Minute Pulmonary Meningothelial-like Nodule Syndrome

Frank Schneider1; Lewis J. Wessellius2; Henry D. Tazelaar.2 1Duke University Medical Center; 2Mayo Clinic, Scottsdale, Ariz.

Minute pulmonary meningothelial-like nodules (MPMNs) are small, cellular structures of unknown origin that are frequently identified as incidental findings in lung biopsies. Once thought to be chemodectomas because of their association with vessels, MPMNs’ lack of endocrine granules and nerve fibers helps to dispel this notion. The current designation was prompted by MPMNs’ immunohistochemical and ultrastructural features of meningothelial cells; yet, the histogenesis of MPMNs remains unclear. The presence of more than 3 MPMNs in a patient, as identified by imaging and subsequent histologic examination, has been referred to as MPMN-omatosis. Whereas isolated nodules are thought to be of a reactive nature, recent studies suggest that MPMN-omatosis might represent the transition between a reactive and neoplastic proliferation. This rare syndrome is usually asymptomatic. We describe a 69-year-old woman nonsmoker who had a history of asthma for more than 10 years. She presented with a chronic cough and shortness of breath, which did not improve despite intensification of treatment. Imaging studies showed innumerable bilateral small ground-glass opacities in the periphery of the lung. Open biopsies demonstrated multiple MPMNs in each of the 3 lung wedges. In addition, constriction of airways by submucosal fibrosis consistent with obliterative bronchiolitis was found, likely contributing to the patient’s symptoms. After 6 months of steroid treatment, the patient showed neither clinical improvement nor deterioration of her symptoms. It is unclear whether the MPMNs were causally related to the patient’s symptoms or whether they were innocent bystanders.

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Metastatic Carcinoma of the Lung to Male Breast or Anterior Chest Wall on Fine-Needle Aspiration: A Review of 36 Cases

Monica I. Ruiz1; Rodolfo J. Nudelman1; Linda K. Green.2 1Baylor College of Medicine, Houston, Tex; 2Veterans Affairs Medical Center & Baylor College of Medicine, Houston, Tex.

Context: Carcinoma of the breast is uncommon in men. When a man presents with a breast or anterior chest mass, a primary tumor must be distinguished from a soft tissue metastases. Lung cancer is the most common tumor metastasizing to soft tissue. It may be difficult to distinguish from a primary tumor. We designed a study to examine the incidence, characteristics and features of primary breast cancer and metastatic lung cancer to the male breast on fine-needle aspiration (FNA).

Design: We reviewed our files dating from 1986 to 2007 for primary and metastatic carcinomas of the male breast diagnosed by FNA. Each case was reviewed for tumor location, cell type, immunohistochemistry, electron microscopy, clinical history, radiographic findings, and clinical course.

Results: There were 36 metastatic lung carcinomas: 12 (33%) adenocarcinomas, 12 (33%) non–small cell carcinomas, 8 (22%) squamous cell carcinomas, and 4 (11%) small cell carcinomas. There were 10 primary breast carcinomas. The most important aid in arriving at the correct diagnosis was computed tomography and magnetic resonance imaging of the thorax.

Conclusions: In our patient population, metastatic lung carcinoma to the male breast or chest was much more common than primary breast carcinoma. On FNA, a poorly differentiated carcinoma may be primary or metastatic to the breast. Estrogen and progesterone receptors may be seen in both lung and breast cancer. Immunohistochemistry is variable and may not always distinguish a breast primary from a lung primary.
A search for a lung primary should always be considered in a male with a breast or chest mass malignancy.

Metastatic Lung Carcinoma to the Stomach Masquerading as a Primary Gastric Malignancy: A Review of 64 Cases

Rodolfo J. Nuidelman1; Monica I. Ruiz2; Linda K. Green,23 Baylor College of Medicine, Houston, Tex.; Veterans Affairs Medical Center & Baylor College of Medicine, Houston, Tex.

Context: Rarely will lung tumors metastasize to the stomach and present as bleeding ulcerated masses. They may be difficult to distinguish from primary gastric malignancies. Differentiation between the two is crucial for therapeutic management.

Design: The files of our institution from the last 40 years were searched for surgical-, necropsy-, and cytology-proven metastases to the stomach. The tumors proven to be lung in origin by clinical, necropsy, or ancillary tests were selected, and the clinical findings, upper gastrointestinal endoscopy findings, radiographic data, histology, and ancillary tests were reviewed for each case.

Results: There were 123 metastases to the stomach with 64 proven lung cancers. The histopathologic types included the following: 27 (42%) adenocarcinomas, 19 (29%) small cell carcinomas, 12 (19%) squamous cell carcinomas, and 6 (9%) large cell carcinomas. The lesions were often volcano-like in appearance. The lack of transformation from the gastric mucosa was a helpful clue. In some cases, immunohistochemistry was valuable.

Conclusions: Lung cancer can present as an ulcerated lesion in the stomach. Lesions with glandular, squamous, and neuroendocrine differentiation all occur in the stomach; therefore, distinction between the two is difficult. If a lesion has an uncharacteristic endoscopic or gross appearance, a metastatic lesion should be entertained. Immunohistochemistry may be helpful in distinguishing a metastatic lesion from a lung primaries.

Superoxide Dismutase Polymorphisms and Expression in Idiopathic Pulmonary Fibrosis

Patrizia Morbini; Simona Inghilleri; Ilaria Campo; Chiara Villa; Tiberio Oggionni; Maurizio Luisetti.11 Università di Pavia; 2Fondazione IRCCS Policlinico S. Matteo.

Context: Superoxide dismutases (SOD), genetic variants associated with reduced scavenger activity and/or stability, could play a role in the development of pulmonary fibrosis mediated by increased oxidative stress.

Design: The Arg213Gly polymorphism in EcSOD and the Ala16Val polymorphism in MnSOD were investigated in 70 patients with a clinical and histopathologic diagnosis of idiopathic pulmonary fibrosis (IPF), in 38 different patients with confirmed histopathologic diagnosis of usual interstitial pneumonia (UIP) according to ATS/ERS criteria, and in 295 normal subjects. EcSOD and MnSOD expression were assessed immunohistochemically in UIP samples.

Results: MnSOD Ala16Val polymorphism was significantly more frequent in histologically confirmed UIP cases (heterozygous, 38%; homozygous, 25%; P < .05). No difference was found between controls and clinical IPF cases. Arg213Gly EcSOD polymorphism distribution did not significantly differ in the 3 groups. Both MnSOD and EcSOD were moderately expressed in type 1 pneumocytes, airway epithelia, macrophages, endothelia, and vesel miocytes. Fibroblastic foci were negative for both enzymes, while overlying reactive pneumocytes were intensely positive for EcSOD. No difference in staining was observed in cases with or without polymorphisms.

Conclusions: Molecular investigations documented the significant association of a MnSOD genetic variant associated with reduced antioxidant activity in a series of histologically confirmed UIP cases, but not in a series of clinically diagnosed IPF cases. This result stresses the importance of basing molecular association studies of UIP on carefully selected patient series. Negative antioxidant activity in fibroblastic foci, together with the molecular results, suggests that foci may be the site of increased oxidative stress.

Gliomangiomyopericytoma Arising in a Diffuse and Nodular Myofibromatosis-like Process in the Lung With Vascular Endothelial Growth Factor Receptor 3 Expression

Ulrike M. Gruber-Moesenbacher;1 Alicia Morresi-Hauf;2 Helmut H. Popper.3 Teaching Hospital Feldkirch; Fachkliniken Asklepios; 3Medical University of Graz.

