Pleural and Cutaneous Manifestations of Seronegative Kaposi's Sarcoma in an Elderly Patient: A Diagnostic Challenge Resolved by Thoracoscopy.

Abstract

- **Background:** Kaposi's sarcoma (KS) is a low-grade vascular tumor etiologically linked to Human Herpesvirus 8 (HHV-8). While heavily documented in HIV-positive individuals (epidemic form), KS can also arise in HIV-negative patients, particularly in elderly Mediterranean or Eastern European men (classic form). Pleural involvement in HIV-negative KS is exceedingly rare, often mimicking tuberculosis or malignant pleural mesothelioma, which frequently leads to diagnostic delays.
- **Case Presentation:** We report the case of a 69-year-old male farmer presenting with a one-month history of left-sided pleural pain, progressive dyspnea (mMRC grade II), and profound constitutional symptoms (fatigue, anorexia, significant weight loss). Clinical examination revealed a left pleural effusion syndrome and bilateral, painless lower limb lymphedema associated with purplish skin induration. Laboratory findings highlighted an elevated C-reactive protein (119.40 mg/L) and a negative HIV serology. Thoracic computed tomography and ultrasound revealed a large, multiloculated left pleural effusion with infiltrative pleural masses. Initial blind pleural biopsies and bronchoscopy were inconclusive. Definite diagnosis was established via medical thoracoscopy, which visualized characteristic violaceous, highly vascularized angiomatous nodules and a "powdered" thickening of the pleura. Histopathological analysis of the thoracoscopic biopsies confirmed classic Kaposi's sarcoma, revealing a dense inflammatory infiltrate, slit-like vascular spaces, and spindle cell proliferation.
- **Conclusion:** This case underscores that pulmonary or pleural Kaposi's sarcoma must be considered in the differential diagnosis of exudative pleural effusions, even in strictly HIV-negative patients. Medical thoracoscopy remains the gold-standard diagnostic tool when non-invasive cytological and blind biopsy techniques fail to provide a conclusive diagnosis.

- **Keywords:** Kaposi's Sarcoma, HIV-Negative, Classic Kaposi's Sarcoma, Exudative Pleural Effusion, Medical Thoracoscopy, Vascular Neoplasm.

1. Introduction

Kaposi's sarcoma (KS) is a distinct angioproliferative malignancy derived from endothelial cell lineages, fundamentally driven by infection with Human Herpesvirus 8 (HHV-8), also known as Kaposi's sarcoma-associated herpesvirus (KSHV). Epidemiologically, KS is classified into four distinct clinicopathological variants: epidemic (AIDS-associated), endemic (African), iatrogenic (immunosuppression/transplant-associated), and classic (Mediterranean).

While the epidemic form frequently presents with disseminated mucocutaneous and visceral involvement—including the lungs and gastrointestinal tract—the classic form typically manifests as an indolent, slowly progressive cutaneous disease localized predominantly to the lower extremities of elderly men from Mediterranean, Middle Eastern, or Eastern European descents. Visceral dissemination, particularly pleuropulmonary involvement, is widely considered an exceptional feature in classic, HIV-negative KS.

When pleuropulmonary KS does occur in seronegative individuals, its clinical and radiological presentation is highly non-specific. It frequently masquerades as pleural tuberculosis, parapneumonic empyema, or primary pleural malignancies like mesothelioma. Consequently, clinicians face a major diagnostic dilemma, especially when initial cytological fluid evaluations and blind percutaneous pleural biopsies return negative or inconclusive results.

In this report, we present a rare and diagnostically challenging case of primary pleural Kaposi's sarcoma associated with long-standing cutaneous lesions in a 69-year-old HIV-negative farmer, where definitive diagnosis was successfully achieved through direct visualization and sampling via medical thoracoscopy.

