

## Pulmonary placental transmogrification associated with adenocarcinoma of the lung: a case report with a comprehensive review of the literature

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**How to cite:** Hamza A, Khawar S, Khurram MS, et al. Pulmonary placental transmogrification associated with adenocarcinoma of the lung: a case report with a comprehensive review of the literature. *Autops Case Rep* [Internet]. 2017;7(3):44-49. <http://dx.doi.org/10.4322/acr.2017.027>

### ABSTRACT

Pulmonary placental transmogrification (PT) is a rare entity with less than 40 cases reported in the literature. Most reported cases are associated with either bullous emphysema or with pulmonary fibrochondromatous hamartomas. We present only the second case of PT associated with adenocarcinoma of the lung. A 67-year-old female with multiple chronic medical ailments presented with shortness of breath and was found to have a 6-cm mass in the upper lobe of her right lung. A computed tomography (CT) guided core biopsy was performed that showed a well-differentiated adenocarcinoma. Interestingly the normal lung tissue showed placental villous architecture. A unique feature of our case is that the diagnosis was made on a needle core biopsy, unlike all the other cases in the literature. We also provide a comprehensive review of this rare entity.

### Keywords

Emphysema, Hamartoma, Placenta, Solitary pulmonary nodule.

### INTRODUCTION

Pulmonary placental transmogrification (PT) is a rare histopathologic entity first described by Mc Chesney in 1979.<sup>1</sup> PT is a benign lesion and resembles placental tissue morphologically, however, lacks the functionality of the placenta. It is usually diagnosed as an incidental finding, and the exact etiology is still unknown. Some think that it is due to lymphatic or vascular proliferation in emphysematous lung,<sup>2-4</sup> while others believe it to be a component of a congenital malformation,<sup>3</sup> or a hamartoma.<sup>1</sup> Xu et al.<sup>5</sup> found that PT is frequently associated with pulmonary fibrochondromatous hamartomas and may be induced by or associated with a proliferation of lining epithelial components in the hamartomas. Clinically PT is associated with the bullous emphysematous disease. A thorough literature review revealed one case of PT associated with adenocarcinoma of the lung.<sup>6</sup> The PubMed database was searched using keywords "placental transmogrification". 26 manuscripts, most of which were case reports were identified. All these were analyzed with respect to patient demographics, clinical presentation, associated

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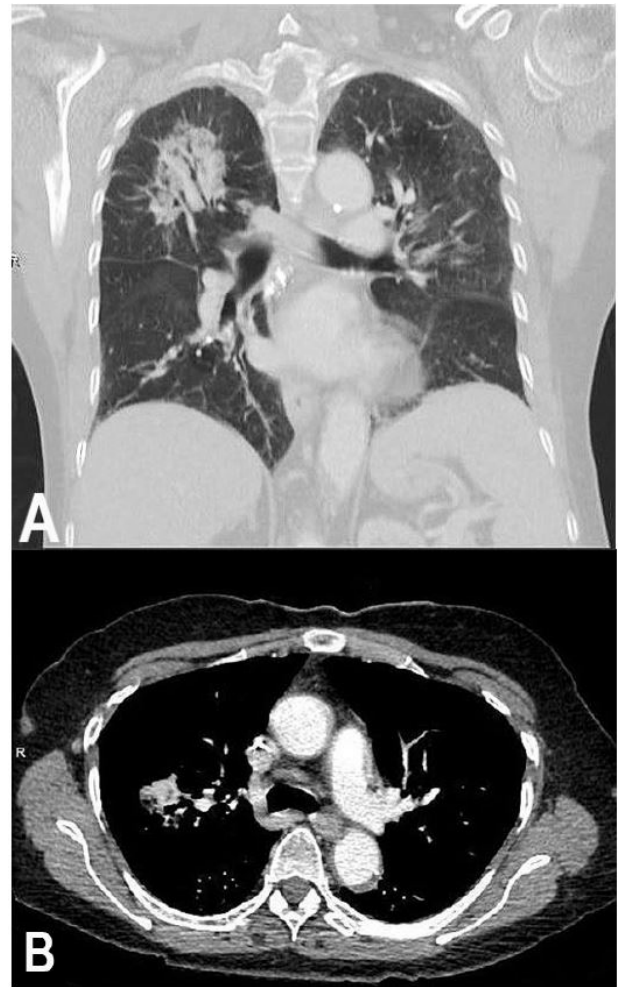


