ISSN: 2469-5696

Rybicka-Ramos et al. Int J Blood Res Disord 2020, 7:050
DOI: 10.23937/2469-5696/1410050
Volume 7 | Issue 1
Open Access

International Journal of
Blood Research and Disorders

CASE REPORT

Atypical Clinical Picture of Breast Cancer with Dominant Symptoms of Hematologic and Gastrointestinal Malignancies

Malwina Rybicka-Ramos[1], Grzegorz Kasiarz[2], Katarzyna Pluta[3], Tomasz Wilczyński[4], Jerzy Pruszyński[1] and Ewa Ziółko[1]*

[1]*Department of Hematology, Specialist Hospital No. 1 in Bytom, Bytom, Poland*
[2]*City Hospital in Ruda Slaska, Ruda Slaska, Poland*
[3]*A. Mielecki Independent Public Clinical Hospital, Medical University of Silesia, Katowice, Poland*
[4]*Provincial Specialist Hospital No. 4 in Bytom, Bytom, Poland*

***Corresponding author:** *Malwina Rybicka-Ramos, MD, PhD, Department of Hematology, Specialist Hospital No. 1 in Bytom, 7 Zeromskiego Street, 41-902 Bytom, Poland, Tel: +48-32-396-32-63*

Abstract

Gastrointestinal malignancy was suspected in a 68-year-old woman with long-term anemia, thrombocytopenia, leukopenia, the presence of fecal occult blood and elevated levels of CEA and CA 19-9. However, malignancy was not confirmed. The patient was later hospitalized in the Department of Hematology where hematologic disease was excluded. Cervical and inguinal lymphadenopathy and atypical bone marrow cells collected by aspiration biopsy gave rise to the suspicion of bone marrow involvement by tumor cells of non-hematologic origin. As a result, trepanobiopsy samples were histologically and immunohistochemically assessed. The results revealed bone marrow metastases of cancer of glandular origin with a phenotype corresponding to breast cancer. Screening mammograms did not reveal lesions suspicious for cancer. A chest CT showed a nodular lesion in the left breast, enlarged lymph node conglomerates in the left axillary region and bone remodeling with the appearance of diffuse metastatic lesions.

Keywords

Anemia, Bone marrow trepanobiopsy, Bone marrow metastases, Mammography, Occult breast cancer

Introduction

Breast cancer is the most common malignancy in women. It is also the main cause of cancer-related death in females [1]. Diagnostic assessment is based primarily on breast and axillary lymph node palpation as well as mammography and ultrasound. Screening includes mammograms every 2 years in women aged 50-69 with no additional risk factors and disease symptoms [2]. Screening recommendations vary widely between many leading organizations. General principles regarding the treatment of pre-invasive forms of breast cancer and early-stage cancer are based on surgical treatment, sometimes combined with radiotherapy and/or systemic treatment [3]. In adults, along with lung and prostate cancers, breast cancer commonly metastasizes to bone. Metastases of the above cancers usually produce skeletal symptoms, including bone pain, abnormalities in complete blood count and anemia in particular [4].

Case Description

A 68-year-old patient was admitted to the Department of Hematology in January 2018 with anemia, leukopenia and thrombocytopenia that were diagnosed in 2017. In January 2017 complete blood count showed the following: Red blood cell (RBC) count 3.02 × 106/µL, hemoglobin (Hb) 8.8 g/dL, white blood cell (WBC) count 2.96 × 103/µL and platelet (PLT) count 63 × 103/µL. In 2017, the patient was diagnosed with fecal occult blood and the patient underwent esophagogastroduodenoscopy and colonoscopy. Helicobacter pylorigastritis was diagnosed and eradication treatment was given. The colonoscopy showed two intestinal polyps of 6-7 mm and 15-18 mm, which were removed in April and September 2017, respectively. Both histological diagnoses revealed low-grade tubular adenoma. Tests for fecal occult blood were positive during the follow-up

Citation: Rybicka-Ramos M, Kasiarz G, Pluta K, Wilczyński T, Pruszyński J, et al. (2020) Atypical Clinical Picture of Breast Cancer with Dominant Symptoms of Hematologic and Gastrointestinal Malignancies. Int J Blood Res Disord 7:050. doi.org/10.23937/2469-5696/1410050

Accepted: June 01, 2020: **Published:** June 03, 2020

despite negative findings for gastrointestinal cancer. In April 2017, routine lymph node ultrasound showed morphologically normal cervical (8 × 3 mm) and axillary lymph nodes (the largest node was located in the left axillary fossa and measured 17 × 11 mm), not detected in physical examination and not biopsied. In September 2017, blood test results were as follows: RBC count 3.1 × 106/μL, Hb 8.6 g/dL, WBC count 2.6 × 103/μL and PLT count 111 × 103/μL and erythrocyte sedimentation rate (ESR) 158 mm/h. Elevated levels of carcinoembryonic antigen (CEA) and CA 19-9 were also found.

