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# Breast Trauma and Triple-Negative Hemorrhagic Cystic Carcinoma: Management and Treatment

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Data Collection B  
Statistical Analysis C  
Data Interpretation D  
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**Conflict of interest:** None declared

**Patient:** Female, 59-year-old  
**Final Diagnosis:** Invasive breast carcinomas of no special type (NST)  
**Symptoms:** Recurrent hemorrhagic cystic lesion  
**Medication:** —  
**Clinical Procedure:** —  
**Specialty:** Surgery

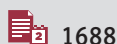
**Objective:** Challenging differential diagnosis  
**Background:** Breast trauma can always have diagnostic pitfalls. In the presence of a recurrent hemorrhagic cysts, cancer should always be suspected.

**Case Report:** A 59-year-old woman noted a palpable mass after breast trauma from falling at home. Radiological exams showed a breast cyst with well-defined margins, with corpuscular and dense fluid components. First, a conservative approach was implemented. One week later, a fine-needle aspiration cytology (FNAC) of the mass showed bloody fluid without atypical cells. Three weeks later, the patient was emergently evaluated due to increased size of the lesion and anemia. To avoid further blood loss and due to suspected malignancy, an urgent surgical excision biopsy was planned. Histopathology revealed a poorly-differentiated carcinoma and the patient was treated with left modified radical mastectomy with axillary dissection. Adjuvant chemotherapy was administered. At 6-month follow-up, the patient was free from recurrences.

**Conclusions:** Recurrent hemorrhagic cysts should always be investigated and considered as a possible cancer lesion. Sonography and cytological exam are the first steps in case of suspicious cysts, but false-negative results are common. In such cases, resection of the cyst should be considered. Immediate resection is valid in cases of diagnostic uncertainty or inability to assess the cyst with imaging or biopsy.

**MeSH Keywords:** Breast Cyst • Breast Neoplasms • Triple Negative Breast Neoplasms

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## Background

A cystic tumor that occurs acutely as a bleeding event after patient-related breast trauma can be diagnosed too late, especially when fine-needle aspiration cytology (FNAC) is reported as negative [1]. These clinical features can be misleading, and cancer diagnosis and differential diagnosis can be challenging. In patients with hemorrhagic cysts, intracystic cancer should be always be considered [2]. In this report, we describe a case of triple-negative breast cancer that appeared as a recurrent hemorrhagic cyst after trauma.

## Case Report

A 59-year-old woman with recent breast trauma from falling at home was referred to our hospital for clinical evaluation. She reported that she had breast pain associated with a new mass in the left breast. Physical examination revealed a palpable mass in the upper inner quadrant of the left breast, without variation of the skin profile and palpable axillary lymph nodes. No personal or familiar oncological history, hematologic disease, anticoagulant therapy, or bleeding tendency was reported. At first, ultrasonography showed a 4-cm breast cyst, with thin well-defined margins. Sonography features of the cyst showed corpuscular and dense fluid, as in organized hematoma. Due to pain, 40 cc of blood was drained, with no residual lesion. The complete blood cell count was in the normal range according to age (hemoglobin 12.3 g/dL). Seven days later, the patient presented a recurrent cystic lesion (4.7 cm). A conservative approach was implemented, and 60 cc of bloody fluid was removed by needle aspiration. Our diagnostic hypothesis was a post-traumatic hemorrhagic cyst and we recommended complete radiological assessment and subsequent surgical reevaluation. Mammography showed a well-defined breast lesion without any suspicious micro-calcification. A second-look sonography confirmed a complicated cyst at the site of the mammography finding. Ipsilateral axillary lymph nodes were reported as not suspicious but with increased volume of 1.5 cm diameter. A surgical visit 10 days after the initial trauma revealed a recurrent breast lump 6.2 cm in diameter. Due to the volumetric increase in nodes and cyst, we drained the cyst for cytological examination and performed FNAC of the axillary nodes. Eight slides were then prepared from the sample using traditional smear and Thin-Prep procedure and stained with hematoxylin-eosin. No atypical cells were found in any of these cytological preparations; we observed the presence of only inflammatory cells, foamy histiocytes, and fibrinonecrotic material (C1 according to European Guidelines) [3]. Core-needle biopsy was not performed due to the hemorrhagic risk and the absence of clear suspicious finding in the cyst wall. Antibiotic therapy was started. Three weeks later, the patient was admitted to the Emergency Department due to increased



