Kaposi sarcoma (KS) is a low-grade mesenchymal tumor involving blood and lymphatic vessels. There are four types, based on clinical presentation: classic, endemic (Africana), iatrogenic (typically involving renal allograft recipients), and AIDS-associated (epidemic). Kaposi’s sarcoma-associated herpes virus infection has been linked along with other factors to the development of KS. The Kaposi’s sarcoma-associated herpes virus interacts and encodes for numerous molecular proteins that play a role in the pathogenesis of KS, including latency-associated nuclear antigen, viral G protein-coupled receptor, viral FLICE inhibitory protein, and viral IL-6. KS primarily affects the skin and causes disseminated disease in a variety of organs. Involvement of visceral organs other than the lining of the alimentary tract is extremely rare. While the chylous pleural effusions of KS may resemble other pulmonary diseases (including lymphangioma, lymphangectasis, and lymphangioleiomyomatosis) with chylous effusions at thoracic CT, differentiating features may allow for more prompt diagnosis and treatment. The presumptive diagnosis of AIDS-related pulmonary KS is often clinical. A tissue diagnosis is not required to establish the diagnosis of pulmonary KS. There are a variety of causes of chylothorax. The primary finding is a near-water-attenuating pleural effusion. The secondary findings of chylothorax can help differentiate the etiology.

Introduction

Chylothorax is a relatively uncommon cause of pleural effusion (1). Lymph in the thoracic duct originates at the cisterna chyli and then passes from the abdomen into the mediastinum through the aortic hiatus. It then ascends superiorly in the posterior mediastinum and, at the level of T5-T6, the thoracic duct crosses to the left side to enter the superior mediastinum (1, 2). Chylous pleural effusions can be diagnosed on CT or MRI. The CT finding of chylous effusions is typically a large unilateral effusion of water attenuation and may demonstrate fat. The MRI findings may demonstrate high signal intensity on T1WI due to fat content.

The causes of chylous effusions can be congenital, traumatic, iatrogenic, malignant, idiopathic, infectious, or inflammatory (1, 2). Congenital chylothorax occurs more due to congenital malformations than to trauma during delivery (1). Chylothorax is predominantly seen following trauma or cardiothoracic surgery (2, 3). Traumatic injury to the thoracic duct is more common with penetrating trauma than blunt trauma, and is seen with hyperextension injuries (2, 4). Generally, an injury to the lower third of the thoracic duct causes a right chylous effusion, to the upper two-thirds of the thoracic duct causes a left chylous effusion, and to the thoracic duct (as it crosses midline) causes bilateral chylous effusions. The thoracic duct can be obstructed from lymphadenopathy (including lymphoma, sarcoidosis, lung cancer, and tuberculosis) (5). We review the less common causes of chylothorax, including lymphangioma, lymphangectasis, and lymphangioleiomyoma-
tosis (LAM). Familiarity with these entities may lead to more prompt recognition and diagnosis.

**Case report**

A 21-year-old homosexual male presented with a chief complaint of abdominal pain and bright red blood per rectum over the preceding three weeks. He had nausea without vomiting, bloody diarrhea, and 10 bowel movements per day. He denied any weight loss, fever, chest pain, or shortness of breath. Colonoscopy with rectal biopsies demonstrated KS on pathology. The rectal bleeding was self-limited. He was managed for a left pleural effusion with a left pleural drain (Fig. 1). Laboratory testing confirmed that he was HIV-positive with a CD4 count of 12 cells/μL (427–1625 cells/μL). He was subsequently discharged home in stable condition.

As an outpatient, a metastatic evaluation was performed starting with PET/CT (Fig. 2), which demonstrated extensive lymphadenopathy. His newly diagnosed HIV was managed with Highly Active Antiretroviral Therapy (HAART), and chemotherapy was initiated for his KS as an outpatient. He then had excision of a right level-five cervical lymph node that was positive for metastatic KS. Over the next five months, the patient experienced shortness of breath with upper- and lower-extremity edema responsive to diuretic therapy (Fig. 3).

He was admitted five months later from his original admission for exacerbations of these symptoms (Figs. 3, 4). He developed recurrent bilateral bloody chylous pleural effusions with progressive shortness of breath and extensive peripheral lymphedema. He was tachycardiac with increasing oxygen requirements requiring BiPAP, and eventually was intubated.

The effusions were resistant to serial thoracentesis and pleural drains (Fig. 4). Multiple samples were sent for cytology, which was negative for atypical and malignant cells. The location of thoracic duct involvement by KS was to be assessed by lymphoscintigraphy before ligation of the duct. There was such extensive inguinal lymphadenopathy that the radiotracer remained at the level of the upper thighs 24 hours post injection (Fig. 5). The thoracic duct at the cisterna chyli was found to be infiltrated with tumor on the chest CT (Fig. 6). The thoracic duct was unable to be safely ligated due to extensive infiltration of the tumor; therefore, bilateral decortications with chest tube placement were performed instead in an attempt to control the chylous effusions. Bronchoalveolar lavage (BAL) demonstrated hemorrhagic secretions with erythema of the bronchioles. An infectious evaluation was negative. The patient expired from cardiopulmonary arrest.
KS is a low-grade mesenchymal tumor involving blood and lymphatic vessels (6, 7). There are four types based on clinical presentation: classic, endemic (Africana), iatrogenic (typically renal allograft recipients) and AIDS-associated (epidemic). Human herpesvirus-8 (HHV8) infection has been linked along with other factors to the development of KS (6). KS is considered an AIDS-defining illness.

