

# Metastatic Adenocarcinoma to the Breast arising from a Mediastinal Mature Teratoma with Somatic Malignancy: A Case Report with a Review of the Literature

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## Case Report

**Keywords:** Mature teratoma, Malignant transformation, Metastasis, Somatic-type malignancies, Mediastinal, Breast

**Posted Date:** December 28th, 2020

**DOI:** <https://doi.org/10.21203/rs.3.rs-135224/v1>

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# Abstract

## Background

Malignant transformation in mature teratomas, especially somatic-type malignancies, are extremely rare phenomena with few cases described in the literature. In the mediastinum, these lesions are often accompanied by metastases, ultimately unmasking them.

## Case presentation

We report an exceptional case of metastatic adenocarcinoma to the breast arising from a mediastinal mature teratoma with malignant transformation in a 31-year-old female. The patient initially presented with a breast lesion that was later diagnosed as either a triple negative ductal carcinoma or a metastatic adenocarcinoma of unknown origin. Extensive clinical workup and radiological imaging revealed an anterior mediastinal mass. Subsequent pathological examination of the mass showed a mature teratoma with malignant transformation equivalent to that found in the breast biopsy.

## Conclusion

Mediastinal teratomas with malignant transformation (TMTs) are rare entities; however these tumors should be suspected in cases of suspicious mediastinal masses presenting with unusual clinical and radiological signs, such as metastasis of unknown primary origin. Pathological corroboration of extensive sampling and meticulous microscopic examination is crucial for the diagnosis in order to tailor subsequent treatment.

## Background

Breast cancer accounts for more than 20% of all cancers affecting women (1). Conversely, metastases to the breast are rare and represent only 0.2% to 1.3% of mammary tumours (2–4). Among occult cancers, 30% are initially presented by breast metastasis (3–5). Imaging studies usually reveal a single well-defined, occasionally speculated mass. The most common origin of these metastases are contralateral breast cancers, however, they can also arise from other neoplasms such as: carcinomas from the lung and ovary, melanomas, lymphomas and rhabdomyosarcomas particularly seen in young female patients (5,6). However, many other primitive sites have been reported (7).

Here we report a highly unusual case of metastatic adenocarcinoma to the breast in a young female arising from a mediastinal mature teratoma with malignant transformation.

## Case Presentation

A previously healthy 31-year-old woman was referred to our cancer center following a recent discovery of a left breast lump. Her family history included an aunt who had died from ovarian cancer. Clinical examination revealed a nodular lesion located at the exterior upper quadrant of the left breast with no signs of inflammation or lymph node involvement. Routine hematological and biochemical investigations were unremarkable. Ultrasound study and mammography both showed a mass measuring 37 mm, classified as ACR4 (8). Biopsy of the mass revealed mammary parenchyma diffusely infiltrated by a moderately differentiated adenocarcinoma composed of variable sized glands in a discreetly fibrous stroma. These glands were lined by tall columnar epithelial cells displaying abundant eosinophilic cytoplasm, moderate atypia and rare mitoses. Some cells had intra-cytoplasmic mucin vacuoles (Figures 1 and 2).

An extensive immunohistochemical panel was performed and showed positivity with epithelial markers: CK7+ (strong and diffuse); CK20+ and CEA + (weak and focal).

Other stains such as: Oestrogen Receptor (ER), Progesterone Receptor (PR), HER2, Mammaglobin, GATA3, TTF1, P40, P63, CD117 and PAX8 were all negative (Figure 3).

The initial diagnosis proposed was a triple negative grade 1 invasive ductal carcinoma according to the modified Scarff-Bloom-Richardson classification system (9).

*Consequent imaging by* Computed Tomography revealed a well-defined cystic anterior mediastinal mass with central necrosis, measuring about 10 cm and compressing adjacent anatomical structures. It also showed atelectasis, pulmonary and pleural thickening, multiple pulmonary nodules as well as regional lymphadenopathy.

Scintigraphy revealed multiple bone foci at the levels of L3, S1 and S2 and at the level of the 6th intercostal rib.

A Positron-emission tomography scan found two suspicious hypermetabolic lesions in the left breast, multiple positive foci at the level of the left pleura, left lung, left adrenal gland and multiple bone sites associated with mediastinal lymphadenopathy. No anomalies in the gastrointestinal tract were found.

