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CASE REPORT

Fluoro-deoxy-glucose-(18f) Positron Emission Tomography in Diagnostic of Carcinoma of Unknown Origin

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Carcinoma of unknown origin is defined as the absence of primary tumor and biopsy proved the existence of metastatic changes. The incidence is about 3% of all cancers. We present a case of a patient who underwent surgery for left breast mammography verified pathological lymphonodes on the left breast and on the left axillary region. Histopathological analysis of excised tissue showed the absence of malignant disease in the breast. A complete diagnostic evaluation also did not confirm the primary lesion. We done fluorodeoxyglucosa positron emission tomography, which had set suspicion of primary breast cancer, but biopsy and pathological reverification were not confirmed. The patient spent six cycles of chemotherapy for cancer of unknown origin. After a year and six months because of sudden right side hemiparesis were performed Computed Tomography and Magnetic Resonance imaging of the head, which indicated that it was a metastatic brain tumour. After metastasectomy, histopathological finding was finally proved to be a metastasis of breast adenocarcinomas. The patient had irradiation of the cranium, and began chemotherapy protocol for breast cancer. In this case, insufficient diagnosis did not affect in the proper therapeutic approach.

Keywords: *carcinoma of unknown origin; positron emission tomography; breast adenocarcinoma*

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Competing interests
The authors declare no competing interests.

INTRODUCTION

Carcinoma of unknown origin is defined as the absence of primary tumour and biopsy proven metastatic developments [1]. It has specific biology with clinical features and rapid progression of atypical metastases. The incidence is about 3% of all carcinoma [1, 2]. A very low percentage of women with confirmed breast cancer [0.3%], and which had isolated axillary metastasis without proven primary site [2]. Adenocarcinoma is the most common histological type carcinoma of unknown origin and as a well differentiated, poorly differentiated or undifferentiated, then followed squamous cell carcinoma. The leading sites are the lung [30%] and pancreas [20%], while the breast is very rare [0.3%] [2.3]. FDG-PET [Fluoro-deoxy-glucose-(18F) Positron Emission Tomography] as a diagnostic method is the most sensitive [100%] and specific [94%] [2-6] in comparison with conventional diagnostic imaging methods and panendoscopy. It is the most specific in detection of primary cancer sites in patients with cervical metastases [2-5]. We present the patient who underwent a brain metastasis rescretion. Previously, we performed positron emission tomography which showed a suspicion of primary breast cancer, although the histological findings after quadrantectomia was negative. This case could be important parameter in the clinical work.

CASE REPORT

In December 2008, 58 years old female patient presented in the Department of Surgery Cantonal Hospital Zenica. She was admitted due to histologicaly proven breast cancer [lympho nodes dissection]. The diagnostic process had a mammogram where the primary lesion was found. There was a lot of lymph nodes in the tail of the left breast and left armpit. The ultrasonography of the abdomen and kidney, lung radiography, spine, cranium and laboratory were normal. A resection of the upper quadrant of the lateral quadrants and histological analysis were performed. The pathologist confirmed the presence of numerous metastatic lymphonodes in the tail of the left breast, but primary breast cancer was not found. The surgeon was dissected the lymph nodes of the second level with an impressive findings of numerous lymph nodes. The hystopathological analysis showed metastatic lymph nodes. After one month the patient was reported oncologist, who indicated an expanded diagnostic evaluation that included: esophagogastoduodenoscopy / EGDS /, colonoscopy, alcal phosphatase / ALP /, hormone receptor-estrogen / ER /, progesterone / PR / and HER 2 / neu including tumour markers CA 15_3, CA 125, CA 19_9, and CEA were nor-