On admission to the Department of Hematology in January 2018, the patient reported increasing general weakness, limited mobility of the right upper limb, loss of appetite, rapidly increasing enlargement of the abdominal circumference with tenderness on palpation and periodic epistaxis. Physical examination revealed pallor with the presence of telangiectasia on the skin of the abdomen and torso, and enlarged hard and immovable cervical and supraclavicular lymph nodes. Significantly enlarged abdominal circumference and abdominal rigidity were found. Abdominal organs were difficult to palpate and lower limb edema was found.

In January 2018, blood results showed severe normocytic anemia - RBC count 2.82 × 106/μL, Hb 7.3 g/dL, leukopenia (WBC 3.6 × 103/μL) and thrombocytopenia (PLT 38 × 103/μL), elevated levels of gamma-glutamyltranspeptidase (GGTP) 45.86 U/l, creatinine 160.78 μmol/l, uric acid 11.21 mg/dl, total calcium 2.79 mmol/l, D-dimers 3070.71 ng/ml, ESR > 120 mm/h and C-reactive protein (CRP) 32.30 mg/L. Levels of CA19-9, Ca 125 and CEA were also elevated: 41.1 U/ml, 496.5 U/ml, 12.38 ng/ml respectively. The suspicion of myelodysplastic syndrome was raised. Bone marrow trepanobiopsy was performed. Cytological examination of trepanobiopsy-3 imprints showed 43% of young cells with myeloblast-like nucleoli and dysplasia in all cell lines. Another bone marrow aspiration biopsy was collected for immunophenotyping. No hematologic malignancy was found in the specimen. The suspicion of bone marrow infiltration with non-hematological cancer cells was raised and further immunohistochemical assessment of trepanobiopsy specimen was performed.

Inguinal lymph node ultrasound showed slightly enlarged hypoechoic structures corresponding to lymph nodes (13.4 × 7.8 mm) forming conglomerates. Axillary and cervical lymph nodes were unremarkable. Abdominal ultrasound showed as cites and the pressure of fluid on abdominal organs was also found. Pericentesis was performed with the evacuation of 5 liters of a straw-yellow fluid. Cytology revealed no cancer cells.

Computed tomography (CT) of the abdomen and pelvis showed transverse colon wall thickening over a length of 8 cm. Colonoscopy showed numerous focal discolorations of the intestinal mucosa, small polyps and narrowing of the splenic flexion of the colon. No biopsy was collected due to low PLT count and mucosal contact bleeding during the procedure.

On 22nd January 2018, mammography showed no pathological calcifications or nodular changes. Axillary fossae were unremarkable (BI-RADS 1), which is similar to the results of the previous examination in 2017. On 24th January 2018, a chest CT revealed a nodular lesion of 12 mm in diameter in the lower lateral quadrant of the left breast. Additionally, a suspicious smaller structure with the diameter of 6 mm was found anteriorly to the lesion. Structures arousing the suspicion of conglomerates of enlarged lymph nodes were found (the largest structure measured 13 × 11 mm). In addition, the presence of fluid in the pleural cavities was indicative of pleural dissemination (a layer at the posterior chest wall of 13 mm in thickness on the right and 20 mm on the left). Additionally, CT showed massive tumor spread as a osteosclerotic metastases in the regions of the ribs, sternum, collarbones, shoulder blades, heads of the humerus, spine, pelvic bones and femurs.

The results of immunohistochemical examination of the trepanobiopsy specimen showed bone marrow metastases of cancer of glandular origin (CK^+, $CK7^+$, $CK20^-$, $GATA\text{-}3^+$, $mammaglobin^+$, $TTF\text{-}1^-$, $CD15^+$, $WT\text{-}1^-$) with a phenotype corresponding to breast cancer without blast cells ($CD34^-$, $CD117^-$) that would otherwise be characteristic of hematologic malignancy. Breast biomarkers were positive for the estrogen receptor (Allred TS 7), progesterone receptor (Allred TS 8), While negative for the HER2 receptor (1^+). The Ki-67 proliferation index was 5%.

The patient was referred to the Oncology Centre - Maria Skłodowska-Curie Memorial Institute in Gliwice, Poland. Positron Emission Tomography (PET) revealed massive tumor spread from the left breast in the regions of the ribs, sternum, collarbones, shoulder blades, heads of the humerus, spine, pelvic bones, femurs, pleura, peritoneum, left axillary and anterior mediastinum lymph nodes. Due to worsening anemia and thrombocytopenia, the patient was referred to a district hospital for blood product substitution. The patient did not report for further treatment at the Oncology Centre in Gliwice.

Discussion

Occult breast cancer (OBC) is a condition in which no evidence of breast tumor is found on physical examination, mammography or ultrasound despite histological confirmation of the presence of breast cancer cells in the metastatic focus. The diagnosis is related to about 0.2%-0.9% of cases [5].

