



Glands in Pleura-Not Always a Malignancy

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Abstract

Normal visceral and parietal pleura contain collagen, elastin fibers, lymphatics, small nerves, and blood vessels and is lined by a monolayer of mesothelium. The presence of epithelial cells in pleural tissue is a concern for a malignant process. We report a case of a 76 year old African American female, presenting with complaint of bleeding per rectum. The computed topography (CT) scan of the abdomen and pelvis showed rectosigmoid wall thickening, a large fluid attenuated mass within the pelvis and a right middle lobe lung nodule. Image guided drainage of the pelvic mass revealed neutrophils and gram negative rods but no evidence of malignancy. Colonoscopy with biopsy of the sigmoid mass revealed invasive moderately differentiated colonic adenocarcinoma. Fine needle aspiration (FNA) of the lung nodule showed clusters of malignant cells with rare acinar configuration and intracytoplasmic mucin. The tumor cells were positive for TTF-1 and CK7 and negative for CK20; these findings were consistent with primary lung adenocarcinoma. The core needle biopsy of the lung nodule did not show evidence of carcinoma. A well-defined cluster of benign epithelial cells with glandular configuration and a separate gland lined by ciliated columnar epithelium were identified in pleura. These benign glands expressed CK7 and TTF-1. The benign mesothelial cells lining the pleura were positive for CK5 and CK7. This case study highlights the importance of recognizing this benign condition, especially in patients with co-existing malignancy in order to avoid a false positive diagnosis of malignancy involving pleura.

Keywords: Pleura; Epithelial inclusion; Mesothelium; Lung adenocarcinoma

Introduction

The normal constituent of pleura is fibrous connective tissue composed of mainly elastic and collagen fibers, along with lymphatic, nerves and blood vessels. The lining of this connective tissue is single layer of mesothelium. A small amount of serous fluid is normally present between the parietal and visceral layers of pleura. Epithelial cells do not constitute normal component of pleura; thus, their presence raises the possibility of malignancy. We report a case of 76 year old African American female who was diagnosed with synchronous primary colon adenocarcinoma and primary adenocarcinoma of the right lung. The benign epithelial inclusions lined by columnar epithelium with glandular configuration were identified in the pleura during biopsy of the right lung nodule. This case study highlights that the finding of epithelial cells within the pleura does not always indicate metastasis, extension of primary lung carcinoma, primary mesothelioma, or endometriosis.

Case Presentation

We report a case of a 76 year old African American female, presenting with rectal bleeding. The computed topography (CT) scan of the abdomen and pelvis showed rectosigmoid wall thickening, a large fluid attenuated pelvic mass, and a right middle lobe lung nodule (Figure 1,2). Image guided drainage of the pelvic mass revealed neutrophils and gram negative rods but no evidence of malignancy. The patient was started on broad spectrum antibiotics. Colonoscopy with sigmoid mass biopsy revealed invasive moderately differentiated colonic adenocarcinoma. CT guided fine needle aspiration (FNA) and biopsy of the lung nodule was performed. FNA showed clusters of malignant cells with rare acinar configuration and intracytoplasmic mucin. The tumor cells were positive for TTF-1 and CK7 and negative for CK20, consistent with primary lung adenocarcinoma. The biopsy of the lung nodule did not show carcinoma in multiple levels. A well-defined cluster of benign epithelial cells with glandular configuration and a separate gland lined by ciliated columnar epithelium were identified in the pleura (Figure 3,4); these bland-appearing cells expressed CK7 and TTF-1 (Figure 5,6). The benign mesothelial cells lining the pleura were positive for CK5 (Figure 7) and CK7.

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Figure 1: CT scan showing right middle lobe lung nodule: Blue arrows outline the mass.

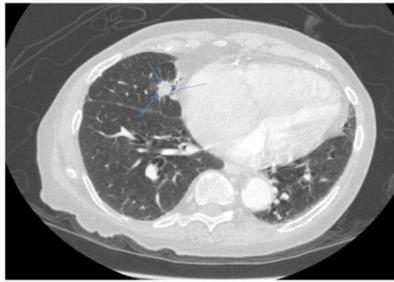


Figure 2: CT scan showing right middle lobe lung nodule: Blue arrows outline the mass.

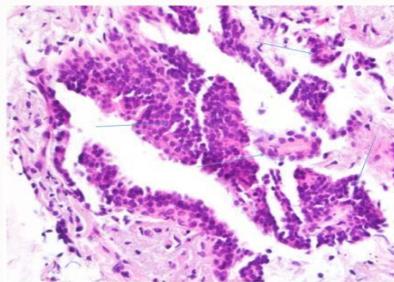


Figure 3: Benign epithelial cells with gland formation, H & E (x400); highlighted by blue arrows.

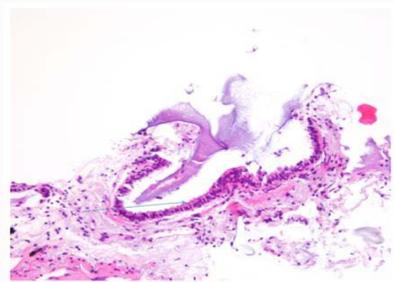


Figure 4: Benign glands lined with ciliated columnar epithelium, H & E (x200); highlighted by blue arrow.