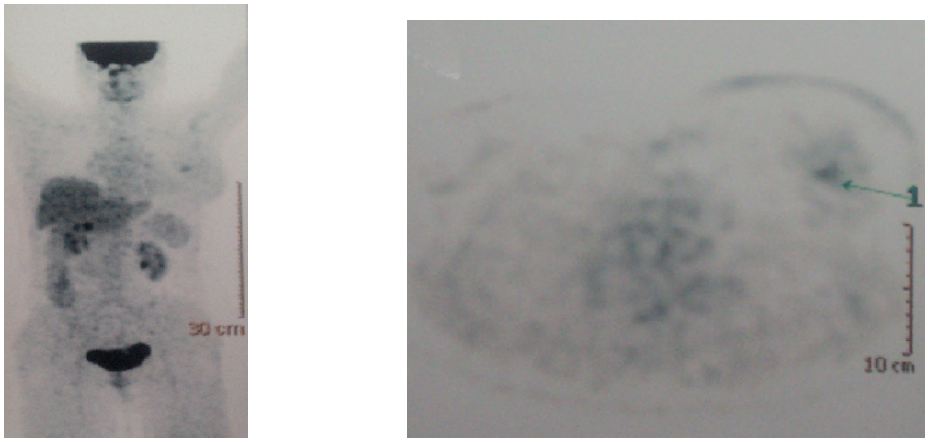

Figure 1. FDG PET-high intense metabolism on the left breast (frontal and axial scans)

mal. After diagnostic the patient presented in the Consilium for breast cancer which decided to start with three cycles of chemotherapy for cancer of unknown origin and to supplement the diagnosis with PET. PET was performed in Polyclinic Department of Radiology and Nuclear Medicine Zagreb, Croatia.

The results PET was that the skin thickened left breast with inhomogeneous parenchyma which was diffusely intensed FDG metabolism (Fig 1 and 2).

But there was also one visible and limited area with high intense metabolism on the chest wall. That area was high suspected on malignant change (Fig 3).

The oncologist indicated histological verification that change. Consilium for breast cancer referred patient to the surgery for biopsy of the lesion visible on FDG PET. Histopathological analysis showed that it was olegranuloma. In spite of the negative histological analysis Consilium for breast cancer decided to continued another three cycles of chemotherapy for cancer of unknown origin. After that followed the reevaluation with ultrasound of breast and lymphonodes drainage, abdomen and pelvis, tumor markers CA 15_3, CA 125, CEA, CA 19_9, ALP, gynecological examination with transvaginal ultrasound [endometrial thickness]. Controlled results showed that the endometrial thickness was 1.53 cm, and we indicated exploratory curettage. Other findings were normal. The histopathological analysis after curettage was normal. The local findings in the breast was also normal. The patient came to the oncologist control every two months. In the September, 2009. we verified the first increase breast tumour marker CA 15-3 which was 37.0. Control mammography / annual / was normal including EHO of the breast, lymphatic drainage and the liver. Also, the values of the other tumour markers CA 125, CA 19-9, CEA and radiography of the lungs were normal. Then there was the first increase in alkal phosphatase / ALP/-147. We indicated the bone scintigraphy / PET was performed before eight months and showed no secondary deposits in the sceleton / which register metastatic changes in the bone of the left hip with suspected pathological fracture of the femur neck. The diagnostic was completed with the target X-ray images pelvis with both hips and thigh which did not confirm that it is secondary deposits in bones. The oncologist decided to make Computed Tomography / CT / of the pelvis. In the April 2010, the control examination local findings in the breast was normal. Complete attached diagnostics were normal, except alkal phosphatase which was still on the rise / CT of the pelvis was still waiting/. The patient had no subjective symptoms related to primary disease. After 12 days of the last control examination, the patient presented to the Department of Neurology General Hospital Tešanj presenting the right hemiparesis. CT of the cranium was performed and showed the metastasis changes into the left supraventricular region of brain. In the same time was also done CT of pelvis which showed pathological fracture of the left femur neck and the metastatic changes in the pelvis bone. After diagnostic the patient was sent to the oncology treating. In the Department of Oncology and Hematology Cantonal Hospital in Zenica, the patient was hospitalised for extended diagnostic