Involvement of visceral organs other than the lining of the alimentary tract is extremely rare (7, 8). Chylothorax is a rare manifestation of KS involving the thoracic duct (9). KS with chylothorax was initially postulated to develop due to metastatic KS to the thoracic duct; more recent findings suggest that this may arise because of in-situ KS in this region (10, 11). KS-related chylothoraces frequently develop with concomitant upper-airway KS disease (9).

**Discussion**

KS is a low-grade mesenchymal tumor involving blood and lymphatic vessels (6, 7). There are four types based on clinical presentation: classic, endemic (Africana), iatrogenic (typically renal allograft recipients) and AIDS-associated (epidemic). Human herpesvirus-8 (HHV8) infection has been linked along with other factors to the development of KS (6). KS is considered an AIDS-defining illness.
Chylothorax in a patient with metastatic Kaposi sarcoma: Differential diagnostic considerations

Fig. 6. Cisterna Chyli infiltrated with tumor. The cisterna chyli is identified adjacent to the right side of the abdominal aorta and posterior to the inferior vena cava. The cisterna chyli appears enlarged and complex in attenuation (arrow).

Pathophysiology/pathogenesis

Human herpes virus-8 (also known as Kaposi’s sarcoma-associated herpes virus [KSHV]) was discovered by Chang and Moore and has been linked to the development of KS as well as lymphoproliferative disorders, including primary-effusion lymphoma and multicentric Castleman disease (12, 13). Infection with KSHV is necessary for the development of KS, although it is not sufficient by itself (13). HIV co-infection significantly increases the risk of KS (13). KS has been found to be more common among persons who are at greater risk for sexually transmitted infections, which led to a search for an infectious etiology (14). KS cells have been screened for infectious agents, including cytomegalovirus, Epstein Barr virus, human papilloma virus, and mycoplasma; these viral sequences are not uniformly found in KS.

KSHV interacts and encodes for numerous molecular proteins that play a role in the pathogenesis of KS, including latency-associated nuclear antigen (LANA), viral G protein-coupled receptor, viral FLICE inhibitory protein, and viral IL-6 (12, 13). LANA acts as a transcriptional regulator binding to tumor-suppressing proteins p53 and retinoblastoma protein, which promotes the replication of the latent viral episome (12). The viral G protein-coupled receptor leads to proangiogenic signals by the upregulation of hypoxia-inducible factor 1-alpha and the subsequent expression of vascular endothelial growth factor (VEGF)-A and activation of VEGF-receptor-2, which in turn activates PI3K-akt and the mammalian target of rapamycin (mTOR) pathway (13). Viral FLICE inhibitory protein is associated with constitutively activated nuclear factor-xB, where it then activates a large number of antiapoptotic genes (12). Viral IL-6 stimulates gp 130 coupled to the JAK-STAT pathway (13). It is secreted by KSHV-infected cells, allowing tumor cells to regulate their own growth through an autocrine pathway (13). A host of other proteins may play a role, including the HIV Tat protein, which has been shown to serve as a growth factor. In animal models, the replication of the HIV virus may enhance the replication of KSHV (13). HIV Tat promotes the migration and proliferation of cytokine-activated endothelial cells, stimulating KS growth (13).

Clinical presentation

KS primarily affects the skin and causes disseminated disease in a variety of organs. Skin lesions range from several millimeters to several centimeters in size. The lesions are usually not painful or pruritic.

Involvement of visceral organs other than the lining of the alimentary tract is extremely rare. Gastrointestinal AIDS-related KS compromise is the most common visceral involvement in disseminated disease, being seen in up to 50% of patients (7). AIDS-related KS can affect any level of the gastrointestinal tract from the oropharynx to the rectum, including the gallbladder (7). The duodenum is the most frequently affected site (7).

Pulmonary involvement with KS, in the majority of cases, occurs in conjunction with extensive mucocutaneous disease (15). Pulmonary involvement can be the initial manifestation (8). Affected patients can present with shortness of breath, fever, cough, hemoptysis, or chest pain, or pulmonary involvement may be asymptomatic. When a new diagnosis of KS is suspected in a patient with HIV infection, the degree of HIV-related immunosuppression is assessed by measuring the CD4 count and HIV viral load (7). In patients with AIDS-related KS, the CD4 count appears to be the most important factor associated with the development of KS.