Tumors of the perivascular system, glomus-tumor, hemangiopericytoma, and PEComas have been reported in the lung. We present a large tumor arising in a nodular and diffuse growing perivascular process with focal myoid and hemangiopericytomatos differentiation for which we propose the term gliomangiomyopericytoma. A 46-year-old woman presented with a mediastinal mass and pulmonary nodular densities on chest x-ray, which were interpreted as Langerhans cell histiocytosis. After 5 years, a large lung tumor developed. Both lungs contained nodules composed of small spindle cells with inconspicuous oval nuclei and indistinct borders of the slightly eosinophilic to clear cytoplasm growing around capillaries in a hemangiopericytoma-like pattern. The large tumor consisted of spindle and epithelioid cells, increased nuclear polymorphism, some multinucleated giant cells, and no necrosis. Immunohistochemistry of the tumor and diffuse proliferation were negative for pancytokeratin, thyroid transcription factor 1, surfactant apoprotein A, neuron-specific enolase, S100 protein, CD56, leukocyte common antigen, CD68, desmin, estrogen receptor, progesterone receptor, vascular endothelial growth factor (VEGF), CD31, cAMP kinase-α, and hamartin, but were positive for vimentin, VEGF receptor 3, endothelium kinase Tie2, tuberin, and focally for smooth muscle actin and CD34. Exclusively in the large tumor, PEComa-like cells expressed HMB-45; 1 to 5% of tumor cells were positive for MIB-1. In the differential diagnosis, lymphangioleiomyomatosis, PEComa, hemangioendothelioma, hemangiopericytoma, histiocytic tumors, and solitary fibrous tumor were considered but could be excluded based on immunohistochemistry. Due to the loss of hamartin, the reticulonodular proliferative process clearly belongs to the spectrum of perivascular tuberous sclerosis complex–related diseases. Hormone therapy with Letrozol and chemomotherapy with doxorubicin were unsuccessful. Bevacizumab and Gemcitabine as second-line therapy stopped progression and resulted in shrinkage of the large nodules.

Hodgkin Lymphoma Presenting as Multiple Cavitary Pulmonary Nodules


Context: Hodgkin lymphoma (HL) involving the lung is uncommon. It may present in a variety of radiographic and histologic patterns, including solid, necrotizing, and cavitory lesions with or without associated mediastinal adenopathy. Histologically, it may masquerade as a necrotizing, inflammatory, or granulomatous reaction and may be misdiagnosed as an infectious process. HL should be considered in the differential diagnosis of pulmonary lesions, particularly those associated with adenopathy.

Design: We report a case of an 18-year-old man presenting with cough, fever, multiple cavitary pulmonary nodules, pleural effusion, and mediastinal adenopathy.

Results: Bronchoalveolar lavage and pleural fluid cytology revealed neutrophilic inflammation. Initial biopsies of both a mediastinal lymph node and lung nodule showed necrotizing, neutrophilic inflammation consistent with abscess. An infectious etiology was the working diagnosis, and multiple cultures and histopathology studies were performed, all of which were negative. The pulmonary nodules increased with enlargement and coalescence. Repeat pulmonary biopsy revealed a marked necrotizing inflammatory reaction with scattered CD30-positive Reed-Sternberg cells and focal areas of fibrosis, consistent with HL, nodular sclerosis type.

Conclusions: HL may involve the lung as a primary alone or more commonly, in association with mediastinal disease. The histology is variable and often masquerades as an inflammatory reaction, which may be misdiagnosed as a presumed infectious process, leading to delay in treatment and progression of disease. HL should be considered in the differential diagnosis of necrotizing, inflammatory, and granulomatous pulmonary lesions.

Expression of Angiostatin Receptor Annexin II in Lung Squamous Cell Carcinoma: A Potential New Therapeutic Target

Kai Zhang; Fan Lin; Jianhui Shi; Ce Zhang. Geisinger Medical Laboratory, Geisinger Health System, Danville, Pa.

We reviewed a total of 44 lung resection cases of lung non-small cell carcinoma, including G2, G3 squamous cell carcinoma (SCC) (n = 20) and G2, G3 adenocarcinoma (ACA) (n = 24). Immunostain (IHC) was done using monoclonal anti-annexin II (ANX2) antibody. Visible cytoplasmic and/or membranous staining was considered as positive staining. The intensity was graded subjectively as weak, intermediate or strong. The distribution was recorded as negative (no staining), 1+ (<25%), 2+ (26%–50%), 3+ (51%–75%), or 4+ (>75%). Western blotting was done on 1 G2 SCC, 1 G2 ACA, benign lung tissues, and a known positive control. β-Actin was used for checking equal loading. The results were as follows: In all 44 benign lung tissues, no cells were positive for ANX2 by IHC.
Positive staining for ANX2 was observed in 19 (95%) of 20 SCCs, and most cases showed strong or moderate staining intensity, with 55% of cases showing 3+ or 4+ staining. In contrast, only 1 case (of 24; 4%) of ACA showed very focal and weak (1+) staining intensity. In addition, the cells located at the basal layers of some of the benign bronchioles near SCCs expressed ANX2, which was not observed in the cases of ACA. Western blotting showed a positive band at 38 kd on SCC and on the positive control sample but not on benign lung tissue and ACA. The Western blotting results were supported immunohistochemical findings. In conclusion, the novel findings of expression of ANX2 on lung SCC provide a basis for a potential new therapeutic target, a useful marker for distinction between SCC and ACA, and a potential role in the pathogenesis of lung SCC.

Metastatic Lung Adenocarcinoma of Fetal Type to the Ovaries

Mostafa M. Fraig. Medical University of South Carolina, Charleston.

This case concerns a 37-year-old woman with a 5-year pack history of smoking who presented with a 7.5-cm well-circumscribed mass in the left lower lobe. Abdominal computed tomography scan performed at the time of presentation revealed no abdominal or pelvic masses. An initial biopsy was reported as carcinoid tumor. A lobectomy was performed, and the tumor was diagnosed as pulmonary blastoma. The woman experienced recurrences in the opposite lung as well as in bone. Six years later, she was found to have a 10-cm ovarian mass that was positive for adenocarci-

noma. Because of morphologic similarities between lung adenocarcinoma of fetal type and endometrioid adenocarcinoma, thyroid transcription factor 1 immunostains were performed on both tumors and proved to be positive in both. The differential diagnosis of both tumors and a review of the literature on the metastatic potential of the well-differentiated fetal adenocarcinoma will be presented.

Solitary Intrapulmonary Cystic Lymphangioma

Hiroshi Minato,1 Sachiko Kaji,2 Eriko Kinoshita; Nozomu Kurono; Tak-ayuki Nojima.1 Kanazawa Medical University, Ishikawa, Japan;2 Chiba Cancer Center, Chiba, Japan.

Context: Intrapulmonary lymphangioma rarely presents as a solitary pulmonary lesion, and the abnormal vessels may be capillary, cavernous, or cystic in type. We experienced a case of solitary cystic lymphangioma of the lung and hereby present its clinicopathologic findings.

Design: A 2-month-old male infant was referred to our hospital because of a persistent cough. Chest radiograph showed a large cyst in the right lung. He was born of a full-term, normal delivery. No other lesion was observed extrapulmonary or intrapulmonary.

Results: An excised specimen contained a septate cystic lesion that measured 5.5 x 5.5 x 4.5 cm. The cyst had a small amount of serous fluid, and the inner surface was smooth. Microscopically, the lesion was composed of a large cystic space and interconnected slitlike spaces surrounding bronchovascular islands. The cysts were lined by a monolayer of flat cells and some multinucleated giant cells. Neither significant smooth muscle proliferation nor lymphoid follicles were observed. Immunohistochemically, the lining cells of the cystic lesion were diffusely positive for D2-40, CD34, and CD31, but were negative for AE1/3 and HMB-45. Postoperative course was uneventful. Differential diagnosis of intrapulmonary lymphangioma may include lobar or interstitial emphysema, bronchogenic cyst, congenital cystic adenomatoid malformation, and alveolar adenoma.

Conclusions: Solitary intrapulmonary lymphangioma is a rare, benign, and localized lesion. D2-40 was useful in differentiating it from other diseases and in determining the extent of the lesion.

Extracorporeal Membrane Oxygenation as a Bridge to Lung Transplantation in a Patient With Active Wegener Granulomatosis

Lakshmi Puttagunta; Khalida Nasim; Dale C. Lien; Kenneth C. Stewart; Joanne Honik; Steven S. Caldwell; Justin Weinkauf. University of Alberta, Alberta, Canada.