conditions, pathogenic hypotheses, radiologic findings, microscopic appearance, treatment modalities and prognosis. We report a case of a well-differentiated, lepidic predominant adenocarcinoma arising in association with PT.

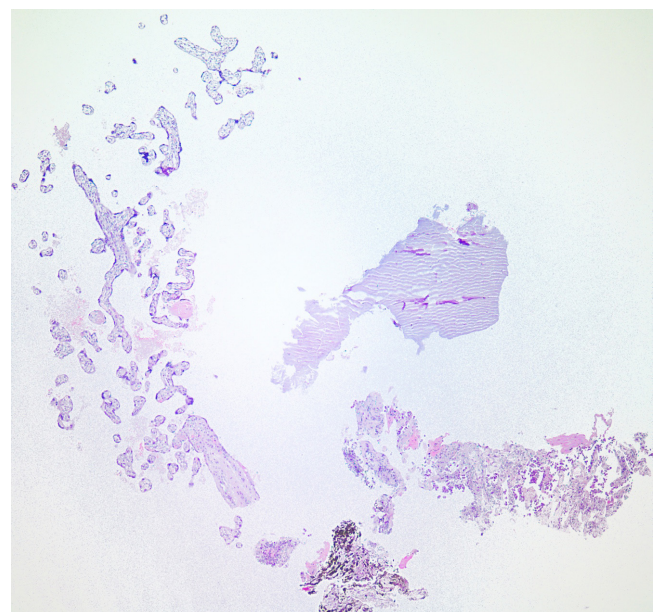
## CASE REPORT

A 67-year-old African American female with a past medical history of hypertension, diabetes mellitus, chronic obstructive pulmonary disease with a smoking history of half pack per day for 17 years, seizure disorder, chronic liver disease due to hepatitis C, multiple GI bleeds and substance abuse (marijuana, crack cocaine and heroin) presented to the emergency department with shortness of breath. On examination patient had decreased breath sounds bilaterally with poor inspiratory effort, hepatomegaly and dry mucous membranes. Point-of-care glucose was noted to be 512 mg/dl (NR: 70-199 mg/dl) and oxygen saturation was 87% (NR: 90-100%) on room air. On laboratory investigations, she was found to be severely anemic with hemoglobin of 7.0 g/dl (NR: 12-16 g/dl) and had hypophosphatemia. A chest x-ray revealed a vague mass-like opacity within the right upper lung zone. Since the mass was suspicious for malignancy a CT scan was done, that demonstrated a 6 cm irregularly-shaped right upper lobe mass with ground glass and solid components (Figure 1A and 1B). The lungs were diffusely emphysematous.

A CT-guided core biopsy of this lesion was performed. Biopsy specimen consisted of flecks of tissue 3 × 2 × 1 mm in aggregate, yet it proved diagnostic (Figure 2). Microscopic evaluation revealed proliferation of atypical, non-mucinous, low columnar to hobnail cells with enlarged, hyperchromatic nuclei. These cells lined the pre-existing alveolar septal architecture which showed slight expansion of the interstitium with fibrosis, a pattern referred to as "lepidic" growth pattern. Although these findings were subtle, yet were sufficient to establish a diagnosis of well-differentiated adenocarcinoma (Figure 3A and 3B). More interesting than this, was that the portion of benign lung tissue showed architectural features of placental villi, consistent with pulmonary placental transmogrification (Figure 3C and 3D). Limited by the fact that the specimen was a core biopsy, it could not be determined with certainty