Imaging manifestations

KS can present with chylothorax. The typical pulmonary CT findings in AIDS-related KS are the presence of bilateral, ill-defined nodules in a peribronchovascular distribution (flame-shaped lesions representing tumor infiltration involving the bronchovascular bundles), areas of ground-glass opacities (representing edema and blood filling the airspace) surrounding nodules (the “halo sign”), peribronchovascular and interlobular septal thickening (representing edema or tumor infiltration), fissural nodularity, mediastinal lymphadenopathy, pleural effusions (common), or pleural implants (rare) (6, 7, 16). The nodules correspond to proliferation of neoplastic cells (6).

Diagnosis

The presumptive diagnosis of AIDS-related pulmonary KS is often clinical (16). A tissue diagnosis is not required to establish the diagnosis of pulmonary KS. Bronchoscopy is frequently performed to diagnose pulmonary KS with stains, culture, and cytology (which are frequently negative). The bronchoscopic appearance of endobronchial KS is considered to be characteristic enough to allow a diagnosis (6). Parenchymal lesions may occur in the absence of tracheobronchial lesions detected by bronchoscopy. Endobronchial KS lesions typically appear violaceous and are macular or papular, often at airway bifurcations (8). Alveolar hemorrhage is frequently diagnosed during BAL (7, 8). Endobronchial and transbronchial biopsies have a low di-
agnostic yield for KS, with the risk of significant hemorrhage following biopsy (8, 17, 18).

In the setting of worsening pulmonary status, the primary diagnostic role of thoracentesis may be to exclude an underlying infection caused by mycobacterium or fungus. KS lesions are found on the visceral but not parietal pleura (7). Pleural fluid cytology and biopsies are not helpful in diagnosis (19).

When chylous effusions are identified at thoracic CT, imaging findings allow lymphangioma, lymphangectasis, and LAM to be differentiated. Lymphangioma can present with chylothorax. The imaging findings of lymphangioma are typically a homogeneous, thin-walled, well-defined, low-attenuating cystic mass, though increased attenuation occurs with high protein content, hemorrhage, or infection. Calcification or contrast enhancement is atypical. These lesions insinuate and cause displacement as they spread throughout the mediastinum, which also makes complete resection difficult (4). The most common location is the superior aspect of the anterior mediastinum. Other rare locations include the pulmonary hila, pericardium, and intrapulmonary.

Lymphangectasis can present with chylothorax. The imaging findings of lymphangectasis include bilateral ground-glass opacities, smooth interlobular septal thickening, marked pleural thickening, and mediastinal soft-tissue infiltration. The imaging findings resemble those of LAM; however, lymphangectasis presents at a younger age with a much more progressive course (2, 4). LAM has dilated lymphatics like lymphangectasis but also has increased number of lymphatics.

LAM can present with chylothorax. The imaging findings of LAM include diffuse, thin-walled, uniform lung cysts (20). LAM is indistinguishable on imaging from tuberous sclerosis complex. It can cause recurrent pneumothorax.

Treatment

There is increasing evidence that HAART and an improved immune response are associated with complete or partial regression of KS lesions (6, 8, 16). Some studies showed that HAART alone can lead to stabilization and regression of KS, often eliminating the need for chemoradiation therapy (6, 16, 19).

For asymptomatic pulmonary KS, typical treatment is initiated with ART without concomitant chemotherapy. For progression of pulmonary KS after initiation of ART or symptomatic pulmonary KS at presentation, systemic chemotherapy is then generally indicated in addition to ART (11). Radiation therapy has been shown to improve symptomatic control, though long-term survival remains poor (8).

Pleural effusions have been managed with repeat thoracentesis in combination with ART and chemotherapy. If the pleural effusion rapidly reoccurs despite thoracentesis, an indwelling pleural catheter can be installed, or talc pleurodesis performed. Chyloous effusions respond poorly to chemical pleurodesis (21).

Conclusion

KS is a low-grade mesenchymal tumor involving blood and lymphatic vessels. Kaposi’s sarcoma-associated herpes virus (KSHV) infection has been linked along with other factors to the development of KS. KSHV interacts and encodes for numerous molecular proteins that play a role in the pathogenesis of KS, including latency-associated nuclear antigen (LANA), viral G protein-coupled receptor, viral FLICE inhibitory protein, and viral IL-6. KS primarily affects the skin and causes disseminated disease in a variety of organs. Involvement of visceral organs other than the lining of the alimentary tract is extremely rare. While the chyloous pleural effusions of KS may resemble other pulmonary diseases with chyloous effusions at thoracic CT including lymphangioma, lymphangectasis, and LAM, differentiating features may allow for more prompt diagnosis and treatment. The presumptive diagnosis of AIDS-related pulmonary KS is often clinical. A tissue diagnosis is not required to establish the diagnosis of pulmonary KS. There are a variety of causes of chylothorax. The primary finding is a near-water-attenuating pleural effusion on thoracic CT. It is the secondary findings of chylothorax that can help differentiate the etiology.

References

10. Konstantinopoulos PA, Dezube BJ, Pantanowitz L. Morphologic and immunophenotypic evidence of in-