Context: Lung transplantation is a rare indication in patients with Wegener granulomatosis (WG) with failed medical treatment. Ventilator dependence and extracorporeal membrane oxygenation (ECMO) have traditionally been regarded as relative contraindications to lung transplantation. We report on a patient with WG who was maintained on ECMO until the lung allografts became available and were successfully transplanted.

Design: A 17-year-old adolescent boy was diagnosed with WG based on clinical history, positive c-antineutrophil cytoplasmic antibodies (ANCA), a renal biopsy, and a subsequent lung explant pathology report. Despite rigorous weak (1+) staining with cyclophosphamide, methyl prednisolone, hemodialysis, plasmapheresis, and rituximab, his condition deteriorated, and he developed massive pulmonary hemorrhage and hypoxic respiratory failure. On day 11 of his admission, the patient was started on venoarterial ECMO along with anticoagulation, but with no improvement in his bilateral lung function. After 15 of his hospitalization and was taken off ECMO intraoperatively. He received standard immunosuppressive therapy and continued with intermittent hemodialysis. He subsequently regained nearly normal renal function and his ANCA titer became negative. He is now 550 days post-transplant and is doing well.

Conclusions: To our knowledge, this is the first report of successful use of ECMO as a bridge to lung transplantation.

Diffuse Lymphangiomatosis Mimicking Intestinal Lung Disease

Helmut H. Popper; Jana Polachova. Medical University of Graz.

A 67-year-old woman presented having experienced cough and dyspnea for months. From an x-ray, infection was suspected, and treatment with antibiotics was started. The process worsened. On high-resolution computed tomography, ground glass and consolidation areas were seen. Total body irradiation showed organizing pneumonia. Bronchoalveolar lavage diagnosed a lymphohytic, CD4-dominated, and mildly granulo-
cytic alveolitis. A video-thoracoscopic biopsy was taken. The tissue was processed routinely. Sections were stained with hematoxylin-eosin and Movat. Serial sections were immunostained for CD31, VEGF-C/D, VEGF receptor 3, podoplanin (D2-40). On frozen section, a diffuse complex intestinal lung disease was made, composed of organizing pneumonia and focal intestinal fibrosis resembling usual interstitial pneumonia and nonspecific interstitial pneumonia. However, there was also intestinal edema and several foci of an angiomatoid proliferation. These vessels showed a single layer of endothelia, usually flattened, and a thickened wall composed of thickened connective tissue without a muscle layer. In Movat-stained sections, adjacent veins and arteries were highlighted by their elastic laminae. The angiomatoid proliferation, however, was devoid of any lamina elastic. Immunohistochemical staining for CD31, VEGF-C, podoplanin, and VEGF receptor 3 was performed on the vascular proliferation and were found positive. A diagnosis of diffuse pulmonary lymphangiomatosis was made. Diffuse pulmonary lymphangiomatosis is a rare disorder that usually affects children and young adults. A systemic form (Gorham-Stout syndrome or vanishing bone dis-
ese) can affect lymphatic ducts in bone, mediastinum, soft tissues, and also lungs, liver, and spleen. We present here this rare disease in an adult, combined with complex interstitial pneumonias. No treatment other than transplantation has been successfully applied in isolated pulmonary lymphangiomatosis.

Primary Malignant Melanoma of the Pleura: Report of an Autopsy Case

Toshiaki Kawai; Takayuki Haga; Kuniki Nakanishi.1 National De-

defense Medical College, Tokorozawa, Saitama, Japan; National Higashi Saitama Hospital, Hasuda, Saitama, Japan.

Melanoma metastatizing to the lungs is common, but primary pulmo-

nary or pleural melanoma is extremely rare. We present an autopsy case of malignant melanoma of the pleura in a 49-year-old man. The patient presented with cough and right back pain. On admission to hospital, 2.5 months before he died, the man was found to have an elastic, hard, subcutaneous mass the size of a thumb in the right chest. The large amount of pleural effusion was bloody and was diagnosed cytologically as negative. From fine-needle aspiration cytology, the right chest mass was diagnosed as spindle cell sarcoma. Autopsy showed that a yellow-white tumor primarily located in the right visceral pleura had invaded into the right lung and also into the right thoracic wall and had metastasized into the left lung, visceral pleura, thyroid, and left adrenal. No primary site was found (including skin and other mucous membranes). Histologically, the predominantly spindle cell foci exhibited a fascicular growth pattern with elongated, beefy red cells possessing oval, nuclear pleomorphism and vague nucleoli, accompanied by areas of a nuclear palisading pattern and extensive necrosis. Some nested and epithelioid foci were seen, intermingled with cartilage-like differentiation. Some finely granular brown pigment was present within tumor cells and macrophages. Most of the pigment with Fontana-Masson positive and bleached by potassium permanganate. Immunohistochemical analysis showed the tumor cells to be positive for S100 and focally positive for HMB-45, but...
negative for other markers (including keratin, CAM 5.2, and calretinin). Ultrastructural examination of formalin-fixed wet tissue showed the neoplastic cells had a melanosome-like structure.

Platlet-Derived Growth Factor Receptor β, a Potential Target for Molecular Chemotherapy, Is Expressed in Malignant Mesothelioma

Patrizia Morbini1; Chiara Villa1; Simona Inghilleri2; Camillo Porta2
1University of Pavia; 2Fondazione IRCCS Policlinico S. Matteo.

Context: The synergistic combination of gemcitabine or pemetrexed with tyrosine kinase (TK) inhibitor imatinib mesylate seems to be effective in controlling malignant mesothelioma (MM), both in experimental and in as of yet unpublished clinical settings. Imatinib blocks TK-associated receptors, including c-Kit/CD117 and platlet-derived growth factor receptor β (PDGFR-β), by inhibiting kinase binding with adenosine triphosphate. PDGF autocrine production seems to be relevant in mesothelioma cell growth. Furthermore, one of the most common genetic abnormalities observed in MM involves chromosome 22q13, where the PDGFRβ gene is mapped. PDGFRβ was documented in MM cell cultures, but it has never been investigated in MM tissue samples.

Design: PDGFR-β (Rb-1692, Labvision, Fremont, Calif) and CD117 (A4502, Dako Cytomation, Carpinteria, Calif) expression was investigated immunohistochemically in 138 MM cases and correlated with clinical and tumor data (histological type, patient survival, and type of exposure to asbestos).

Results: One hundred five cases (76%) were moderately or intensely reactive for PDGFR-β; 33 (24%) showed weak or absent immunoreactivity. Consistent expression of CD117 was observed in 16 cases (11.5%), which was never been investigated in MM tissue samples.

Design: PDGFR-β (Rb-1692, Labvision, Fremont, Calif) and CD117 (A4502, Dako Cytomation, Carpinteria, Calif) expression was investigated immunohistochemically in 138 MM cases and correlated with clinical and tumor data (histological type, patient survival, and type of exposure to asbestos).

The Role of c-Kit (CD117)–Positive Mast Cells and Its Ligand (Stem Cell Factor) in Chronic Fibrosing Bronchiolitis Obliterans Including Chemical Exposure: Is There a Potential for Treatment With Imatinib (Gleevec)?

Neil Fuehrer1; Alberto Marchevsky1; Jasheer Jagdarn1
1University of Texas Health Science Center, San Antonio; 2Cedar Sinai Medical Center, Los Angeles, Calif.

Context: In many fibrosing lung diseases, it is not clear what leads to the progression of fibrosis following a remote injury. Immune-mediated progression may be a reason. c-Kit (CD117)–positive mast cells (M cells) have been associated with chronic fibrosing diseases and carry a potential to be treated with imatinib (Gleevec), a tyrosine kinase inhibitor. We evaluate the role of M cells in fibrosis associated with bronchiolitis obliterans (BO).

Design: Four cases of BO (household cleaner exposure, ammonia exposure, idiopathic, and posttransplant) were compared with asthma/emi

Results: M cells were concentrated within the involved subepithelium of small airways in BO (122 cells per mm), unlike asthma/epi

Conclusions: M cells appear to be concentrated in the involved small airways subepithelium in BO, suggesting that early administration of imatinib may be of value in preventing progression to fibrosis.