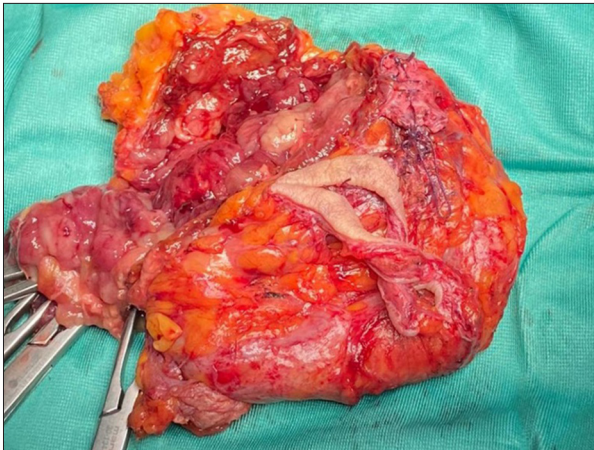
**Figure 1.** Huge palpable mass in the upper inner quadrant of the left breast. The size of the mass was gradually increasing.



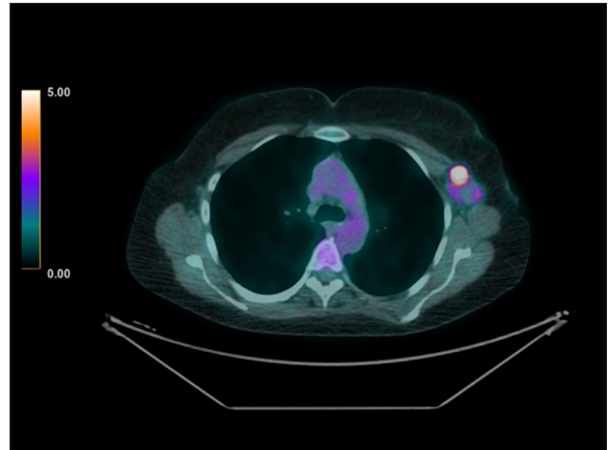
**Figure 2.** The mass had modified skin profile.

size of the mass, skin profile distortion, and anemia (hemoglobin 9 g/dL) (Figures 1, 2). The cyst was about 11.5 cm in size. To avoid further blood loss and due to suspected malignancy, an urgent surgical excision biopsy was planned. A clear surgical cleavage plane could not be achieved from the pectoralis major muscle. En bloc resection of the lesion and pectoralis major fascia was completed and extemporaneous biopsy with frozen section showed an indeterminate small-cell tumor. Macroscopically, the lesion presented as a cyst 11 cm in maximum diameter, filled with necrotic-hemorrhagic material, with an infiltrative neof ormation in the lumen. Sampling for intraoperative cryostatic examination was carried out on the neoplasia and on the intracystic material. The analysis of the frozen slides quickly revealed the malignant nature of the lesion, showing a poorly-differentiated neoplasm with solid growth buried by fibrous branches and high nuclear grade, consisting of large markedly atypical cells with evident central eosinophilic nucleolus, areas of necrosis, and atypical mitosis. The macroscopic characteristics of the lesion and the poor differentiation of the tumor made it difficult to define its primitiveness, postponing any diagnostic clarification to the final