Subsequent biopsy of the mediastinal mass revealed a moderately differentiated adenocarcinoma similar in morphology to that found in the breast biopsy. Interestingly, the immunohistochemical study showed a strong positivity for CK8/18 and CK7, a focal positivity for CEA and a mitotic index of 60%. All other immunostains including CK20, CDX2 and breast tissue markers were negative. Based on these findings, a left anterior thoracotomy was performed to remove the mediastinal lesion.

On gross examination, the resected tumor measured 12 x 10 x 7 cm and weighed 99 g. It was well demarcated with no obvious signs of rupture. No definite capsule or lung parenchyma were identified. The external surface had a glistened variegated appearance with alternating yellowish and congested areas. On sectioning, the mass was unilocular with a predominantly smooth wall and contained grumous material with hair.

Multiple thickened bourgeon areas measuring up to 1.5 cm associated with small yellowish colored granules were discovered inside the wall and on its interior surface. No papillary excrescences were found.

Microscopically, the cystic wall consisted of fibrocollagenous tissue lined by cuboidal and/or tall columnar mucin secreting epithelium with areas of minimal chronic inflammation and vascular congestion (Figure 5). On sectioning of the thickened areas, mature elements of all three germ layers were found:

- mesodermal derivatives such as adipose tissue, cartilage, and muscle bundles,
- endodermal derivatives such as gastrointestinal tract tissue and ciliated bronchial tissue
- and ectodermal derivatives such as stratified squamous epithelium and sebaceous glands.

There were no immature teratomatous elements or other germ cell components associated. Furthermore, we noted multiple foci of atypical cells, arranged in groups or glands and surrounded by a reactive fibrous stroma. These cells contained abundant eosinophilic cytoplasm, sometimes with intracytoplasmic vacuoles and displayed a moderate degree of pleomorphism and atypia (Figure 5). The immunohistochemical profile was similar to that found in the breast biopsy and showed a positivity for cytokeratines, BerEP4 and CDX2, suggesting a digestive origin (Table 1).

A final diagnosis of a mature teratoma with somatic-type malignant transformation, most likely an adenocarcinoma, with secondary breast metastasis was concluded.

The patient's postoperative course was uneventful and she was subsequently discharged. Unfortunately, the patient died a few months later.

## Discussion And Conclusion

Triple-negative ductal carcinomas account for only 15% of mammary tumours but are responsible for a disproportionate number of deaths. In fact, these tumours are most often of high grade; low grades (or grade I) represent only 9.8 to 15.1% of these cases (10,11). Due to the overall rarity of this type of tumour, it is necessary to be cautious when establishing this diagnosis by thoroughly eliminating all other differentials, including metastasis. This case reports a metastatic adenocarcinoma to the breast in a young female arising from a mediastinal mature teratoma with somatic-type malignant transformation. Teratomas belong to germ cell tumours (GCTs), divided into: seminomas, malignant "non-seminomatous GCTs" (such as embryonal carcinoma, yolk sac tumours, choriocarcinoma and mixed germ cell tumors), and teratomas both mature and immature. Mediastinal teratomas account for 50 - 70% of all mediastinal GCTs and 7 to 9,3% of mediastinal tumours (12).

According to the most recent World Health Organization definition, a teratoma with somatic-type malignancy is a teratoma containing one or more components of a non-germ cell malignant tumour,

which may be a sarcoma or a carcinoma. These tumours represent 10 to 20% of all mediastinal GCTs with somatic-type malignancies (12). Histologically, it seems that the malignant component is often carcinomatous (13,14) but this somatic-type only represents 37% of all GCTs with somatic-type malignancies (15). These tumours mostly always occur in males (12), between the ages of 20 to 40 years; however a few cases concerning females have been reported in the literature, mainly as case reports (14,16–22).

Same clinical features are also used to classify these tumours into two categories: TMTs induced by chemotherapy and/or irradiation and naturally occurring TMTs (14,16,18). Most reported cases have been from the former group, chiefly occurring in young patients with an initial presentation of a malignant germ cell tumour. On the other hand, naturally occurring TMTs in the mediastinum are extremely rare and occur in older patients in the context of mature teratomas of long standing duration, generally with good prognoses (14,16). In our case, the malignant transformation most likely occurred naturally due to the absence of chemotherapy or radiation exposure. Contrarily, the breast metastasis demonstrates an aggressive nature to this tumour. To our knowledge, this is the first reported case of a mediastinal TMT unmasked by breast metastasis.