Abstracts

Malignant Mesothelioma: Guidelines for Pathologic Diagnosis

Aliya N. Hasain1; Alain Borczuk2; Philip T. Cagle2; Andrew Churg3; Thomas V. Colby4; Françoise Galateau-Sallé5; Allen R. Gibbs6; Allen M. Gown7; Samuel P. Hammar8; Thomas Krausz9; Leslie A. Litzky10; Nelson G. Ordonez11; Victor L. Roggli12; William D. Travis13; Mark R. Wick14 1University of Virginia Medical Center; 2Columbia University Medical Center; 3The Methodist Hospital; 4University of British Columbia; 5Mayo Clinic College of Medicine; 6Laboratoire d’Anatomie Pathologique; 7Llandough Hospital; 8PhenoPath Laboratories; 9Diagnostic Specialties Laboratory; 10University of Pennsylvania Medical Center; 11M. D. Anderson Cancer Center; 12Duke University Medical Center; 13Memorial Sloan Kettering Cancer Center; 14University of Virginia Medical Center.

A pathology panel was convened in October at the International Mesothelioma Interest Group (IMIG) biennial meeting to discuss guidelines for the pathologic diagnosis of malignant mesothelioma (MM). This resulted in a consensus opinion, which can be divided into the following:

1. distinguishing between benign and malignant mesothelial proliferations (both epithelioid and spindle cell lesions);
2. cytologic diagnosis of MM;
3. key histologic features of pleural and peritoneal MM;
4. use of histochemical and immunohistochemical (IHC) stains;
5. differentiating epithelioid MM from various carcinomas (lung, breast, ovarian, and colonic adenocarcinomas, as well as squamous cell and renal cell carcinomas);
6. diagnosing sarcomatoid mesothelioma;
7. use of molecular markers in the differential diagnosis;
8. electron microscopy; and
9. what not to use in the diagnosis;
10. pitfalls in the diagnosis of MM.

The IHC panels are suggested, the exact makeup of which is dependent on the differential diagnosis, experience of the pathologist, and antibodies available. The panel should contain both positive and negative markers, with at least 60% sensitivity and specificity. Interpretation of positivity generally should take the number of cells staining (>10%) and the localization of the stain (eg, nuclear vs cytoplasmic) into consideration. These guidelines are meant to be a practical reference for the pathologist, rather than a mandate or review of the literature.

Financial disclosure: Dr Travis receives financial compensation from plaintiffs and defendants for expert testimony on malignant mesothelioma.

Kiln Burner Pneumoconiosis

Izidor Kern, Katarina Osohnik. University Clinic of Respiratory and Allergic Diseases.

Context: Charcoal can be produced by carbonization of wood in kilns. It is a traditional seasonal job. When the pyrolysis is complete, a kiln burner manually removes the charcoal. While doing this, he is exposed to smoke and charcoal dust. We report a case of so-called kiln burner pneumoconiosis.

Design/Results: A 71-year-old man, who was a nonsmoker and farmer, was admitted to the hospital because of bilateral pneumonia. Antibiotic therapy was efficient. Two months after complete resolution of radiologic lung infiltrates and normalization of his laboratory results, pulmonary function testing disclosed a restriction pattern (vital capacity 67% and forced expiratory volume in the first second 75% of predicted values) with diminished diffusion capacity (74% of predicted value). With time, pulmonary function did not improve. High-resolution CT scan showed a diffuse centrilobular ground-glass nodular pattern with subpleural small areas of consolidations. Transbronchial biopsy revealed deposition of black pigment in the bronchiolar interstitium, similar to the histologic appearance of simple coal workers pneumoconiosis, with no signs of fibrosis. A lot of black amorphous material was found in bronchialveolar lavage. Additional environmental history was taken to elucidate the patient's lifelong occupation as a kiln burner.

Conclusions: We report a case of lung disease due to inhalation of carbonaceous materials. The patient was exposed to incomplete combustion of wood burning and large amounts of charcoal dust while kiln burning for a long period.

Benign Lymphocytic Angiitis and Granulomatosis

Belinda E. Clarke. Queensland Health Pathology Service.

A 55-year-old obese diabetic woman presented with 6 months of fluctuating skin lumps, dry cough, exertional dyspnea, and mild fatigue. No environmental exposures were documented. Serology for infections, connective tissue diseases and vasculitis was negative. Serial computed tomography scanning demonstrated multiple fluctuating pulmonary nodules. Excision of a skin nodule yielded a diagnosis of nodular vasculitis. Video-assisted thoracoscopic lung biopsy revealed an area of infarctlike necrosis associated with lymphocytic and granulomatous vasculitis. There

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was no atypia of the lymphoid infiltrate, which consisted predominantly of CD4+ CD56- T cells. Results of Epstein-Barr virus in situ hybridization (EBV-EH) were negative, and polymerase chain reaction for T-cell receptor and immunoglobulin heavy chain rearrangements demonstrated polyclonal DNA. A diagnosis of benign lymphocytic angiitis and granulomatosis (BLAG) was made. The patient was started on chlorambucil with little measurable benefit. Since the original description of 14 cases of BLAG in 1977, controversy has surrounded its existence as an entity distinct from lymphomatoid granulomatosis. Understanding the histogenetic basis of BLAG has evolved during that time. Liebow described the classic triad of changes in 1972, but only during the 1980s was it recognized to be an angiocentric lymphoma, thought to be of T-cell origin. Not until 1994 were most shown to be T-cell-rich, EBV-driven B-cell lymphomas. Cases of otherwise typical LYG in which the cytologically malignant lymphoid cells mark as T cells and lack evidence of EBV infection are now classified as peripheral T-cell lymphomas. Cases such as that reported here have been designated angiocentric immunoproliferative lesions, grade I. Some have been shown subsequently to progress to malignant lymphoma.

Primary Epithelioid Angiosarcoma of the Pleura

Kirtree Rishi1; Philip T. Cagle1; Timothy C. Allen2. 1 The Methodist Hospital, Houston; 2 University of Texas Health Center at Tyler.

A 61-year-old man presented with shortness of breath and right-sided chest pain. On physical examination, he was found to have a large right-sided pleural effusion and a large right-sided pleural mass with adjacent pleural thickening. He underwent thoracotomy, and approximately 750 ml of bloody fluid was drained from his right chest. A hemorrhagic, circumscribed mass was excised from the right pleura. On sectioning, the mass was hemorrhagic and necrotic. Histologic sections showed sheets of epithelioid cells with large, vesicular nuclei and prominent nucleoli. At higher power magnification, similar features with scattered cytoplasmic vacuoles and occasional mitoses were seen. The neoplastic cells were immunopositive for CD31 and factor VIII and focally immunopositive for keratin.

Spontaneous Pleuropulmonary Endometriosis in Baboons: Insights Into Pathogenesis

Jaiitree Jagirdar1; Jeffrey Christal1; Matthew Martin1; Gene Hubbard2. 1 University of Texas Health Science Center; South West Foundation for Biomedical Research.

Context: Endometriosis is a common gynecologic disorder in women. Spontaneous pleuropulmonary endometriosis (PPE) is rare. The pathogenesis of endometriosis, particularly of PPE, remains unclear. Major theories include the following: coelomic metaplasia, embolization from the diaphragmatic migration of endometrium. Although not reported, PPE is the pathogenesis and to refine management.

Design: Ten cases of PPE and 4 cases of intra-abdominal endometriosis were identified at necropsy in baboons (Papio spp.). Hematoxylin-eosin stain and immunohistochemistry were performed on sections, using antibodies to estrogen receptor (ER), progesterone receptor (PR), thyroid transcription factor 1 (TTF-1), CD10, and the proliferation marker Ki-67.