Discussion

Histological finding of glands within pleura is concerning for the presence of metastasis, advanced primary lung adenocarcinoma, or primary mesothelioma since pleura normally consists of connective tissue with interspersed nerves, lymphatics and blood vessels and a lining of mesothelial cells. The most common type of malignancy involving the pleura is adenocarcinoma characterized by the presence of malignant glands in the pleura. It is often accompanied with

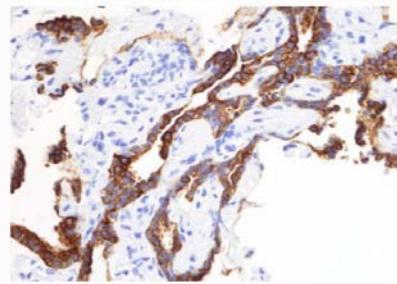


Figure 5: Benign glands express CK7 immunostain, H & E (x200).

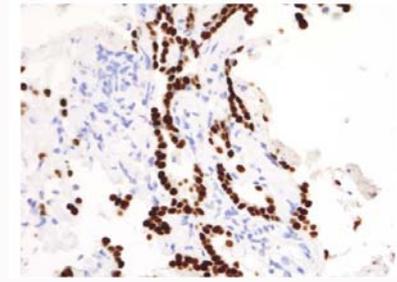


Figure 6: Benign glands express TTF-1 immunostain, H & E (x200).

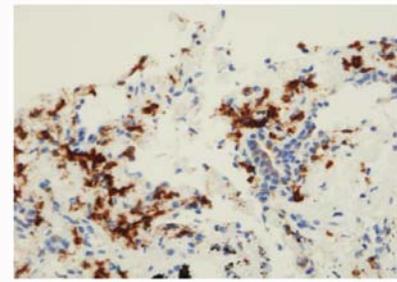


Figure 7: Benign mesothelial cells express CK5 immunostain, H & E (x200).

malignant pleural effusion and dyspnea. The most common causes of malignant pleural effusions include primary lung adenocarcinoma (35%), metastasis from breast carcinoma in females (23%) and lymphoma (10%) [1-3]. The metastasis from gastrointestinal tract and gynaecological tract are rare in pleura. Although benign causes of glands in pleura are rare, endometriosis (endometrial implants in pleura) is the most significant cause [4,5].

Epithelial and/or nonepithelial inclusions are most commonly reported in lymph nodes [6-12]. Patients with endometriosis may have endometrial glands in pelvic and para aortic lymph nodes [13]. Ectopic glands are relatively rare above the diaphragm, most commonly found in cervical and axillary lymph nodes. Ectopic glandular breast tissue and cystic structures lined by squamous epithelium are found in axillary lymph nodes [14,15]. Ectopic thyroid tissue is found occasionally in cervical lymph nodes. Among nonepithelial implants, the most common are mesothelial inclusions in mediastinal lymph nodes [16,17] peritoneum [17,18] as well as below the diaphragm in abdominal lymph nodes. Peritoneal endometriosis and surface epithelial inclusions of ovary are some examples of extranodal glandular inclusions.

There are several theories for the explanation of ectopic glands. Among lymph node implants, one theory proposes maldevelopment at the embryonic level when glandular cells were entrapped within

lymph nodes and survived. The other possibility may be the mobilization of glands from their original site via lymphatics to the lymph nodes. The cause of mobilization may be inflammation or infection at the original site as seen in endometriosis where the inflammation due to menstruation dislodges the glands and they are transported via lymphatics to regional and/or distant lymph nodes. These two theories also hold true for ectopic mesothelial inclusions [19,20]. Epithelial implants on mesothelium can also be explained by metaplasia. Embryonic coelomic and/or subcoelomic mesenchyme undergoes metaplastic change to mesothelium. Chronic inflammation may play a role in it. Regardless of the cause, these implants usually raise the suspicion for malignancy but the benign causes of these ectopic glands must be ruled out. This is especially important if the patient has a history of malignancy as lung is a common site of metastasis or coexisting/history of primary lung adenocarcinoma.

We expect to see elastic and collagen fibres in pleura, along with nerves, blood vessels and lymphatics, lined by a single layer of mesothelium. Diagnosis of malignant glands in pleura makes lung carcinoma inoperable and in the case of distant metastasis indicates stage IV. This case study suggests that the false positive diagnosis of pleural malignancy should be avoided and presence of benign glands in pleura must be identified based on morphology.

Conclusion

There is no specific immunostain to distinguish benign glands from primary lung adenocarcinoma in pleura. Careful evaluation of morphology is the key to establish the diagnosis. This case study highlights the importance of considering the presence of benign glands in pleura in order to avoid the false positive diagnosis of advanced malignancy or stage IV metastatic disease from nonpulmonary cancers. This might be particularly challenging in patients with synchronous lung and non-pulmonary carcinoma.

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