicine during a period of 7 years: diet without sugar and animal products; regular vitamin B17 treatments; almond kernel cure; high-dose intravenous vitamin C treatment for; intravenous ozone therapy; apitherapy with bee venom (from 1 to 20 bees progressively placed on the posterior face of the thorax); oral administration of cannabis oil during the past four years until now; regularly physical therapy sessions, to maintain joint suppleness and muscle strength. The patient has a height of 152 cm, weighing 43 kg at the onset of the disease and 37-38 kg at present. The study was approved by the Ethical Committee of the Balneal and Rehabilitation Sanatorium of Techirghiol, Rehabilitation Division (approval no. 1734 from 02.02.2022).

### 4. Conclusions

Multidisciplinary approach in this cases is the key for the good results after the complex treatments using surgical, oncological, neurological and orthopedic methods, associated with rehabilitation for increasing the quality of life. Also, this case can contribute to our experience of clinicians regarding the standard protocols for treatments.

**Author Contributions:** conceptualization, NDC, DVG, CO and AO ; methodology, EVI.; software, AEC; validation, EVI and MGI; formal analysis, MGI; investigation, CO; resources, BO, EG and RP; data curation, NDC; writing—original draft preparation, EVI;

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## References

- Ranniere Gurgel Furtado de Aquino; Paulo Henrique Diogenes Vasques; Diane Isabelle Magno Cavalcante et al. *Invasive ductal carcinoma: relationship between pathological characteristics and the presence of axillary metastasis in 220 cases*. Rev. Col. Bras. Cir. 2017, 44(02): 163-170. <https://doi.org/10.1590/0100-69912017002010>
- Popescu RC; Tociu C, Brînzan C; Cozaru GC; Deacu M; Dumitru A; Leopa N; Mitroi AF; Nicolau A; Dumitru E. Molecular profiling of the colon cancer in South-Eastern Romania: Results from the MERCUR study. *Medicine (Baltimore)* 2021, Jan 8, 100(1):e24062. DOI: 10.1097/MD.00000000000024062
- Follana P; Barriere J; Chamoney E; Largiller R; Dadone B; Mari V et al. *Prognostic factors in 401 elderly women with metastatic breast cancer*. *Oncology* 2014; 86(3): 143-51. DOI: 10.1159/000357781
- Budzik MP; Sobieraj MT; Sobol M; Patera J et al. *Medullary breast cancer is a predominantly triple-negative breast cancer – histopathological analysis and comparison with invasive ductal breast cancer*. *Arch Med Sci* 2019, 2022: 18(2). DOI: <https://doi.org/10.5114/aoms.2019.86763>
- I Jatoi; S G Hilsenbeck; G M Clark; C K Osborne; *Significance of axillary lymph node metastasis in primary breast cancer*; *J Clin Oncol*. 1999 Aug; 17(8):2334-40. doi: 10.1200/JCO.1999.17.8.2334.
- Degnim AC; Griffith KA; Sabel MS; Hayes DF; Cimmino VM; Diehl KM et al. *Clinicopathologic features of metastasis in non-sentinel lymph nodes of breast carcinoma patients*. *Cancer* 2003; 98(11): 2307-15. doi: 10.1002/cncr.11803.
- Sakorafas GH; Tsiotou AGH. *Ductal carcinoma in situ (DCIS) of the breast: evolving perspectives*. *Cancer Treatment Reviews* 2000, 26: 103-125. DOI: 10.1053/ctrv.1999.0149
- Schnitt SJ; Silen W; Sadowsky NL et al. *Ductal carcinoma in situ (intraductal carcinoma) of the breast-current concepts*. *N Engl J Med* 1988,318: 898-903.
- Barth A; Brenner J; Guiliano AE. *Current management of ductal carcinoma in situ*. *West J Med* 1995, 163: 360-366.
- Solin LJ; Fourquet A; McCormick B. et al. *Salvage treatment for local recurrence following breast-conserving surgery and definitive irradiation for ductal carcinoma in situ (intraductal carcinoma) of the breast*. *Int J Radiat Oncol Biol Phys* 1994, 30: 3-9. DOI: 10.1016/0360-3016(94)90512-6
- Zangouri V; Akrami M; Tahmasebi S; Talej A; Hesarooeih AG. *Medullary breast carcinoma and invasive ductal carcinoma: a review study*. *Iran J Med Sci* 2018, 43(4): 365-371.
- Price P; Sinnett HD; Gusterson B et al. *Duct carcinoma in situ: predictors of local recurrence and progression in patients treated by surgery alone*. *Br J Cancer* 1990, 61: 869-872. DOI: 10.1038/bjc.1990.194
- Solin LJ; Kurtz J; Fourquet A et al. *Fifteen-years of breast-conserving surgery and definitive breast irradiation for the treatment of ductal carcinoma in situ of the breast*. *J Clin Oncol* 1996, 14: 754-763. DOI: 10.1200/JCO.1996.14.3.754
- Fisher B; Constantino J; Redmont C et al. *Lumpectomy compared with lumpectomy and radiation therapy for the treatment of intraductal breast cancer*. *N Engl J Med* 1993, 328: 1581-1586. DOI: 10.1056/NEJM199306033282201
- Galasko CSB. *The anatomy and pathways of skeletal metastases*. In *Bone Metastasis*. Weiss L & Gilbert HA (eds) p. 49. G.K. Hall: Boston, Massachusetts 1981.
- Coleman RE; Rubens RD. *The clinical course of bone metastases from breast cancer*. *Br J Cancer* 1987, 55: 61-66. DOI: 10.1038/bjc.1987.13
- Guisse TA; Chirgwin JM. *Molecular mechanisms of breast cancer metastases to bone*. *Clinical Breast Cancer* 2005, Vol 5 Supplement 2, p. S46-S53.
- Tahara RK; Brewer TM; Theriault; Ueno NT. *Bone metastasis of breast cancer*. *Adv Exp Med Biol* 2019, 1152: 105-129.
- Goblirsch M.J.; Zwolak P.P.; Clohisy D.R. *Biology of bone cancer pain*. *Clin. Cancer Res.* 2006,12:6231–6235. DOI: 10.1158/1078-0432.CCR-06-0682