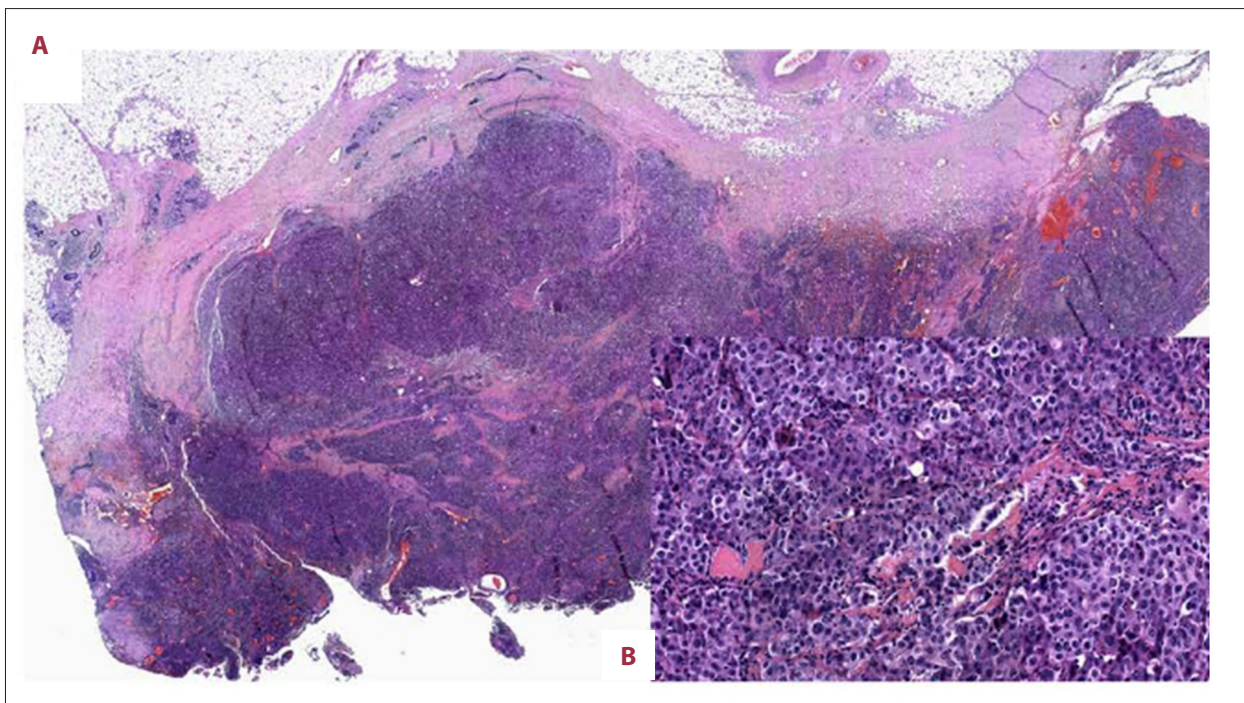
**Figure 3.** En bloc resection of mass was completed.



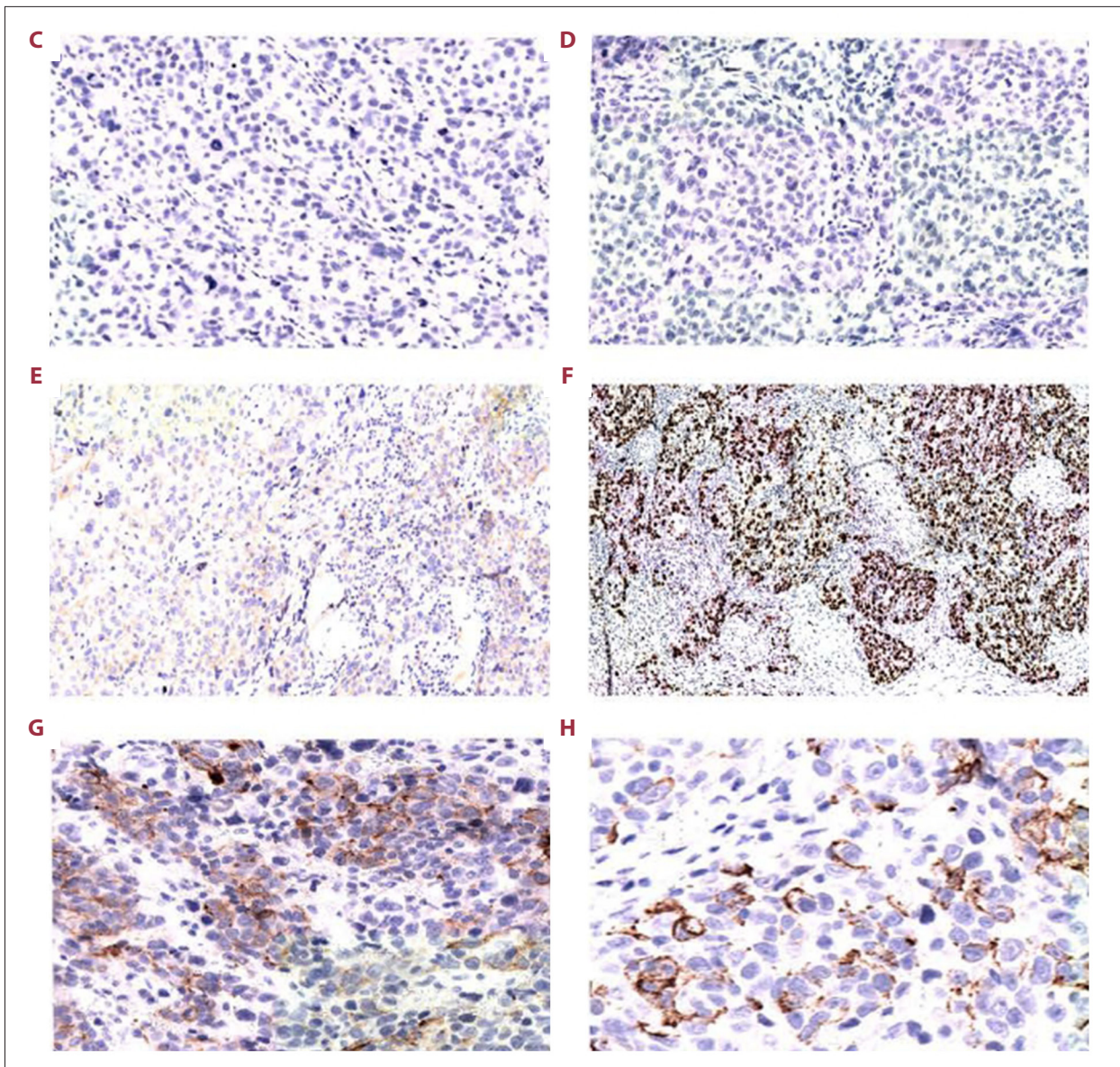
**Figure 4.** Axial image of PET/TC scan showing an intense hypermetabolism enhancement in left axilla.