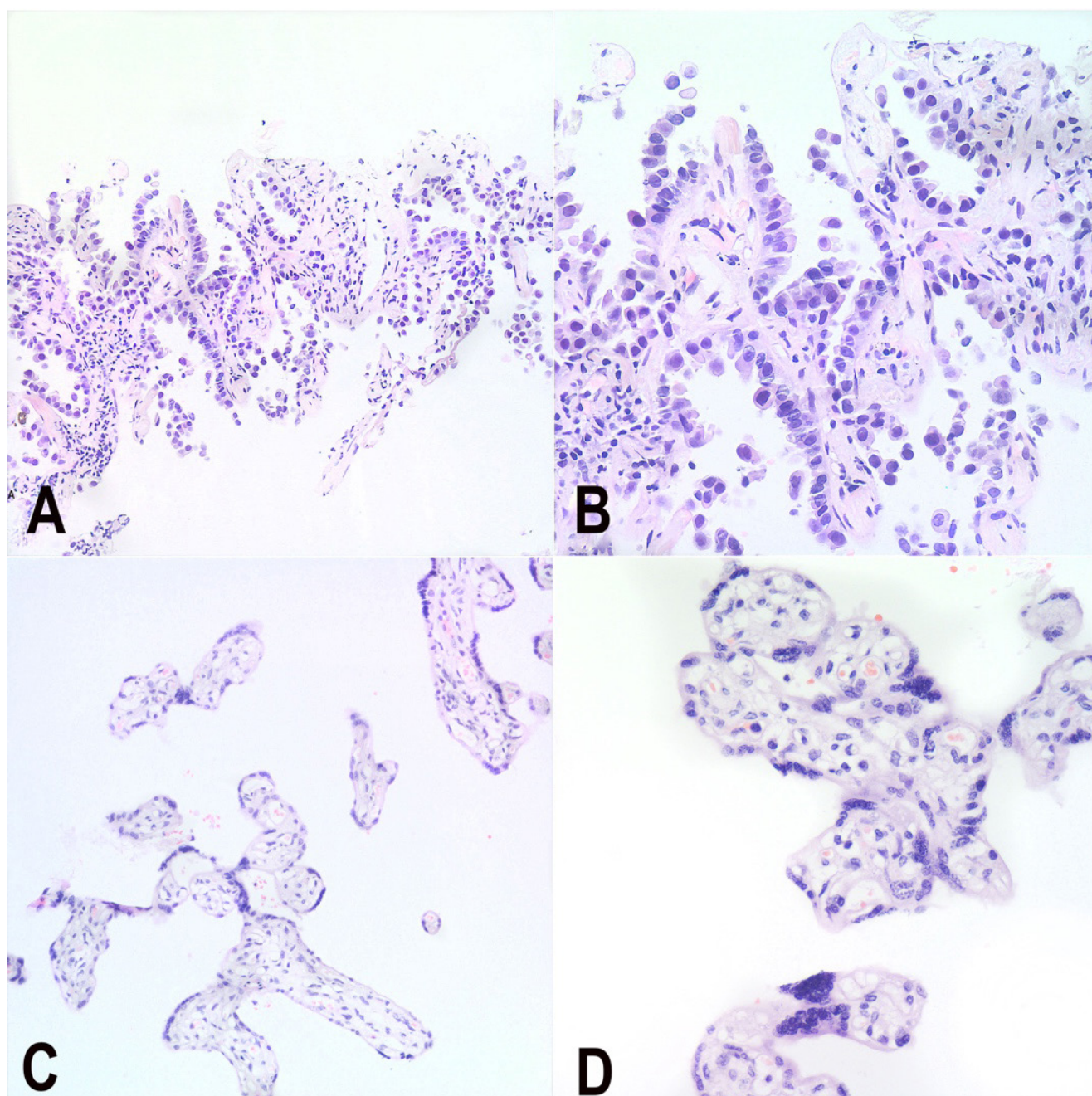


**Figure 1.** Thoracic CT showing right upper lobe mass with solid and ground glass components in a background of diffusely emphysematous lungs. (A - coronal plane; B - axial plane).



