

# Rare paraneoplastic syndrome in an elderly woman with breast cancer-a case report

## Abstract

Paraneoplastic syndromes in cancer patients are important because they can obscure clinical picture of disease. Due to its rarity, it is difficult to diagnose them. I described maybe for the first time exophthalmos-strabismus syndrome in an elderly woman with breast cancer.

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## Introduction

Paraneoplastic syndromes are rare complexes of signs and symptoms which may accompany any malignant disease with incidence about 10% of patients. Their most characteristic feature is occurrence distally from primary tumor place so these cases are difficult to recognize. The small cell lung cancer, gastrointestinal carcinomas, breast, hepatocellular and renal cell carcinoma are amongst the most frequent causes of these syndromes.<sup>1</sup> There are wide range of symptoms: endocrinologic, neurologic, gastrointestinal, hematologic, cutaneous and others. In this report a case of elderly breast cancer patient with unusual paraneoplastic syndrome is described.

A 67-years old woman was admitted to Ambulatory Clinic after pathologic fracture of her right arm. She complained of broken arm pain and a lump in right breast. Her past medical history discovered deep vein thrombosis of extremities. On physical examination the patient general condition was good, she was overweight and her right arm was fixed in a sling. There was 4 cm pathologic mass in right breast, without skin invasion, lymph nodes were unpalpable. No other signs were discovered. All necessary diagnostic procedures were carried out (CT of abdomen and chest, mammography, bone scintigraphy) and right breast cancer diagnosis was confirmed. The scintigraph examination uncovered more bone metastases: to skull, ribs, hip, right femur and right arm. Clinical stage was T2N0M1. Biopsy of the tumor was performed and pathologic examination revealed invasive ductal carcinoma, grade 2 (according to Elston and Ellis classification), with lymphatic vessels invasion.<sup>2</sup> In line with Sorlie classification there was luminal type A (estrogen and progesterone receptors were positive in almost 100% malignant cells, no HER-2/neu expression was found) and Ki 67 activity was seen in about 10% of cells.<sup>3</sup> Laboratory tests were performed. Hematologic, hepatic, nephrotic, electrolytic tests were within normal range of limits. Also 15.3 level was normal (11.3U/ml). Because of intense pain in the right arm, chemotherapy with paclitaxel was introduced as well as an intravenously bisphosphonate. She received six cycles of this cytotoxic without any major adverse effects. Then hormonotherapy was started. Due to history of deep vein thrombosis, overweight (Body Mass Index-27.8) and postmenopausal status, therapy with an aromatase inhibitor was recommended.

After six months she was admitted urgently due to diplopia. No headache was acknowledged. Left eye exophthalmos and left upper

lid ptosis as well as unilateral divergent strabismus were visible. Left pupil was fixed and stiff. Immediate head CT examination was performed but no pathologic lesions were detected. Head magnetic resonance disclosed only minor vascular lesions. The patient was directed to ophthalmologist and neurologist. The ophthalmologist reported: right eye- acuity of vision, tension and mobility correct, anterior part of eyeball and optic centrum normal, hypertonic angiopathy grade 2; left eye- acuity of vision 0.8, tension normal, eyeball with divergent strabismus directed down, diplopia in all directions of sightseeing, optic centrum normal, medium width pupil with lack of reaction to light and accommodation, hypertonic angiopathy grade 2. Conclusions: central damage left optical nerve. The neurologist confirmed the diagnosis of left optic nerve damage but lumbar puncture was not done. This is why Positron Emission Tomography [18] F-fluorodeoxyglucose-CT was performed. The examination confirmed only presence of multiple bone metastases (SUV 38.3) with no lesions within central nervous system. The Ca 15.3 level raised slightly to 18.6U/ml. The other laboratory tests maintained in normal range of limits. Because of lack evident proofs of disease progression, previous treatment with the same aromatase inhibitor was continued.

During next several weeks her bone pain exaggerated and she became weak. Samar therapy was performed and the pause between bisphosphonate infusion was shorten to three weeks. Unfortunately, these measures were insufficient. After one month she was brought in a wheelchair. Her general condition according to ECOG (Eastern Cooperative Oncology Group) classification was only four. She was cachectic and her ocular signs worsened. Laboratory tests revealed anemia-hemoglobin level 10.5g/dL (lower range limit-13.5g/dL), creatinine level 1.45mg/dL (upper range limit-1.05mg/dL), calcium level 10.5mg/dL (upper range limit- 10.1 mg/dL) and Ca 15.3 lever raised to 134.8U/ml. An urgent treatment was necessary. The patient was unsuitable for chemotherapy so hormonotherapy with intramuscular fulvestrant (loading dose 500mg every two weeks and then 500mg every month) was introduced. The next month she was stable but then she became better. Her general condition was better, bone pain subsided, diplopia and strabismus lessened, creatinine level dropped to 1.27mg/dL. After three months she came in on her own using crutches, diplopia and vision greatly improved. She was on hormonotherapy over two and half years with no signs of progression but ocular signs persisted (Figure 1).



**Figure 1** Hormonotherapy over two and half years with no signs of progression but ocular signs persisted.

## Discussion

Despite their rarity, occurrence of paraneoplastic syndromes is very important to cancer patients and oncologists. This is because these syndromes can be the first symptoms of malignant disease, they can mimic metastatic process and they can worsen quality of patients' life.<sup>4</sup> But they can be used also as an indicator of successful or unsuccessful treatment. The accurate diagnosis is especially difficult in elderly patients because of their comorbidities and naturally impaired reserves so any additional burden of neoplastic disease can lead to fast deterioration of their general condition. There are several paraneoplastic syndromes connected with breast cancer, for example: cerebellar degeneration, stiff person syndrome, retinal degeneration, opsoclonus-myoclonus with possible ataxia, dermatomyositis, erythema gyratum repens or hypercalcemia.<sup>5-8</sup> Described here ocular syndrome exophthalmos- strabismus is to my knowledge first in the literature.

In order to regard this syndrome as paraneoplastic a few aspects should be taken into consideration. The paraneoplastic clinical signs appeared several weeks before overt disease progression. Despite careful radiologic work-up, no signs of metastases were discovered. Unfortunately, lumbar puncture was not done due to quite obvious for medical staff reason- dissemination of neoplastic disease. So leptomeningeal involvement could not be excluded. The only clue to connect at this stage the syndrome with breast cancer was a minor raise (seven units) of Ca 15.3 level, although it was still in normal range of limits. In my opinion the most important reason to consider exophthalmos-strabismus syndrome as paraneoplastic was reasonable resolution of its signs after hormonotherapy introduction. There was another central nervous system magnetic resonance done and again

no signs of metastatic process was discovered, despite of left eye symptoms persisted. There is one more question to be answered. Should the treatment be changed when ocular signs developed? This patient therapy was not changed because there was no valid radiologic or laboratory evidence for disease progression. But the later course of disease indicated clearly, that the reason for ocular symptoms was neoplasm progression.

## Conclusion

1. Lack of radiologic or laboratory evidence for disease progression not always means inactive disease.
2. Because neoplastic disease can produce unexpected signs and symptoms, clinical suspicion should make oncologists to consider treatment change.
3. Any new cancer syndrome should be promptly described in literature.
4. Fast and correct diagnosis of paraneoplastic syndrome is of paramount importance in elderly patients.

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## Conflicts of interest

The author declares that there is no conflicts of interest.

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