Exceptional Site of Metastatic Adenocarcinoma of the Lung

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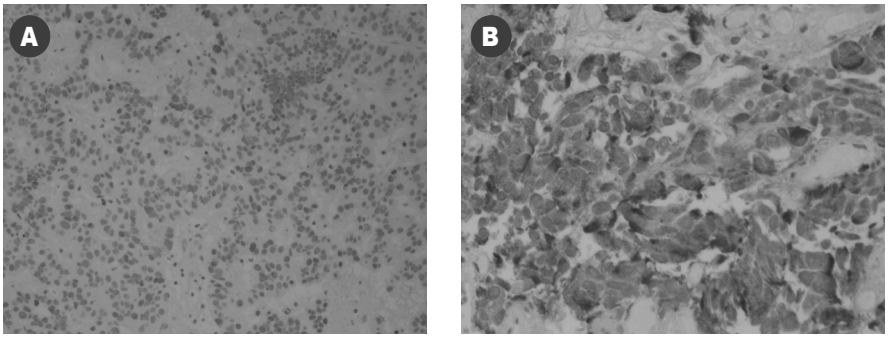
The urinary bladder may become a landing site for metastasis from various distant primaries. The most common primary tumors to metastasize to the bladder are prostate, ovary, uterus, breast, kidney and stomach. Other less frequent primaries are malignant melanoma, leukemia and lymphoma [1]. Adenocarcinoma of the urinary bladder accounts for less than 2% of all bladder tumors, rarely as a primary tumor and more commonly as a result of direct invasion from the surrounding organs. To the best of our knowledge. We report to the best of our knowledge, the first case of lung adenocarcinoma metastasis to the urinary bladder.

Patient Description

A 75 year old man underwent left lower lobectomy for stage Ib moderately differentiated adenocarcinoma of the lung 3 years after right lower lobectomy, with the same histology. Two years later he underwent open prostatectomy. No gross pathology of the urinary bladder was reported at the time of the operation.

Six months later, computerized tomography demonstrated thickening of the urinary bladder wall with no evidence of metastatic spread in a metastatic workup. The patient was asymptomatic and no hematuria was noted. Cystoscopy and urinary bladder biopsy confirmed the diagnosis of metastatic adenocarcinoma, moderately differentiated, that was consistent with the findings of the primary lung tumor. Both specimens were positive for the following immunostains: cytokeratin 7, thyroid transcription factor-1 [Figure A], surfactant protein-B [Figure B], and carcinoembryonic antigen. Chemotherapy was recommended but the patient refused. He underwent two sessions of palliative radiotherapy to the pelvic region (600 cGy each) for pain relief. Eight months later the patient died due to disseminated metastatic disease. An autopsy was not performed.



Histologic demonstration of urinary bladder wall biopsy, mucosa involved by metastatic lung adenocarcinoma confirmed by immunopositivity for **[A]** TTF-1 (x 10), and **[B]** surfactant protein-B (x 1).

Comment

In the United States lung cancer is the leading cause of cancer death in both men and women and in all races. Of all lung cancer types, only 15% of patients have local disease at diagnosis, 25% have disease spread to regional lymph nodes, and 60% have distant metastases. The various cell types have different natural histories and responses to therapy. At presentation, the small-cell type carcinomas have usually already spread such that surgery is unlikely to be curative, and they are managed primarily by chemotherapy with or without radiotherapy. In contrast, non-small-cell cancers (epidermoid, adenocarcinoma, large cell carcinoma, bronchioloalveolar carcinoma, and mixed versions of these) are found to be localized at the time of presentation and may be cured with either surgery or radiotherapy [2].

Rarely, adenocarcinoma of the urinary bladder may arise from primary urothelial mutation. More commonly, bladder adenocarcinoma arises from local invasion from adjacent organs, such as: prostate, urachus, colon, cervix, ovary and endometrium [3]. Adenocarcinomas originating from different organs have a similar histologic appearance. Therefore, locating the tissue's site of origin is a diagnostic challenge. Tumor immunohistochemical staining profile may be helpful in determining the primary origin of the neoplasm. With the exception of prostate-specific antigen and thyroglobulin, no single immunohistochemical marker is entirely site-specific [4].

Many techniques have been developed to determine the site of origin of tumors, and a panel of tumor markers may helpful to differentiate the site. TTF-1 was shown to be positive in adenocarcinoma originating from the lung, but negative in non-pulmonary adenocarcinoma. TTF-1 is a highly specific marker for primary lung adenocarcinomas, and is included in a panel of antibodies for the differential diagnosis between primary and metastatic adenocarcinomas of the lung [5]. Therefore, in patients presenting with

TTF-1 = thyroid transcription factor-1

possible metastatic adenocarcinoma of an unknown primary site, TTF-1 is used to prove or exclude the pulmonary origin.

Recognizing an uncommon location of lung tumor metastasis is crucial for an appropriate follow-up and management mainly in cases of a single metastasis. The present report highlights the possibility that adenocarcinoma found in the urinary bladder may be a metastasis originating from a primary pulmonary malignancy. In the event of urinary symptoms or hematuria, the physician should consider including pelvic CT in the metastatic workup in lung adenocarcinoma. Bladder wall findings on imaging studies in patients with lung cancer may warrant a bladder biopsy, and if found to be a single metastasis, surgical removal should be considered.

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Capsule

Lymph node tracks

Lymph nodes are crucial staging posts from which immune responses are launched throughout the body. To achieve this, naive lymphocytes must locate and respond to their specific antigens, which are relatively scarce. The active migratory tendency of lymphocytes helps to achieve this, and the structural organization of the lymph node itself also improves the chances of antigen encounter. Bajenoff et al. find that organized networks of stromal cells provide trackways for lymphocytes to travel around lymph nodes. With a combination of microscopy and real-time intravital imaging, T cells were seen to enter the lymph node paracortex by interacting with fibroblastic reticular cells (FRCs). Inside the lymph node, the FRC formed a three-dimensional network along which a large proportion of T cells could crawl. Antigen-presenting dendritic cells also associated with the FRC network, which is consistent with the idea that this would optimize the rate of encounter between the two types of cell. B cells were also seen to move along the FRC tracks within the paracortex, transferring to a similar network of dendritic cells once they had entered the lymph node follicle. It will now be interesting to elucidate the molecular cues that govern migration along these cellular highways and byways.

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Capsule

IgG stimulate phagocytosis

Phagocytes engulf microbes by enveloping them in a patch of membrane that invaginates to form a phagosome; this then fuses with a lysosome, which contributes the enzymes that destroy the internalized pathogen. Trivedi and co-authors exposed mouse macrophages to latex beads to investigate how immunoglobulin G (IgG), which stimulates phagocytosis, might promote the latter stages of this process. When macrophages incubated with beads coated with either bovine serum albumin or IgG at 15°C (allowing bead engulfment but not fusion) were warmed to 37°C, the association of IgG-coated beads with phagolysosomes was faster than that of the albumin-coated beads. Cytosol from cells transfected with human Fcgamma receptor (making them phagocytic) and incubated with IgG beads promoted phagosomelysosome interactions more effectively than that from unexposed cells, an effect enhanced by transfection of the cells with protein kinase C (PKC). Inhibition of PKC abolished the stimulatory effect of IgG, and further pharmacological analysis indicated that IgG stimulated the actin-dependent tethering or docking (or both) of phagosomes and lysosomes. Thus, facilitation of phagosome-lysosome attachment by way of PKC appears to be one mechanism whereby IgG signaling stimulates phagocytosis.

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