2. Case Presentation

2.1. Patient History and Clinical Examination

A 69-year-old male, a lifelong farmer with a 40-year history of agricultural occupational exposure, presented to our pulmonology department with a one-month history of persistent left-sided pleuritic chest pain. This was accompanied by progressively worsening exertional dyspnea, categorized as grade II on the modified Medical Research Council (mMRC) scale. He reported no cough, hemoptysis, expectoration, or nocturnal sweats, but described a severe deterioration of his general health status, characterized by profound asthenia, anorexia, and substantial unquantified weight loss over the preceding weeks.

His medical history was remarkable only for essential arterial hypertension, well-controlled with irbesartan (ICARD) at a dose of 150 mg daily. He had no history of surgical interventions, no known toxic habits or tobacco smoking, and no known history of immunodeficiency or immunosuppressive therapy.

Upon admission, the patient was conscious, well-oriented, and hemodynamically stable, with a Glasgow Coma Scale (GCS) score of 15/15 and an Eastern Cooperative Oncology Group (ECOG) Performance Status (PS) of 2. Respiratory rate was 18 breaths per minute, and arterial oxygen saturation (SpO_2) was 97% on ambient room air. Physical examination of the respiratory system revealed a classic left-sided pleural effusion syndrome, evidenced by abolished vocal fremitus, dullness to percussion, and absent breath sounds at the left pulmonary base.

Remarkably, a detailed dermatological inspection revealed bilateral, painless, non-pitting lower extremity edema extending above the ankles. This lymphedema was accompanied by structural skin hardening (induration) and a distinct, confluent violaceous-to-purplish discoloration(figure 1) .

2.2. Diagnostic Workup and Laboratory Findings

Baseline laboratory investigations revealed a microcytic hypochromic anemia with a hemoglobin level of 10 g/dL. The white blood cell count was 6,800/μL, with predominant polymorphonuclear neutrophils (PNN at 5,100/μL). Platelet count was within normal parameters. A striking systemic inflammatory response was noted, with a C-reactive protein (CRP) markedly elevated at 119.40 mg/L. Repeated enzyme-linked immunosorbent assays (ELISA) for Human Immunodeficiency Virus (HIV-1 and HIV-2) were strictly negative.

A formal dermatological consultation and dermoscopic evaluation of the lower limb plaques were performed. Dermoscopy revealed characteristic "rainbow patterns" (multicolored shiny zones under polarized light) superimposed on a deep violaceous background, highly suggestive of cutaneous Kaposi's sarcoma (figure 2).

Upon deeper questioning, the patient recalled that a small, asymptomatic purplish plaque had initially appeared on his lower leg roughly 8 years prior, which he had neglected due to its indolent nature.

2.3. Imaging and Initial Interventions

A conventional posteroanterior chest radiograph demonstrated a large left-sided pleural effusion causing a homogeneous opacification of the lower two-thirds of the left hemithorax, along with a secondary homolateral band of passive atelectasis. A subsequent thoracic ultrasound confirmed a voluminous, heavily septated and multiloculated liquid effusion split into several dense fluid pockets.

A contrast-enhanced computed tomography (CT) angiogram of the chest was performed, confirming a massive, multiloculated left pleural effusion associated with thickened, nodular pleural surfaces and infiltrative pleural masses, raising high suspicion for a malignant process.

Diagnostic Tool	**Key Finding / Outcome**
HIV Serology (ELISA)	Strictly NEGATIVE
C-Reactive Protein (CRP)	119.40 mg/L (Highly Elevated)
Dermoscopy (Lower	Rainbow vessels on a violaceous background

Diagnostic Tool	Key Finding / Outcome
Extremities)	(Classic KS)
Chest CT Angiogram	Large multiloculated left pleural effusion with infiltrative masses
Pleural Fluid Analysis	Exudate, 99% lymphocytes, ADA: 15 UI/L, BK negative
Blind Percutaneous Pleural Biopsy	Inconclusive (Non-specific fibrinous and inflammatory remodeling)
Flexible Bronchoscopy	Mucosal thickening at the carina and left bronchial tree (Biopsies inconclusive)
Medical Thoracoscopy	Direct visualization of vascularized, violaceous angiomatous nodules
Histopathology (Thoracoscopy)	Spindle cell proliferation and slit-like vascular channels (**Final Diagnosis**)