20. Patchell R.A.; Tibbs P.A.; Regine W.F.; Payne R.; Saris S.; Kryscio R.J. Mohiuddin M., Young B. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: A randomised trial. *Lancet*. 2005 366:643–648. DOI: 10.1016/S0140-6736(05)66954-1
21. Li BT; Wong MH; Pavlakis N. *Treatment and Prevention of Bone Metastases from Breast Cancer: A Comprehensive Review of Evidence for Clinical Practice*. *J Clin Med* 2014. Mar; 3(1): 1–24. <https://doi.org/10.3390/jcm3010001>
22. Wong M.H.; Pavlakis N. Optimal management of bone metastases in breast cancer patients. *Breast Cancer Targets Ther.* 2011. 3:35–60.
23. Becker KP; Baehring JM. Spinal cord compression. DeVita VT Jr, Lawrence TS, & Rosenberg SA. *Cancer: Principles & Practice of Oncology*. 9th ed. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins 2011. 145: pp. 2136 - 2141.
24. Kaplan M. Spinal cord compression. Kaplan M (Ed.). *Understanding and Managing Oncologic Emergencies*. 2nd ed. Pittsburgh: Oncology Nursing Society 2013. 9: pp. 337 – 383.
25. Basaran R; Tiryaki M; Yavuzer D; Efendioglu M; Balkuv E; Sav A. *Spinal Intramedullary Metastasis of Breast Cancer, Case Reports in Medicine* Volume 2014. Article ID 583282, 3 pages. <https://doi.org/10.1155/2014/583282>
26. Stanciu M; Ristea RP; Popescu M; Vasile CM; Popa FL. Thyroid Carcinoma Showing Thymus -like Differentiation (CASTLE): A Case Report. *Life*. 2022. 12(9):1314. EISSN 2075-1729. <https://doi.org/10.3390/life12091314>. <https://www.mdpi.com/2075-1729/12/9/1314>.
27. Iliescu M; Bordei P; Iliescu DM; Ciobotaru C; Lucescu V; Covaleov A and Ionescu C. Anatomico-clinical and imaging correlations within the lumbar discopathy. *Surg Radiol Anatomy*. 31(145) 2009.
28. Iliescu DM; Micu SI; Ionescu C; Bulbuc I; Bordei P; Obada B; Voinea F; Gheorghe E; Iliescu MG. Axial and para axial loading response evaluation on human cadaver harvested lumbar vertebral blocks: In vitro experiment with possible clinical implications for clinical practice. *EXPERIMENTAL AND THERAPEUTIC MEDICINE* 22: 1192 2021. doi: 10.3892/etm.2021.10626.
29. Popa F.L.; Iliescu M.G.; Stanciu M.; Georgeanu V. Rehabilitation in a case of severe osteoporosis with prevalent fractures in a patient known with multiple sclerosis and prolonged glucocorticoid therapy. *Balneo and PRM Research Journal* 2021. 451, 12 (3): 284–288, doi:10.12680/balneo.2021.451.
30. Stanciu L.E.; Ionescu E.V.; Oprea Carmen; Almășan E.R.; Vrăjitoru A.B.; Iliescu M.G. Rehabilitation in Osteoporosis – therapeutic challenge?. *Balneo and PRM Research Journal* 2020.388, 11(4):501-506, doi: 10.12680/balneo.2020.388.