TMTs should be suspect under certain clinical and radiological presentations such as: a voluminous mediastinal tumour measuring at least 10 cm in size (14) , adhesion to surrounding structures with or without invasion, local wall thickening with fatless solid areas and a contrast-enhancing capsule with a rough and uneven internal surface (13, 22).

These non-germ cell malignancies are postulated to originate either from totipotential germ cells differentiating to somatic type cells or from pre-existing mature teratoma elements to non-germ cell malignancy (14,20,22). Molecular studies have shown an isochromosome 12p (i[12p]) genotype with no clearly defined consequence in carcinogenesis, that is shared by both the somatic-type malignancy and its associated germ cell tumor component (12). The latter hypothesis is favored by the finding that “pure” mature mediastinal teratomas show no chromosome 12 abnormalities while a shared i(12p) abnormality is characteristic of teratomas that are clonally related with somatic type malignancies.

Interestingly, the majority of somatic-type malignancies do not immunohistochemically express PLAP, AFP, beta-hCG, or CD30, which are normally expressed in GCTs, but rather stain like their counterparts found elsewhere in the body. Cytokeratin immunostains, such as CK7 and CK 20, can be used to distinguish adenocarcinomas from other types of malignancies (21).

According to the literature, prognosis is poor compared to other GCTs, and depends mainly on surgical resection which is currently the recommended treatment. Other factors include, the primary tumor site and its margins, the type of transformed histology and the number of prior chemotherapy regimens before the development of TMT (23). Due to its rarity, the treatment of these tumors does not have a standardised chemotherapy protocol. However, adapted chemotherapy based on the TMT somatic malignant component is hypothesized to improve the overall outcome of these patients (13,24–26).

Despite their rarity, mediastinal TMTs should be suspected in all clinically diagnosed cases of mediastinal mature cystic teratomas with unusual metastasis. Unfortunately, clinical and radiological examinations cannot always predict the malignant component of these tumors. Therefore, pathological corroboration with extensive sampling and meticulous microscopic examination is crucial for accurate diagnosis, and for a tailoring subsequent treatment.

## Abbreviations

- TMTs : teratomas with malignant transformation
- GCTs : germ cell tumours
- CK : Cytokeratin
- ER : Oestrogen Receptor
- PR : Progesterone Receptor
- CEA : carcinoembryonic antigen

## Declarations

### *Ethics approval and consent to participate*

Ethical approval was obtained according to the agreement of the tumor biobank of Rouen University Hospital (tissue sample collection n° DC2008-689) by the institutional review board of Rouen University Hospital and the French Ministry of Scientific Research.

### *Consent for publication*

Not applicable

### *Availability of data and materials*

All data supporting the conclusions of this article is included within the article.

### *Competing interests*

The authors declare that they have no conflicting interests

### *Funding*

Not applicable

### *Authors' contributions*

Gwenaëlle ARHANT and Dahlia MIRDAD equally contributed to this work, they wrote the article and reviewed the literature.

Anca BERGHIAN and Nicolas PITON diagnosed the case.

Nicolas PITON and Jean-Christophe SABOURIN revised the article.