**Figure 2.** Low magnification (H&E, 40X) view of the entire specimen showing the fragment involved by well-differentiated adenocarcinoma and classic PT changes.





**Figure 3.** Photomicrograph of the lung biopsy showing a well-differentiated adenocarcinoma (**A** - H&E, 200X; **B** - H&E, 400X) and pulmonary placental transmogrification (**C** - H&E, 200X; **D** - H&E, 400X).

whether the benign PT changes were within the mass or arose simultaneously in the normal adjacent lung parenchyma.

## DISCUSSION

Pulmonary placental transmogrification (PT) is a histologic diagnosis, characterized by papillary projections and placental structures with myxoid, lipomatous and edematous changes; minimal inflammatory infiltrate and lack of pulmonary fibrosis.

PT is predominantly observed in males in the 2<sup>nd</sup> to the 5<sup>th</sup> decade of life. The youngest reported case was a 14-year-old boy with involvement of 2 lobes.<sup>7</sup> The few cases that are reported in the literature have a wide geographical distribution with cases from North America, Germany, Japan, Korea, Portugal and India. Some patients had history of smoking; however, not enough data is available to prove an association with smoking if there is any.

Clinically, the patients may or may not be symptomatic. PT usually presents as bullous

emphysematous disease resulting in dyspnea, chronic obstructive pulmonary disease, bronchopneumonia, and respiratory distress.<sup>2-11</sup> It can also present as tension pneumothorax,<sup>12</sup> solitary lung nodule<sup>13</sup> and occasionally as incidental mass discovered by radiography.<sup>1,11</sup> There is no predilection with respect to lung laterality or lobe.<sup>5</sup>

Pathogenesis of PT is poorly understood. As most of the reported cases of PT are associated with bullous disease, most researchers believe that PT either develops from bullous emphysema or is a reaction to it.<sup>2-4,11</sup> Others believe that PT may be related to lymph-vascular malformation, owing to the frequent presence of lymphatic and dilated vascular channels within the stroma of PT.<sup>3,4</sup> Yet others are of the opinion that PT is an independent lesion, possibly of congenital hamartomatous origin.

Our patient certainly had underlying emphysema, and PT morphology was classic, however, dilated vascular or lymphatic channels were not observed and due to limited core biopsy material, not enough tissue was available for vascular or lymphatic immunohistochemical markers. There was no radiologic or morphologic evidence of a hamartomatous lesion.

Xu et al.<sup>5</sup> proposed that PT is associated with pulmonary fibrochondromatous hamartomas with epidemiology, morphology and pathogenic mechanism possibly different from PT associated with bullous emphysema (Table 1). In one of the largest studies on PT to date, Xu et al.<sup>5</sup> tried to investigate the pathogenesis of PT. By evaluating the immunohistochemical profile of lining epithelium of PT, they proposed that the lining epithelium of PT is respiratory in origin and that the exaggerated proliferation of lining epithelial cells results in placental villi like structures.

In a retrospective study of 103 cases of pulmonary hamartoma and 410 cases of emphysema, Ortiz et al.<sup>14</sup> found PT in 3 cases, of which 1 was associated with hamartoma and 2 were associated with emphysema. All 3 patients were male with ages 55, 54 and 61 years, and there was no difference in the morphology of the 3 cases contradicting to the proposal of Xu et al.<sup>5</sup>

Cavazza et al.<sup>15</sup> proposed that undifferentiated clear cells in the stroma of PT may be involved in the pathogenesis of the disease. This hypothesis, however, like many others is limited due to demonstration in just 2 reported cases.