Results: Grossly, clear hemorrhagic, 0.5- to 2-mm cystic lesions were noted on the lung surfaces and within the lung parenchyma in the 10 baboons. The cysts were lined by TTF-1 and ER and focally immunopositive for keratin as TTF-1+ epithelial cells were found with variable Ki-67+ proliferative activity. In contrast, the epithelium and stroma in abdominal endometriosis was TTF-1-, ER-, and Ki-67-. Conclusions: The abdominal endometriosis differs from the PPE in that the latter is lined by TTF-1+ cells, which suggests that the pathogenesis of PPE is other than what is speculated above. The presence of deep parenchymal interstitial aberrant nodular stromal aggregates suggests that the stroma is the driving force in PPE upon which the lung-specific epithelium condenses and may require a novel approach to therapy.

Tumor Lymphangioimmunoblastic Lymphoma and Micrometastasis in Stage I Lung Cancer Using D2-40 Immunohistochemistry

Irene Castaneda-Sanchez; Elizabeth Kurian; Philip T. Cagle; Jaiitree Jagirdar1. 1 The University of Texas Health Science Center, San Antonio; 2 The Methodist Hospital, Houston.

Context: Stage I non–small cell lung cancer (NSCLC) carries survival rates of approximately 70% at 5 years, with approximately 30% of patients experiencing poor outcome, despite complete surgical excision. Squamous cell carcinomas (SCCs) fare slightly better. In the search for prognostic markers, this study proposes to evaluate lymphatic invasion, micrometastasis, and lymphangiogenesis in stage I lung cancer, using a specific marker of lymphatic endothelium (D2-40/podoplanin).

Design: Paraffin-embedded tissue sections of tumor and lymph nodes from 60 patients with stage I NSCLC were retrospectively analyzed for lymphatic invasion, micrometastases and lymphatic microvessel density (MVD) using D2-40. The presence of these pathologic factors were correlated with clinical factors in the search for prognostic markers in early disease. Tumor types included the following: 35 adenocarcinomas (ACAs), 9 bronchioloalveolar carcinomas, 10 SCCs, and 7 large cell carcinomas.

Conclusion: Although lymphatic invasion is uncommon, it trended toward poor outcome. MVD was uniformly low in SCC. Minimal lymphatic MVD was noted in peritumoral areas in all types of stage I NSCLC. Incidence of increased lymphatic MVD was highest in scar areas (2+ to 3+), particularly in ACAs. Larger scar size correlated with increased lymphatic microvessel density and with a poor prognosis.

Conclusions: The increase in lymphatic density in the tumor scar may account for the prognostic significance of scar size in ACAs. The better prognosis of stage I SCCs may be due to low lymphatic MVD and absence of scar. D2-40 is a valuable marker for lymphatic invasion in stage I lung cancer.

A Case of Pulmonary Epithelioid Hemangioendothelioma With an Unusual Presentation and an Aggressive Clinical Course

Armita Bahrami1; Philip T. Cagle2; Timothy C. Allen. 1 Baylor College of Medicine, Houston; 2 The Methodist Hospital and Weill Medical College of Cornell University, Houston; 3 University of Texas Health Center at Tyler.

A 37-year-old white man presented with a 1-year history of progressively severe posterior chest wall pain. Magnetic resonance imaging of the spine revealed an intrathoracic mass, which on a chest computed tomography scan was described as a 4-cm solid left upper lobe lung mass, arising from the left hilum. Initial attempts by bronchoscopic and transbronchic biopsies failed to obtain diagnostic material. The patient underwent thoracotomy and was found to have a locally advanced, surgically unresectable tumor involving the pleura, pericardium, and diaphragm. Bone imaging studies showed loss of periosteum of several ribs in the area where the patient complained of pain. Results of the metastatic work-up were otherwise negative. The patient failed to respond to radiochemotherapy and died 11 months following the diagnosis with large pleural and pericardial effusion, tamponade, and metastasis to the skin of the thoracoabdominal wall. Histologically, the tumor had a biphasic (epithelioid and spindled) appearance, suggestive of mesothelioma. The epithelioid cells had round-oval vesicular nuclei, with mild to moderate nuclear pleomorphism without significant mitoses, arranged in nests and strands within a dense hyalinized to chondromyxoid stroma. Immunohistochemically, neoplastic cells expressed endothelial markers CD31, CD34, and FLI-1 and were negative for mesothelioma markers. Cytokeratin AE1/AE3 was focally positive. The tumor was diagnosed as epithelioid hemangioendothelioma. Despite lack of unequivocal high-grade histologic features, the tumor was felt to have an aggressive biological behavior. It is our impression that epithelioid hemangioendothelioma is a rare tumor in the lung that can mimic other more common pathologic entities. It should be considered in an approach to unusual pulmonary neoplasms with epithelioid or biphasic morphology.

Angiogenesis in Bronchial Dysplasia and Angiogenic Squamous Dysplasia Is Associated With the Formation of Immature Vasculature

Daniel T. Merrick; Elizabeth S. Buyers; York E. Miller; Robert L. Keith; Timothy C. Kennedy; Wilbur A. Franklin. 1 Denver Veterans Administration Medical Center; 2 University of Colorado Health Sciences Center.

Angiogenic squamous dysplasia (ASD) is a dysplastic lesion of the bronchi of smokers that is distinguished from other dysplasias by virtue of the presence of characteristic vascular morphology with projection of microvessels into the overlying dysplastic epithelium. To date, we have identified ASD in 167 of 721 patients who have undergone LIPF bronchoscopy at the University of Colorado Health Sciences Center: in nonmalignant airways of 37 patients with invasive carcinoma (28 prevalent carcinomas and 9 incident carcinomas) and in 130 patients without carcinoma. ASD can be associated with marked stromal matrix remodeling. These changes are associated with high stromal matrix metalloproteinase factor expression and high microvessel densities (MVD) in comparison to normal bronchial epithelium. We examined the microvessel maturation...
index (MMI) (actin+/MVD/CD31− MVD) of 12 ASD lesions and 4 samples of normal mucosa. The mean MMI for dysplastic lesions was significantly less than that measured for 4 normal bronchial biopsies (MMI, 0.62 vs 1.02, respectively; P = .04). When analyzed independently, the vessels that project into the intraepithelial papillae of ASDs showed the lowest MMI of 0.56. This was not statistically different than the MMI for the dysplasia group as a whole, but was significantly decreased in comparison to normal MMI (P = .71 and .04, respectively). Incomplete vascular maturation is associated with a change in the phenotype of smokers and is most striking in the vascular structures of ASD. In this respect, ASD is similar to invasive carcinoma. Increased delivery of protumorigenic factors, such as growth promoting factors and mutagenic substances, may be facilitated by immature vascular networks in premalignant airways.

Malignant Solitary Fibrous Tumor of the Pleura

Jerald M. Gardner; Philip T. Cagle; Timothy C. Allen. The Methodist Hospital, Houston; University of Texas Health Center at Tyler.

A 65-year-old woman presented with a pleural-based mass of the right lower lobe. The mass was surgically resected, and the gross specimen was a 14-cm, 858-g nodular tumor with a white whorled cut surface. Microscopically, some areas of the tumor were composed of irregularly arranged pleomorphic spindle cells with intervening dense collagen and a hemangiopericytoma-like vascular pattern. These areas were confluent with areas of highly pleomorphic spindle cells with prominent nucleoli and numerous atypical mitotic figures. Multinucleated tumor giant cells and haebroblasts were also seen, as well as focal areas of tumor necrosis. The specimen was diagnosed as a malignant solitary fibrous tumor (MSFT). MSFT is a very uncommon lesion. Such tumors may have the architectural features of a benign solitary fibrous tumor but with malignant cytologic features, or they may resemble obvious high-grade sarcoma. Most MSFTs are CD34 positive, but CD34 negativity has been reported. Although there is potential for local recurrence as well as distant metastasis, many patients can be cured of MSFT by complete surgical resection. Interestingly, radiation and chemotherapy may actually decrease survival in patients with this lesion. This case of MSFT is particularly unique because representative areas of both typical solitary fibrous tumor and high-grade MFH-like sarcoma are seen within the same lesion.