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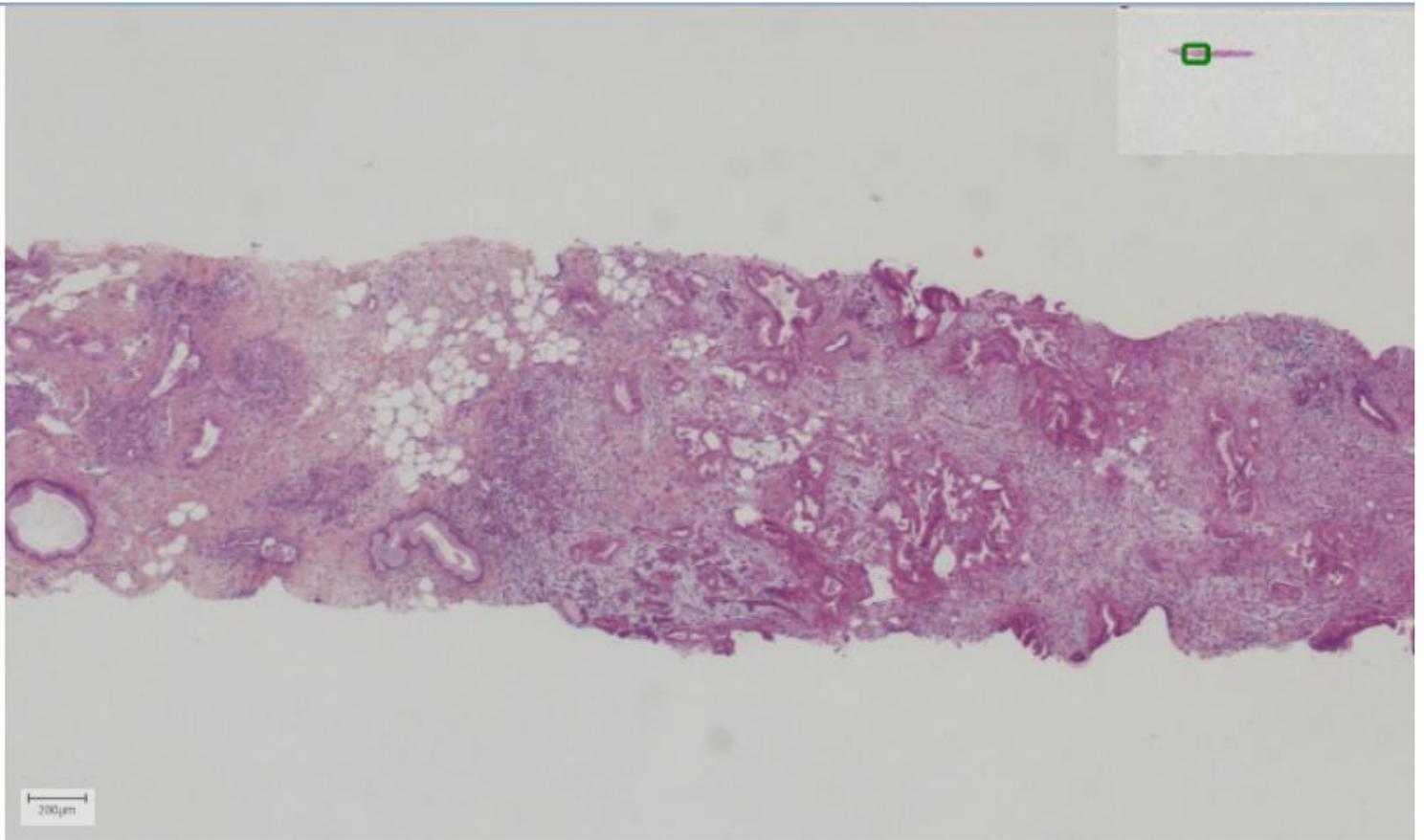
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# Tables

**Table 1.** Comparison of immunohistochemical profile of the breast and mediastinal mass.

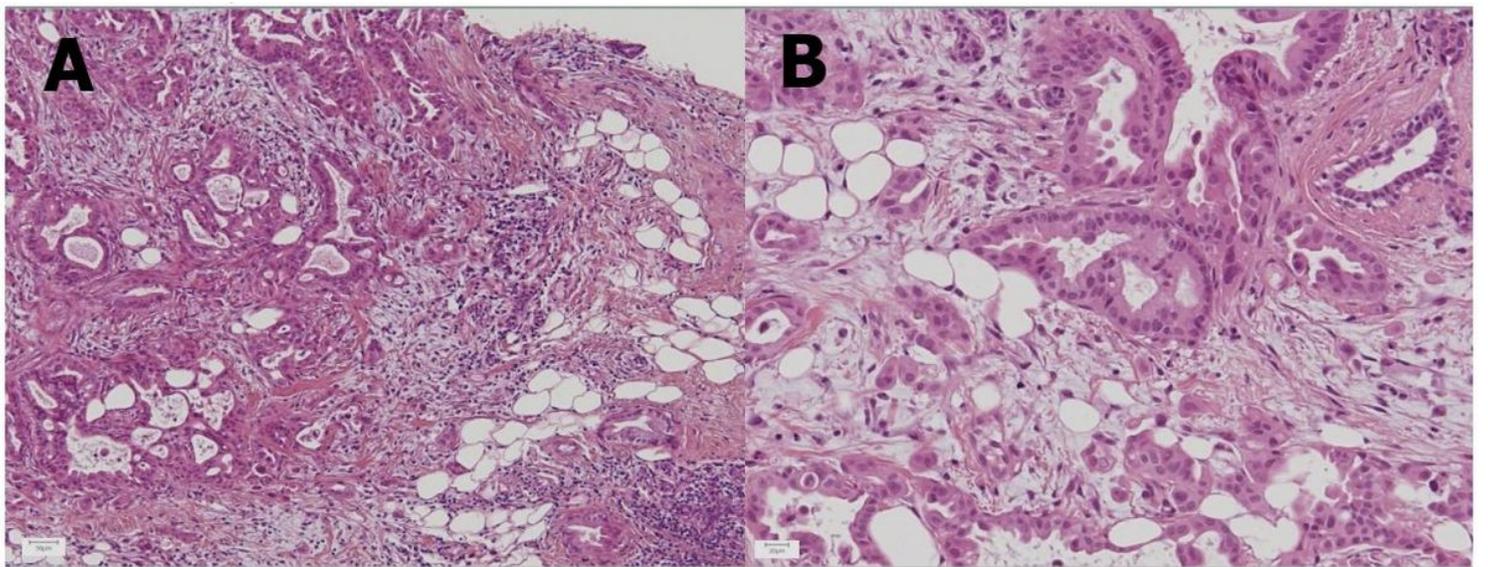
<i>Immunohistochemical Stain</i>	<i>Tumor Cells in mediastinum</i>	<i>Tumors Cells in breast lesion</i>
<i>ER</i>	Negative	Negative
<i>PR</i>	Negative	Negative
<i>HER2</i>	Negative	Negative
<i>GATA 3</i>	<i>Not performed</i>	Negative
<i>Mammoglobine</i>	<i>Not performed</i>	Negative
<i>CK7</i>	Positive (strong and diffuse)	Positive (strong and diffuse)
<i>CK20</i>	Positive (weak and focal)	Negative
<i>CDX2</i>	Positive	Positive (weak)
<i>BerEP4</i>	Positive	<i>Not performed</i>
<i>TTF1</i>	Negative	Negative
<i>Calretinin</i>	Negative	<i>Not performed</i>
<i>CEA</i>	<i>Not performed</i>	Negative
<i>PAX 8</i>	<i>Not performed</i>	Negative