examination (Figure 3). Axillary lymph node dissection (ALND) was not performed because we could not exclude the breast as a secondary site tumor. The patient underwent a total-body PET/CT scan, which described pathological uptake in the ipsilateral axilla (SUV max 15) with no further distant pathological enhancement (Figure 4). Only the exhaustive sampling and fair immunohistochemical evaluation permitted us to assess the observed tumor using the following markers: CK7+, CK20-, GATA3+, TTF1-, S100-, beta HCG-, CK5/6, and CK14 focally+, ER- (positive internal control), PR- (positive internal control), HER2- (positive external control), AR+ in 10% of neoplastic cells, and Ki67 index 80%. It could therefore reasonably be concluded that the tumor belonged to the category of

Invasive Breast Carcinomas of No Special Type (NST) according to WHO 2019, of grade 3 (G3) according to Nottingham Grading (tubules: score 3; pleomorphism: score 3; mitosis: score 3), and immunophenotype “triple-negative” [4] (Figure 5). The patient was treated with left modified radical mastectomy with immediate reconstruction due to an aesthetic defect with axillary dissection. No further tumor tissue was found in the breast specimen and 5 out of 23 lymph nodes were sites of metastasis (pT3N2a). Adjuvant chemotherapy was administered. Two weeks after mastectomy, a hematoma appeared in the surgical site. The fluid was fully analyzed: the entire volume (400 cc) was fixed in formalin, centrifuged, and 8 cytological preparations were prepared from the sediment. No







**Figure 5.** Histopathological features of the described tumor. The histological diagnosis was NST invasive breast cancer with a cystic wall, poorly-differentiated, of grade 3 (G3), as observed by hematoxylin and eosin staining at magnification  $\times 1$  (A) and  $\times 20$  (B). Immunohistochemical features of ER (C), PR (D), and HER2 (E) at magnification  $\times 20$ . ER, PR, and HER2 staining results were all negative. The Ki-67 labeling index was 80% (F) at magnification  $\times 20$ . The result of staining with basal cytokeratins, CK 5/6 (G), and CK14 (H) was focally positive at magnification  $\times 20$ .

neoplastic cells were found, only red blood cells and figured blood elements (C1, in according to European Guidelines) [3]. At 6-month follow-up, the patient was free from distant and loco-regional neoplastic recurrence.