Adenoid Cystic Carcinoma of the Trachea

Melissa L. Stanton; Philip T. Cagle. University of Texas at Houston Medical School; The Methodist Hospital, Houston.

Primary pulmonary adenoid cystic carcinoma (ACC) is a rare, slow-growing tumor histologically similar to that found in the salivary glands. Most tumors are intraluminally within the trachea, main stem, or lobar bronchi. They are generally well circumscribed but can have infiltrative margins along the tracheobronchial wall, extending far beyond the localized mass. Histologically, cribriform, tubular, or solid growth patterns are seen within the tumor. Cribriform glands may be seen in 70% of ACC tumors, and these are composed of single-cell columns of neoplastic epithelial cells separated by myxomatous stroma. There is often intraductal papillary proliferation of the neoplastic epithelial cells. The tumor grows in small streams along the basement membrane. The tumor cells are negative for epithelial membrane antigen, monoclonal antibodies to keratin, and keratin 7, and positive for carcinoembryonic antigen, chromogranin, synaptophysin, and actin. Electron microscopic examination showed ducts with thick basal lamina, and basement membranes could be demonstrated. Cytokeratin 14, 17, and 19 were positive, and the tumor cells were negative for sialomucins and epithelial membrane antigen. The tumor cells were positive for claudin-1 and -2, and negative for S100, keratin 8, 18, 19, and 20, and carcinoembryonic antigen.

Ectopic Bronchial Primary Pruritic Glandular Meningioma

Enrique M. Gomez. University of Texas in Houston.

Primary pulmonary meningioma (PPM) is a very rare entity, with only 33 reported cases in the literature. PPMs are usually benign and located in the peripheral pulmonary parenchyma. None of the previously reported cases had an endobronchial location. To our knowledge, we report the first endobronchial benign PPM case. This case presented in a 34-year-old woman who was admitted with symptoms of hemoptysis. Radiographic and bronchoscopic studies revealed an endobronchial mass obstructing the right intermediary bronchus. A right lobectomy was performed. On gross evaluation, a 2.5 × 2.0-cm unencapsulated well-demarcated mass was identified, with associated distal pulmonary atelectasis. Histologically, the lesion was composed of whorls and bundles of bland polygonal to fusiform cells with oval to round nuclei and dispersed chromatin. Immunohistochemical studies were performed, supporting a diagnosis of meningioma. Immunohistochemical staining pattern and ultrastructural findings were characteristic of a malignant glomus tumor. Glomangiosarcomas (malignant glomus tumors) of the lung are extremely rare tumors with only a few cases described to date. Rarity of this tumor and its histologic similarity to more common primary and metastatic neoplasms makes this a very challenging diagnosis. This case emphasizes that clinical, histologic, and immunohistochemical examination are essential in establishing a diagnosis of glomangiosarcoma.

The Concordance of Clinical Asbestosis With Pathological Asbestosis: A 10-Year Survey

Richard Luther Attanoos; Gareth Rowlands; Allen R. Gibbs. Llandough Hospital.

Context: In the United Kingdom, recent governmental guidelines recognize clinical asbestosis without a requirement for supportive pathology. Moreover, diffuse intestinal fibrosis (DIF) without asbestos bodies and/or or low fiber burdens are not considered of value in questioning the clinical diagnosis of asbestosis. This survey was performed to compare the post-mortem pathology diagnosis of asbestosis with diagnoses made on clinical grounds.

Design: Of 4800 postmortem examinations from 1997 to 2006, 355 (7.4%) cases were selected for detailed examination on the basis of a history of asbestosis exposure and/or DIF. According to established College of American Pathologists-National Institute for Occupational Safety and Health guidelines, lung tissue was sampled and the diagnosis of asbestosis evaluated according to the 1997 Asbestos, Asbestosis, and Cancer report (Sand J Work Environ Health). Asbestos fiber counts were performed by transmission electron microscopy with energy-dispersive x-ray analysis.

Results: One hundred three cases with an asbestos history had non-neoplastic changes clinically deemed asbestosis. Twenty-three (22.3%) cases showed DIF, 73 (71%) cases showed no significant fibrosis, and in 7 (7%) cases, the lung was insufficient for diagnosis. Of the 23 DIF cases, 5 (21.7%) cases were diagnosed as asbestosis, 3 showed fewer than 2 asbestos bodies per square centimeter of lung, and 15 showed no asbestos bodies. After mineralogic analysis, only 1 of 3 and 1 of 15 cases were subsequently diagnosed as asbestosis.

Conclusions: Significant (70%) discordance between the clinical and pathologic diagnoses of asbestosis exists. The validity of basing compensation on clinical asbestosis alone is questionable. There exists a requirement to standardize pathologic and mineralogic criteria for asbestosis. Other causes of DIF recognized pathologically are misdiagnosed clinically.

Financial disclosure: Drs Attanoos and Gibbs receive financial compensation for expert testimony on asbestos-related disease in various countries.

Primary Glomangiosarcoma of the Lung

Munir Shahjahan; Donna M. Coffey; Philip T. Cagle. The Methodist Hospital, Houston.

A 40-year-old woman presented with a right lung mass and underwent subsequent lobectomy of the upper lobe. The tumor measured 9 cm in greatest dimension with extension into the adjacent bronchus. Initial clinical impression and gross examination pointed toward a neuroendocrine tumor. Microscopic examination revealed no nuclear atypia or necrosis. However, focal areas with increased mitoses (up to 7 per 10 high-power fields) and features of lymphovascular invasion were identified. Tumor cells were immunopositive for actin, vimentin, collagen type IV, and calponin but negative for chromogranin, synaptophysin, S100, pankeratin, cytokeratin 14, epithelial membrane antigen, desmin, CD90, CD10, inhibin, and progestoreone receptor. Electron microscopic examination showed cells with cytoplasmic bundles of microfilaments, external lamina, and micropinocytotic activity. No desmosome-like junctions and no dense core neurosecretory granules were seen. Presence of lymphovascular invasion with increased focal mitotic activity together with the immunohistochemical staining pattern and ultrastructural findings were characteristic of a malignant glomus tumor. Glomangiosarcomas (malignant glomus tumors) of the lung are extremely rare tumors with only a few cases described to date. Rarity of this tumor and its histologic similarity to more common primary and metastatic neoplasms makes this a very challenging diagnosis. This case emphasizes that clinical, histologic, and immunohistochemical examination are essential in establishing a diagnosis of glomangiosarcoma.
Bronchiolitis and Peribronchiolar Interstitial Disease in 4 Patients Exposed to World Trade Center Smoke and Dust

Maoxin Wu; Maria Padilla; Jacqueline Moline; Robin Herbert; David Mendelson2; Virginia Litle2; William Travis; Joan Gil; ‘Mount Sinai School of Medicine; ‘Mount Sinai Medical Center; ‘Memorial Sloan-Kettering Cancer Center.

Persistent respiratory conditions have been described among rescue and recovery workers exposed to smoke and dust from the World Trade Center (WTC) disaster. Sarcoid-like pathologic findings have been reported in some cases. We report findings in 4 patients (ages 42–56 years) with WTC exposure, compounding on September 11 or 12, 2001, who are being followed at the Mount Sinai WTC Medical Monitoring and Treatment Program. Patients presented with complaints of shortness of breath and nonspecific radiologic findings (diffuse interstitial disease and rarely nodules) and underwent video-assisted thoracoscopic biopsies. The 4 biopsies all revealed generally severe bronchiolitis with variable characteristics. In some cases, the degree of interstitial fibrosis was so extensive that the peribronchial origin was less ascertainable. One of the cases was remarkable for areas of honeycombing isolated in an otherwise unremarkable alveolar parenchyma; another case showed eosinophils with very poorly organized granulomas, also present in the lymph nodes. The overall appearance was unusual in that it did not correspond to any of the common interstitial diseases. In none of the cases were classic patterns of usual interstitial pneumonia, nonspecific interstitial pneumonia, or organizing interstitial pulmonary fibrosis seen. Some affected lobes appeared slightly more affected. We conclude that these findings represent an uncommon pathologic reaction to the inhalation of the smoke and dust generated from the WTC disaster.