Our patient presented with the symptoms mimicking hematologic malignancy and gastrointestinal cancer. Initially, the diagnostic assessment was mainly directed at searching for a malignant lesion in the gastrointestinal tract due to the presence of fecal occult blood, anemia

and elevated levels of CEA and Ca19-9. After the exclusion of neoplastic changes on endoscopic examinations (except for benign polyps) and the absence of significant abnormalities on ultrasound, a suspicion of hematological disease was raised. Worsening anemia, leukopenia and thrombocytopenia supported this suspicion. Based on bone marrow immunophenotyping, the suspicion of solid tumor metastasis (breast cancer) to the bone marrow was raised. The tumor was confirmed by chest CT (with negative mammograms) and immunohistochemical assessment of the trepanobiopsy specimen (of the metastatic lesion). According to scientific reports, in cases when the primary tumor cannot be located, immunohistochemical assessment from the site of metastasis is recommended. Positive results for estrogen and progesterone receptors as well as $CK7^{+}/CK20^{-}$, $GATA3^{+}$, $mammaglobin^{+}$ are characteristic for breast cancer. In turn, negative TTF-1 staining results differentiate breast cancer from metastases of lung adenocarcinoma in which this marker is usually positive [6].

Liu, et al. described a similar case of a 58-year-old female patient with thrombocytopenia (PLT 51 × 103/µL), anemia (Hb 8 g/dL) and general weakness which were the first symptoms of the disease. Initially, lymphadenopathy was not found and the breasts were normal on palpation, which also shows the similarity between the initial clinical picture of their patient and our case. Breast ultrasound was unremarkable. However, contrary to our case, mammography showed multiple small nodular lesions. Immunohistochemical staining of the bone marrow sample showed atypical cells with positive CK and GCDFP-15, which indicated the diagnosis of OBC. The patient did not continue further treatment [7].

Solid tumor metastases to the bone marrow can pose diagnostic difficulties when hematological symptoms are the first and dominant symptoms in their course. The clinical picture may then indicate a suspicion of hematological malignancy, particularly when the primary tumor cannot be detected in basic imaging studies. Bone marrow metastases are a relatively common phenomenon in breast cancer. In small tumors (T1) without lymph node involvement (N0), bone marrow infiltration is found in 13%-60% of cases [8]. Micrometastases to the bone marrow have been reported even in as many as one third of patients diagnosed with stage I-III breast cancer at the time of diagnosis [9]. In early breast cancer, they occurred in 15%-30% of cases [10]. Anemia (40%-60%), leukopenia and/or thrombocytopenia (12%-25%) [11] are the most common symptoms of bone marrow involvement by breast cancer cells, which was observed in our case.

Conclusions

The presented case shows the complexity and atypical presentation of symptoms in the cancer disease and the associated diagnostic difficulties. Some basic diagnostic and screening examinations (such as mammography in the case of breast cancer) and a typical clinical picture are not always sufficient to rule out the suspicion of cancer. Our case also stresses a crucial role of immunophenotyping and immunohistochemical examination of a metastatic lesion in primary tumor detection.

Conflict of Interest

None declared.

Statement of Equal Contribution

Authors declared equal contribution of the paper.

References

1. Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, et al. (2015) Global cancer statistics, 2012. CA Cancer J Clin 65: 87-108.
2. Senkus E, Kyriakides S, Ohno S, P Poortmans, F Penault-Llorca, et al. (2015) Primary breast cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol 26: 8-30.
3. Jassem J, Krzakowski M, Bobek-Billewicz B, et al. (2013) Zalec. postępowania diagnostyczno-terapeutycznego w nowotworach złośliwych. Rak Piersi 1: 211-258.
4. Cotta CV, Konoplev S, Medeiros LJ, Bueso-Ramos CE (2006) Metastatic tumors in bone marrow: Histopathology and advances in the biology of the tumor cells and bone marrow environment. Ann Diagn Pathol 10: 169-192.
5. Sohn G, Son BH, Lee SJ, Kang EY, Jung SH, et al. (2014) Treatment and survival of patients with occult breast cancer with axillary lymph node metastasis: A nationwide retrospective study. J Surg Oncol 110: 270-274.
6. Yang M, Nonaka D (2010) A study of immune histochemical differential expression in pulmonary and mammarycarcinomas. Mod Pathol 23: 654-661.
7. Liu L, Zhang J, Chen M, Ren S, Liu H, et al. (2017) Anemia and thrombocytopenia as initial symptoms of occult breast cancer with bone marrow metastasis: A case report. Medicine (Baltimore) 96: e8529.
8. Hartkopf AD, Banys M, Krawczyk N, Staebler A, Becker S, et al. (2012) Bone marrow versus sentinel lymph node involvement in breast cancer: A comparison of early hematogenous and early lymphatic tumor spread. Breast Cancer Res Treat 131: 501-508.
9. Duma N, Wang Z, Miranda C (2015) Bone marrow involvement as the initial presentation of breast cancer. American Journal of Medical Case Reports 3: 177-180.
10. Artac M, Koral L, Toy H, Guler T, Boruban MC, et al. (2014) Complete response and long-term remission to anti-HER2 combined therapy in a patient with breast cancer presented with bone marrow metastases. J Oncol Pharm Pract 20: 141-145.
11. Freyer G, Ligneau B, Trillet-Lenoir VV (2000) Palliative hormone therapy, low-dose chemotherapy and bisphosphonate in breast cancer patients with bone marrow involvement and pancytopenia: Report of a pilot experience. Eur J Intern Med 11: 329-333.