# Figures



**Figure 1**

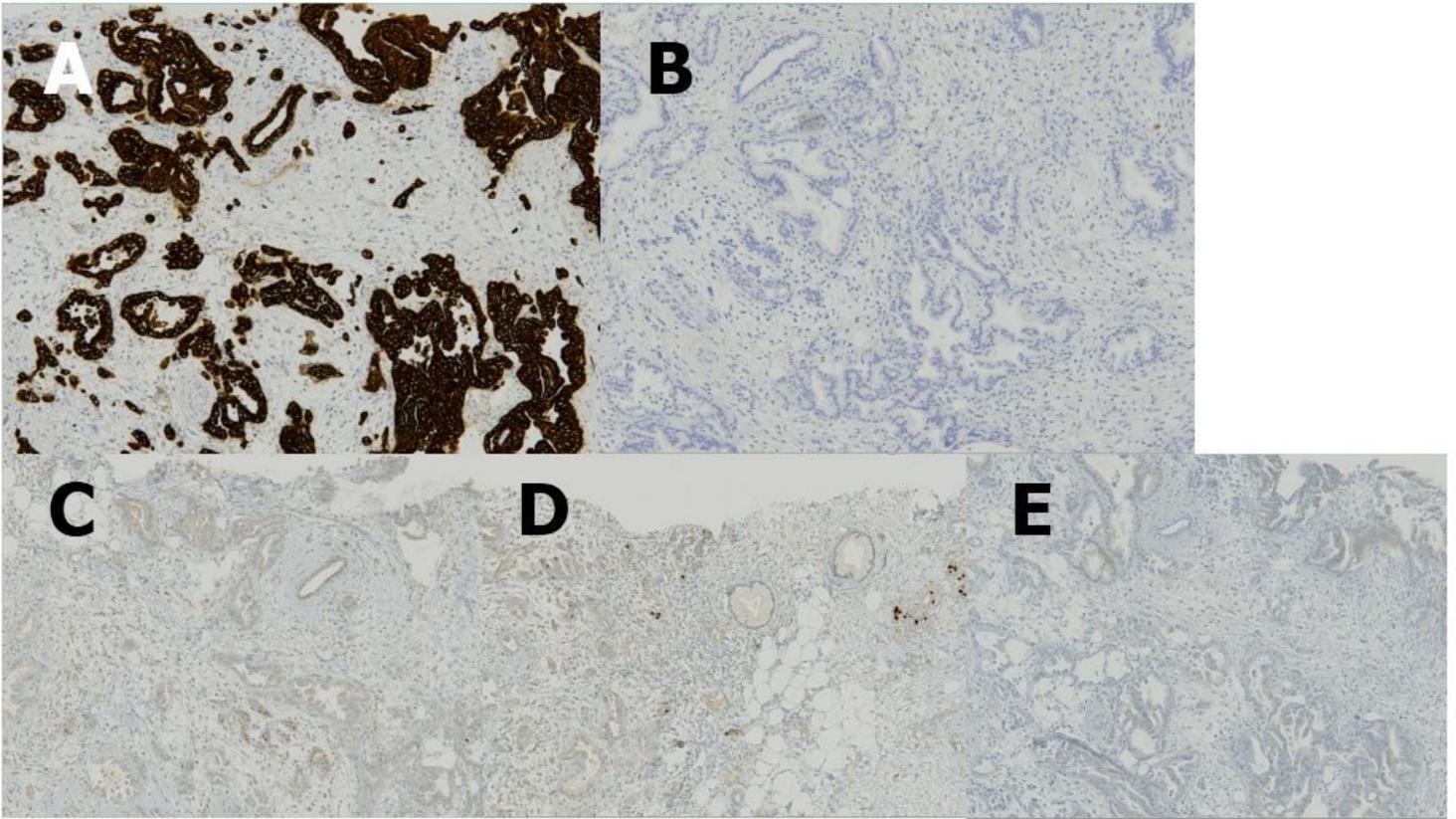
Tumour infiltration into the breast parenchyma with surrounding fibrous stroma. (Hematoxylin and eosin stain, X2.5).