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New Biomarkers in the Cancerous Stroma: Podoplanin, SPARC, and Galectin-9; Tissue Microarray Analysis

Junya Fukuoka; Haruhisa Kitano; Yuta Sakai; Tomonori Tanaka; Kishio Kuroda; Kazuhiro Nomoto; Naoko Kumagai; Takashi Horii. Toyama University Hospital, Toyama, Japan.

In a multi-institutional collaboration (some antibodies were obtained from National Cancer Institute [Bethesda, Md], Kinki Chuo Chest Medical Center [Sakai, Japan], Kyoto University [Kyoto, Japan], National Institute of Advanced Industrial Science and Technology [Tsukuba, Japan], DAKO [Kyoto, Japan], and Shiga University of Medical Science [Osu, Japan]), we have dedicated ourselves to archiving a protein expression database of lung cancer using tissue microarray. Of the nearly 100 evaluated markers, we found 3 new markers (podoplanin, SPARC, galectin-9), and galactoside–binding lectin family members that are selectively stained in the cancerous stroma, mainly fibroblasts, and significantly associated to cancer progression. Podoplanin is a marker widely used to detect lymphatic endothelial cells. We found that stromal podoplanin expression was significantly associated with nodal metastasis (P < .01). Significant association was also detected in the interstitial cells of inflammatory diseases. SPARC is a calcium-binding glycoprotein that associates with morphogenesis, remodeling, cellular migration, and proliferation. The stromal SPARC expression was significantly associated with pT (P = .02) and lymphatic invasion in adenocarcinoma (P = .03). Cases with SPARC expression showed a trend of poorer survival in adenocarcinoma that was not statistically significant (P = .34). Galectin-9 is a member of the β-galactoside–binding lectin family associated with apoptosis and cell aggregation. The stromal expression of galectin-9 was significantly associated with more favorable survival for patients with lung cancer (P = .02). Here we found 3 possible biomarkers selectively expressed in the cancerous stroma. Although most research of biomarkers is focused on the cancer cells, there are some markers specifically found in the stromal cells. Considering the difficulty in staging the cancer cells, it is important to focus mutation and tolerance to medicine, stromal cells can be easier targets to control. Here we propose the importance of finding biomarkers in the cancerous stroma, which may throw some light on upcoming cancer therapy.

Multinodular Neuroendocrine Carcinoma With Intraepithelial Extension of the Large and Small Airways

Patrizia Morbini; Chiara Villa. Università di Pavia.

A 64-year-old male smoker complaining of cough and fever underwent upper left lobectomy after a computed tomography scan showed concentric stenosis of the upper left lobar bronchus with distal inflammatory opacities and endobronchial biopsy–documented atypical squamous cells. Macroscopic examination showed thickened lobar and segmental bronchial walls and multiple peripheral nodules ranging from 3 to 15 mm in diameter. A histologic examination revealed peripheral nodules consisting of neuroendocrine cell proliferations consistent with atypical carcinoma and/or moderately differentiated neuroendocrine carcinoma (NEC) with extensive fibrosis. Distorted airways were observed in the center of some nodules. Bronchial cartilaginous bronchi showed in situ carcinoma, extending to peribronchial glands, and marked fibrosis. The epithelium of many segmental and terminal bronchioli and of some surrounding air space was also severely atypical. Dysplastic bronchial and bronchiolar epithelia were diffusely immunoreactive for high-molecular-weight (HMW) cytokeratins and cytokeratin 7. Poorest expression of neuroendocrine markers was also observed. Neoplastic cells invading peribronchial mucus glands expressed neuroendocrine markers and cytokeratin 7, while HMW cytokeratins were expressed in a small number of cells, mostly negative for neuroendocrine markers. Mixed neuroendocrine and squamous cell carcinoma is a well-documented entity; however, the coexistence of neuroendocrine and squamous cell markers in intraepithelial bronchial carcinoma extending distally into the bronchial tree, with multiple moderately differentiated NECs, has not been described before. The present case offers many subjects of investigation: Is squamous and neuroendocrine cell proliferation independent? Is endobronchial tumor spread responsible for multinodular dissemination? Could the bronchocentric distribution of neuroendocrine proliferation be related to diffuse idiopathic neuroendoctrine cell hyperplasia?

Pulmonary Capillary Hemangiomatosis—like Histologic Changes and Severe Clinical Pulmonary Hypertension in Intstitial Lung Diseases: Report of 3 Explant Cases


Pulmonary hypertension (PH) has been suggested to play an important role in the prognosis of interstitial lung disease (ILD) in patients. However, it is not clear whether PH in ILD is a reflection of the extent of histological remodeling or an independent process. Clinical studies have demonstrated that severe PH in ILDs can occur in the absence of advanced pulmonary dysfunction or hypoxemia. Recent studies reported that there are increased alveolar capillary densities in ILDs. We have also noted that some ILD cases show extraordinary capillary proliferations that may represent isolated pulmonary capillary hemangiomatosis (PCH) or the PCH-associated with pulmonary veno-occlusive disease. Herein, we report 3 ILD cases with severe clinical PH for which the patients underwent double lung transplantations. Explanted lungs showed diffuse PCH-like reactions, hemisiderin deposition, muscularized pulmonary arterioles, and occasional occluded pulmonary veins or venules, as well as ILD. The first patient was a 59-year-old woman who had a clinical diagnosis of systemic sclerosis. The explanted lungs showed the features of fibrosing nonspecific interstitial pneumonia. Pulmonary artery pressures (PAPs) by right heart catheterization (RHC) measured 75/22/39 mm Hg, in systolic, diastolic, and mean pressure, respectively. The second patient was a 64-year-old man with no underlying disease who was diagnosed as having usual interstitial pneumonia (UIP). PAPs by RHC were 62/29/35 mm Hg. The third patient was a 35-year-old woman who had the clinical diagnosis of scleroderma, and her explanted lungs showed UIP. Her PAPs were 103/42/67 mm Hg. Widespread PCH-like changes in these cases might have caused an increase in pulmonary vascular resistance and severe PH.

Significance of Molecular Alterations in Alveolar Cells in Usual Interstitial Pneumonia With or Without Lung Cancer

Sylvie Lantuejoul; Andrew G. Nicholson; Dimitri Salameire; Christopher Pison; Gilbert Ferretti; Elisabeth Brambilla. ‘CHU A Michallon; ‘Royal Brompton Hospital.

Context: Idiopathic pulmonary fibrosis, the most common interstitial lung disease with the worse prognosis, is characterized histologically by a usual interstitial pneumonia (UIP) pattern. Incidence of lung cancer on UIP is higher than that of lung cancer alone. As molecular abnormalities were reported in atypical or metastatic alveolar cells in UIP, we hypothesized that they could characterize carcinoma precursor cells.

Design: Immunohistochemical expression of proteins involved in proliferation or apoptosis, p53, cyclines D1 and E, p21, Bax, Bcl-2 and p16, were scored and compared in 29 UIP cells with cancer, 15 UIP cells without out cancer, 11 fibrotic nonspecific interstitial pneumonia (NSIP) cells, and 10 inflammatory lungs. We have analyzed concomitantly the phenotype of tumor cells.

Results: Numerous atypical and/or metastatic alveolar cells were...
found in 39% and 43% UIP with and without cancer, respectively, but in 9% of NSIP and in none of the inflammatory cases. p53, cyclin D1, p21 and p16 expression and a Bax:Bcl-2 ratio of <1 were found in 70% to 100% of all peripheral tumors from UIP and NSIP, but not in atypical cells from inflammatory lungs. Cyclin E was not expressed except in tumor cells. Immunophenotype of lung carcinomas on UIP was comparable to that reported in lung cancer alone.

Conclusions: Molecular abnormalities in UIP atypical alveolar cells are more frequent than those found in NSIP. However, they are not specifically related to the presence of cancer but are likely a normal DNA damage response to alveolar cell injury leading to apoptosis or G1 arrest for DNA repair.