## Discussion

Modern preoperative breast cancer evaluation usually consists of triple assessment, defined as mammography, ultrasound,

and pathological examination. About 5-10% of women who undergo breast surgery do not have a pathological diagnosis, and breast cancer is rarely treated with urgent surgery [5]. Some authors have described a few cases of breast carcinoma with a huge cyst due to a rupture of the tumor vessels accompanied with a bloody discharge from skin erosion; most of these cases were hemorrhagic cysts [6]. Cystic carcinomas of the breast encompass a heterogeneous spectrum of tumors. Radiological findings of breast cystic lesion are well described [7]. Huge cysts pose a diagnostic challenge, as in our

case [8]. Sonography and biopsy are the main steps in case of suspicious cysts. However, there are high rates of false-negative results due to necrotic debris, abundant obscuring blood, and sparse cellularity, especially in huge cysts [9]. The fluid physical examination can give clues for the differential diagnosis and for determining the benign vs. malignant nature of a cyst. In malignant cysts, however, the presence of blood is not pathognomonic for cancer, but its absence does not exclude malignancy [9]. Recurrent hemorrhagic cysts, when associated with a history of breast trauma, might be misleading, as in our case. In certain cases, the diagnosis can be confirmed by needle-core biopsy, taking into account 2 major limitations. Firstly, the target of the biopsy is often the center of the cystic lesion, which rarely is a site of invasive carcinoma compared with peripheral cells [10]. Secondly, performing needle-core biopsy can be difficult, especially when cysts distort the breast, as in our case. For these reasons, we decided to attempt a cytological examination of the aspirated fluid during the diagnostic process, but this did not reveal any atypical cells. This result seems to confirm the limitations of the cytological examination in the diagnosis of cystic lesions of the breast, which is well-defined in the literature as regards papillary lesions [8]. This result can be interpreted in 2 ways: on the one hand, as a result of a real absence of neoplastic cells in the fluid because triple-negative tumors typically have a pushing border and central necrotic area, known as the “acellular zone” [11]; on the other hand, the result could be a consequence of the limitations of the sampling method, considering the absence of specific guidelines. Concurrently with the recurrence of post-mastectomy hematoma, the second cytological examination was performed, referring to the current guidelines for breast seroma, which recommend analyzing the total amount of the fluid [12]. However, even in this case, no cancer cells were found. Triple-negative breast cancer accounts for approximately 15% to 20% of all breast cancers [13]. Biologically, the behavior tends to be more aggressive, with a higher incidence of metastatic progression, early recurrence, and worse survival, compared with other subtypes [14]. As there is evidence in the literature suggesting that basal-like tumors have a peculiar biological behavior compared to the other triple-negatives of which they are part [4], and considering that in our laboratories we could not carry

out microarray-based expression profiling studies necessary for their correct characterization [15], we attempted immunohistochemical analysis. The triple-negative immunophenotype, the expression of genes usually found in basal or myoepithelial cells of the normal breast (CK5/6 and CK14), and the immunohistochemical positivity for the androgen receptor (AR) reasonably suggests a basal-like phenotype [15,16], or, more precisely, a “core basal phenotype” [4]. Despite the aggressive clinical picture and the poor prognosis, a subset of patients appears to be particularly chemo-sensitive, achieving a pathological complete response and improved long-term outcome after neo-adjuvant chemotherapy [17]. On the one hand, our patient, with triple-negative advanced disease, according to histological tumor subtype, would have been a candidate for neo-adjuvant chemotherapy. On the other hand, from a clinical point of view, the challenging and complicated diagnosis made this strategy impractical. Moreover, in this clinical situation, one must consider the recurrent hemorrhagic cyst and increasing risk of bleeding associated with primary medical treatment, although lymph node needle-core biopsy showed a higher sensitivity than FNAC and might have provided a better chance of diagnosis in our patient [18,19]. Diagnostic open biopsy provides a sufficient amount of tissue for correct assessment, but, although the ERAS protocol and awake breast procedure can reduce surgical trauma, the risk of repetitive surgical stress on the immune system should be always considered in cancer patients [20–23].

## Conclusions

Recurrent hemorrhagic cysts, when associated with a history of breast trauma, might be occult malignancy, so they should always be investigated. Sonography and biopsy are the first steps in case of suspicious cysts, but there is a high rate of false-negative results. In these cases, timely and immediate resection is a valid tool in cases of diagnostic uncertainty or inability to assess the cyst with imaging or biopsy.

## Conflicts of interest

None.

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