**Figure 2**

Tumor histology. A) Moderately differentiated adenocarcinoma composed of glands of various sizes and shapes (Hematoxylin and eosin stain, X10). B) Malignant glands are lined by columnar epithelium

exhibiting moderate atypia (Hematoxylin and eosin stain, X20).



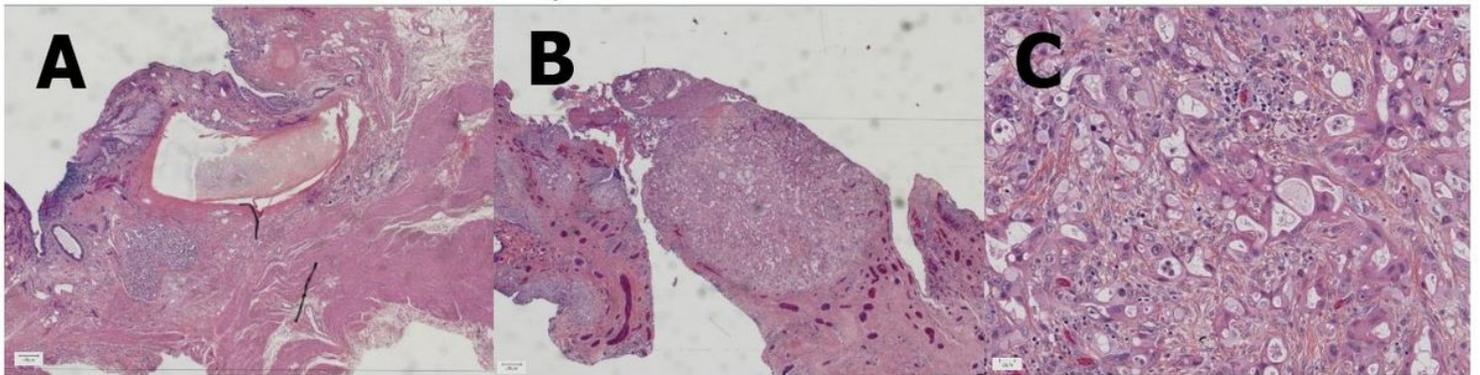
**Figure 3**

Immunohistochemical stains on the breast biopsy. A) CK7+ strongly and diffusely positive. B) CK20 negative. C) Triple negative (PR-, RE- and HER2-).



**Figure 4**

Macroscopic appearance of resected mediastinal mass. Well demarcated. No lung parenchyma was identified. On section, the mass was unilocular with areas of wall thickening associated with small yellow granules inside and on the interior surface of the cystic wall.



**Figure 5**

Tumor histology. A) Mature Teratoma Germ cell layers (Hematoxylin and eosin stain, X2.5). B and C) Mature Teratoma with Somatic Malignancy demonstrates a moderately differentiated adenocarcinoma

(Hematoxylin and eosin stain, X2.5 and X20).