Three Cases of Diffuse Miliary Lesions in Asymptomatic Human T-Cell Lymphotropic Virus Type 1 Carriers

Junya Fukuoka; Kazuya Ichikado; Tomonori Tanaka; Kishio Kuroda; Moritaka Suga; 1Toyama University Hospital, Toyama, Japan; 2Saiseikai Kumamoto Hospital.

Human T-cell lymphotropic virus type 1 (HTLV-1) is a retrovirus that causes adult T-cell leukemia (ATL). Besides that, similar to HIV carriers, those with HTLV-1 occasionally can contract other inflammatory disorders, including arthropyathy and bronchopneumonopathy. “HTLV-1 Associated Bronchiolo-Alveolar Disease (HABA)” is an immune-mediated pulmonary reaction proposed by Kimura et al in 1989. Several additional articles in scientific literature have described 2 major morphologic patterns: diffuse panbronchiolitis and lymphocytic intestinal pneumonia. However, the reports are limited in Japan, and the disease entity is not completely established. We have experienced 3 unique cases showing diffuse miliary lesions in HTLV-1 carriers. The lung wedge biopsies obtained before treatments showed 1- to 3-mm multiple nodules with marked lymphoid infiltration, granuloma, and tissue eosinophilia. Various degrees of organizing pneumonia with airspace fibrid were found inside the nodules in all cases. Two cases showed tiny foci of necrosis in the center of nodules. Most nodules were located around airways, but some were in the periphery of the secondary lobule. No atypical lymphoid cells were identified, and immunohistochemical profile did not show monoclonal proliferation or aberrant expression indicating neoplasm. In situ hybridization against Epstein-Barr virus was negative. Genetic analysis done in one case did not show monoclonal proliferation. However, involvement was found in none of the cases. Examinations, including culture, serum antibodies, and special staining, did not reveal evidence of infection. All patients experienced improvement within a month either by observation alone or with low-dose steroids, and no recurrence was found on follow-up at 0.5, 4, and 6 years. Those cases may be distinctive and self-limited lymphoproliferative disorders associated with HTLV-1.

Primary Lung Neoplasms

Primary Lung Mesothelioma

Machiya Nishino; Philip T. Cagle. 2Baylor College of Medicine, Houston; 2The Methodist Hospital, Houston.

Primary mesothelioma of the lung is an exceptionally rare pulmonary malignancy. While metastatic melanoma with pulmonary involvement is not uncommon, fewer than 30 cases of primary lung melanoma have been reported in the literature. These tumors involving lung typically arise from sebaceal mucosa associated with the diaphragm. The histopathology of mesothelioma of the lung presents as a solitary mass in adults with a peak incidence during the fifth decade of life. Its diagnosis is established based on a combination of clinicoradiographic and histopathologic information. Overall, this entity is estimated to account for less than 0.01% of primary lung neoplasms. We report the case of an 85-year-old man who presented with a 2-week history of productive cough, hemoptysis, progressive dyspnea, fatigue, and weight loss. Fiberoptic bronchoscopy revealed an obstructive left endobronchial mass, and bronchial washings yielded malignant cells with melanin pigment. Histologically, the tumor was characterized by irregular coalescent nests and sheets of pleomorphic cells with enlarged hyperchromatic atypical nuclei and dense eosinophilic cytoplasm. Variable amounts of melanin pigment deposits were identified both intracellularly and extracellularly. Immunohistochemistry of tumor cells demonstrated diffuse reactivity with S100 and HMB-45 and negative immunostaining with pancytokeratin. In the appropriate clinical setting and absent history of other cutaneous, mucosal, or ocular melanoma, the histopathological characteristics of this neoplasm were consistent with primary melanoma of the lung.

Desmoplastic Mesothelioma: Clinicopathologic Features of a Subtle Case

Jeffrey T. Bunning; Therese J. Bocklage; Robyn L. Gaffney. University of New Mexico Health Sciences Center.

A 47-year-old woman presented with a 3-week history of progressive dyspnea, fatigue, and a 12-kg weight loss during the past 2 months. Chest x-ray showed bilateral pleural effusions. Computed tomography imaging revealed bilateral loculated effusions, as well as an ill-defined, right-sided pleural-based mass. Bilateral pleural biopsies were obtained; they re-

squamous morules were also seen associated with underlying glandular stroma. The histopathologic features of this tumor are characteristic of a well-differentiated fetal adenocarcinoma. Fetal adenocarcinoma is a uniquely rare type of pulmonary and immune-distinctive histologic characteristics. The more common well-differentiated variant shows striking histologic resemblance to the epithelial elements of biphasic pulmonary blastoma; this shared histology has contributed to their confusion and previous diagnostic overlap. Well-differentiated fetal adenocarcinoma can be distinguished from pulmonary blastoma by the absence of any sarcomatoid mesenchymal component characteristic of the latter entity. Furthermore, the histopathology of fetal adenocarcinoma has been infrequently described in the presence of other histologic subtypes of pulmonary adenocarcinoma.
vealed hypocellular, dense pleural fibrosis with an associated chronic inflammatory response. Scattered throughout the collagenized stroma and the adjacent adipose tissue were plump spindle cells demonstrating mild to moderate cytologic atypia and rare mitoses. These spindle cells showed strong positivity for cytokeratin AE1/AE3 and focal weak positivity for calretinin and mesothelin. Cytokeratin 5/6 and CD34 stains were negative, and p53 appeared overexpressed in the cells of interest. The immunohistochemical studies also highlighted numerous cytokeratin-positive spindle cells infiltrating the chest wall adipose tissue. This latter finding, along with the paucicellular histology and clinicoradiographic findings, confirmed the diagnosis of desmoplastic mesothelioma.

Chronic Pneumonia Presenting as a Suspicious Lung Mass on Computed Tomography and Positron Emission Tomography Scans

Lizabeth S. Rosenbaum1; Jess D. Schwartz2; Therese J. Bocklage.2 1University of New Mexico, School of Medicine; 2University of New Mexico.

A 46-year-old Hispanic nonsmoking man presented with a 10-year history of recurrent “flu,” bronchitis, and pneumonia. He was treated multiple times with antibiotics, with only transient improvement after each course. Within the last few months, the patient developed hemoptysis, low-grade fevers, and mild shortness of breath. A chest x-ray showed a right upper lobe infiltrate. The patient traveled to Mexico for further work-up, as care in the United States was too costly. A computed tomography scan performed shortly before the surgery showed a 1.9-cm nodule in the right middle lobe, a 1.5-cm nodule in the left lower lobe, and multiple small nodules bilaterally. Eighteen months after surgery, she was alive and well; the remaining pulmonary nodules were stable, and there was no evidence of extrapulmonary disease. Histologic examination of the right middle lobe nodule revealed marked organizing pneumonia with a prominent lymphocytic and plasmacytic infiltrate, multiple bronchial based abscesses, and a bronchus forming a cavitary lesion lined by metaplastic squamous epithelium. No tumor was identified. This case illustrates the hazard of overdiagnosing marked reactive atypia of type II pneumocytes as carcinoma.

Unusual Neoplasm With Glandular and Squamous Differentiation

Andras Khoor. Mayo Clinic, Jacksonville, Fla.

A 71-year-old woman underwent tricuspid and mitral valve repair, Maze procedure, and wedge biopsy of a right middle lobe nodule. Her medical history included pulmonary nodules for more than 10 years. A chest computed tomography scan performed shortly before the surgery showed a 1.9-cm nodule in the right middle lobe, a 1.5-cm nodule in the left lower lobe, and multiple small nodules bilaterally. Eighteen months after surgery, she was alive and well; the remaining pulmonary nodules were stable, and there was no evidence of extrapulmonary disease. Histologic examination of the right middle lobe nodule revealed an unusual neoplasm with glandular and squamous differentiation. The glandular component was composed of mainly cuboidal cells. The squamous component was well differentiated with focal keratin pearl formation. Both the glandular and squamous components were positive for cytokeratin AE1/AE3 and epithelial membrane antigen. The glandular component was also positive for thyroid transcription factor 1. To our knowledge, no similar lesion has previously been described.