Apart from the current report, only one other case<sup>6</sup> was reported in the English literature in which PT was associated with lung adenocarcinoma. Therefore no one has investigated into any possible relationship between PT and carcinoma.

Radiologic appearance of PT is dependent mainly upon the clinical presentation and whether it is associated with bullous emphysema or hamartoma. Kim et al.<sup>16</sup> classified the radiologic appearance of PT into three distinct patterns: (i) bullous emphysema being the most common; (ii) a mixed pattern of cystic lesion and nodule; and (iii) the rare solitary nodule pattern. When a solitary nodule is identified, the radiographic appearance may or may not be typical of a hamartoma.<sup>5,17</sup> PT can also present with typical clinical and radiographic appearance of tension pneumothorax owing to the rupture of bullae.<sup>12,18</sup>

The gross appearance varies with the disease process associated i.e. bullous emphysema or hamartoma. Those associated with bullous emphysema have cystic appearance with papillary projections while those associated with hamartomas are usually well circumscribed with tan-white, rubbery cut surfaces.

**Table 1.** Epidemiology, morphology and pathogenesis of PT

PT associated with bullous emphysema	PT associated with pulmonary hamartoma
Predominantly males during 2 <sup>nd</sup> to 5 <sup>th</sup> decade of life.	Relatively older asymptomatic patients. No gender predilection.
Placentoid structures with prominent lymph-vascular proliferation and dilation.	Placentoid structures with prominent fibroadipose stroma.
Reaction to emphysema / lymph-vascular malformation.	Exaggerated proliferation of lining epithelial cells / congenital hamartomatous origin.

Microscopically PT is composed of immature placental villi in a myxoid or edematous stroma. The stroma is composed of lymph-vascular channels,<sup>3,4</sup> fibroadipose tissue,<sup>5</sup> interstitial clear cells<sup>15</sup> and in rare instances the adipose tissue comprises the major bulk of the stroma.<sup>10</sup>

PT is a benign lesion and surgery is usually curative. Brevetti et al.<sup>19</sup> favored minimal resection and avoidance of lobectomy. This approach of minimal resection, however, is dependent on extent of underlying bullous disease and size of hamartoma / nodule, and in cases where it is associated with carcinoma (Hano et al.<sup>6</sup> and current case) the extent of surgery is dictated by tumor stage.

As with the treatment, prognosis depends on underlying associated disease process. Recurrence is not known. Limited follow up data is available. 3 patients from experience of Ortiz et al.<sup>14</sup> had a mean follow of 72 months with no evidence of recurrent disease or new tumors in other locations. Another patient reported by Shapiro et al.<sup>20</sup> showed relief of respiratory symptoms following surgery and at 2 year follow up. Our patient was alive and doing well except for complications of her multiple chronic diseases 7 months post diagnosis.

## CONCLUSION

The notion that PT is a benign lesion may not be true anymore. Although most cases are associated with bullous lesions of lung and fibrochondromatous hamartomas, the possibility of adenocarcinoma needs to be ruled out for adequate patient management. Also, since it has been proposed with evidence that PT is due to exuberant proliferation of lining epithelial cells, studies need to be carried out to confirm if PT represents an intermediate stage in progression of benign lesions to carcinoma.

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**Author contributions:** All authors have significantly contributed, and are in agreement with the content of the manuscript. Hamza A designed and wrote the manuscript after gathering all the required information. Khawar S did the literature search and made valuable additions to the discussion. Alrajjal A took the pictures and proof read the manuscript. Khurram MS, Ibrar W and Salehi S gathered relevant clinical information, follow up data and contacted radiology. Qu H was the staff pathologist. He proof read the manuscript and provided valuable input to improve it.

**Conflict of Interest:** None

**Financial support:** None

**Submitted on:** June 28<sup>th</sup>, 2017

**Accepted on:** August 8<sup>th</sup>, 2017

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