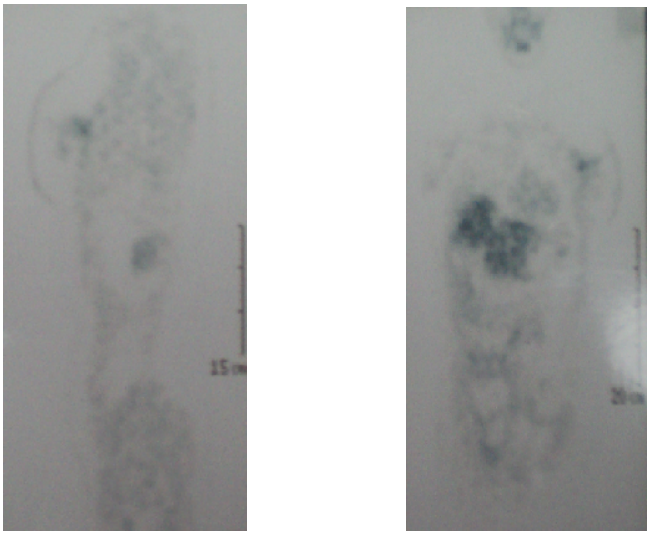

Figure 2. FDG PET-high intense metabolism on the left breast (sagital and frontal scans)

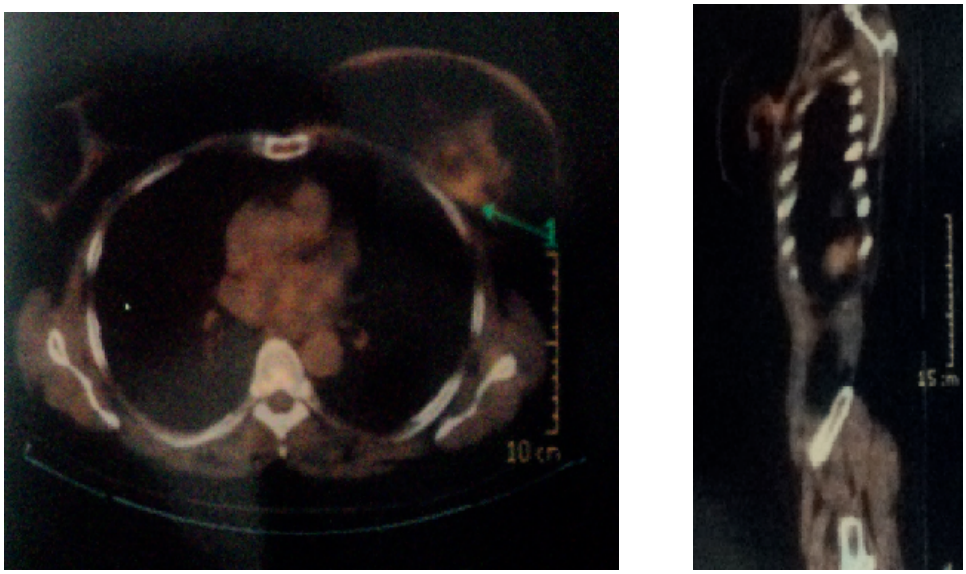

Figure 3. Limited area with high intense FDG PET metabolism on the chest wall

examination when was performed Magnetic Resonance Imaging (MRI) of endocranium. It showed one focal expansive lesion in the left central zone with dimensions 2,2x1,8x2,9 cm (Fig 4).

We consultated neurosurgeon and radioterapeutic. In the June 2010, it was done metastasectomies in the Department of Neurosurgery Cantonal Hospital Zenica (Fig 5).

Patohystological analysis was finally showed metastasis of the breast adenocarcinoma. The patient was treated with palliativ irradiation of neurocranium in the Institute of Oncology and Radiology, University Clinical Centre of Sarajevo. After that, in the September 2010, Consilium for breast cancer decided to start with chemotherapy for breast cancer and bysphosphonates.

DISCUSSION

Carcinoma of unknown origin is defined as the absence of primary tumor and biopsy-proven metastatic developments [1]. The incidence is about 3% of all cancers. In the very small percentage [0.3%] there were isolated axillary metastasis without proven site of primary [1, 2]. PET is a highly sensitive method for detection of primary sites for cancer of unknown origin, which was confirmed by the majority of studies [6-8]. In the most cases this method performed their sensitivity and specifity [2]. PET scans cannot currently be recommended for the standard workup of all patients with unknown primary cancer. Trials that have evaluated the effectiveness of PET scans in patients with unknown primary cancer and negative conventional diagnostic tests. To our knowledge PET scans in patients with unknown primary cancer for the diagnosis of primary tumors has not been studied to date [9]. Three studies have directly compared FDG PET/CT to (CT-based attenuationcorrected) FDG PET alone in CUP. In all three studies [10–12], FDG PET/CT was able to detect a few more primary tumors than FDG PET alone, although these differences were not statistically significant. Nevertheless, a combined PET/CT system is favored above a stand-alone PET scanner in patients with CUP because of its previously mentioned advantages.

In this paper we presented the patient who was referred to oncologist after surgery of the left breast with result of histological analysis. Specifically, it was a metastasis in the left breast and armpit. There did not find the primary site of tumour and the patient underwent a thorough diagnostic evaluation including PET, which certainly did not confirmed the primary site, but it was suspected that it was a primary breast cancer. Histological verification of PET registered changes did not proven that it was breast cancer, only olegranuloma. So, in our case, this diagnostic method was not highly efficacy as we expected at the start. PET was suspected which the patohystological analysis refused. That was oncologists dilemma in the therapeutic approach. It took 18 months to the patohystological confirmed primary process which was suspected in the PET. Fortunately, by this time the patient was given chemotherapy for cancer of unknown origin. This is a really good example for medical doctors how diagnostic sometimes could be insufficient for finally diagnosis. Regular, thor-

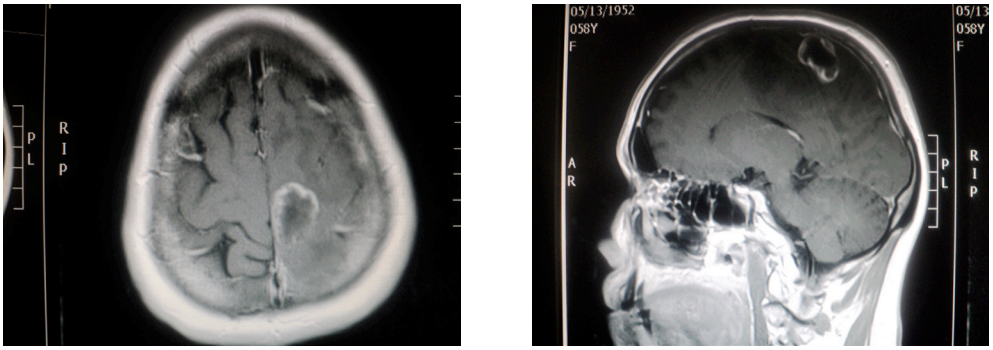

Figure 4. Preoperative MRI of endocranium

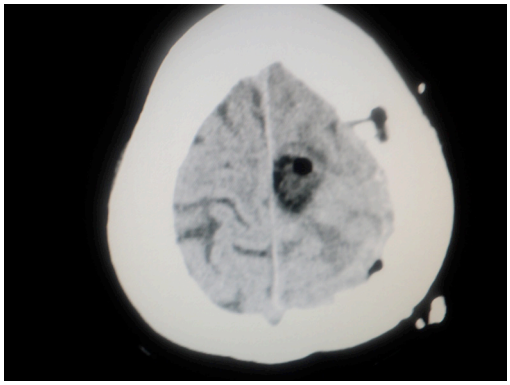

Figure 4. Postoperative CT scan of endocranium

ough and detailed approach to the patient becomes the first and only goal of oncologysts, as part of a multidisciplinary team which use diagnostic as supporting method and not crucial in the treatment of oncologycal patients. Therefore, the limitations of diagnostic methods should not affect in the selection of regular therapeutic approach.

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