A diagnostic thoracentesis yielded a serofibrinous, yellowish-citrine fluid. Biochemical analysis confirmed an exudate characterized by high protein content. Cytological evaluation demonstrated a marked lymphocytic predominance (99% lymphocytes). Adenosine deaminase (ADA) levels were low at 15 UI/L, making pleural tuberculosis highly unlikely. Repeated microscopic examinations and cultures for *Mycobacterium tuberculosis* (Acid-Fast Bacilli/Genexpert) were negative. Two successive sessions of blind percutaneous needle pleural biopsies were performed but yielded inconclusive results, showing only non-specific fibrinous pleuritis and dense inflammatory remodeling without malignant cells.

To rule out endobronchial lesions, a flexible fiberoptic bronchoscopy was carried out. It revealed diffuse mucosal thickening at the level of the main carina and along the left bronchial tree. However, multiple endobronchial biopsies failed to establish a diagnosis, returning only non-specific chronic inflammatory changes.

2.4. Medical Thoracoscopy and Definitive Histopathology

Given the unyielding nature of the initial diagnostic workup and the persistent loculated pleural effusion, the patient was scheduled for a medical thoracoscopy under local anesthesia and conscious sedation.

Upon entering the left pleural cavity and evacuating the loculated fluid, direct thoracoscopic inspection revealed extensive and highly characteristic macroscopic lesions. The parietal and visceral pleura were studded with multiple prominent, highly vascularized, violaceous-to-purplish nodules exhibiting a distinct angiomatous aspect. This was accompanied by diffuse, irregular pleural thickening, dense fibrinous adhesions forming loculations, and a rough, granular, or "powdered" appearance of the pleural surface.

Multiple targeted biopsies were taken directly from these vascularized violaceous nodules. Histopathological examination of the thoracoscopic specimens revealed a dense, polymorphic chronic inflammatory infiltrate mixed with spindle cell proliferation. The tissue featured irregular, slit-like vascular channels dissecting the collagen bundles, extravasated erythrocytes, and areas showing early macular/ulcerated vascular lesions with overlying focal crusts. These findings definitively established the diagnosis of classic pleural Kaposi's sarcoma.

3. Discussion

This case highlights an exceedingly rare clinical entity: extensive pleural dissemination of classic Kaposi's sarcoma in an elderly, immunocompetent, HIV-negative patient. While epidemic KS is renowned for its aggressive visceral involvement, classic KS is typically described as a slowly progressive, benign cutaneous condition restricted to the lower limbs. Visceral involvement in classic KS occurs in less than 10% of cases, and isolated or predominant pleural effusion as the primary presentation is even more exceptional.

The demographic profile of our patient—an elderly male farmer originating from the Mediterranean basin—aligns perfectly with the known geographical distribution of classic KS and HHV-8 seroprevalence. Agriculture and frequent exposure to soil have been proposed in several epidemiological studies as potential environmental cofactors that may promote HHV-8 reactivation or alter local skin immunity, which is highly relevant given our patient's 40-year history as a farmer.

The pathogenesis of KS in HIV-negative patients remains centered on chronic HHV-8 infection. In classic KS, aging is associated with a physiological decline in T-cell-mediated immunity (*immunosenescence*). This mild, age-related immune impairment, potentially coupled with chronic local inflammation (as evidenced by our patient's highly elevated CRP of 119.40 mg/L), can disrupt the latency of HHV-8, driving endothelial proliferation, angiogenesis, and spindle cell transformation.

Diagnosing pleural KS in an HIV-negative patient is notoriously difficult due to its ability to mimic other exudative pleural diseases. Clinically, the presentation of pleuritic pain, exertional dyspnea, and constitutional weight loss strongly echoes pleural tuberculosis or a primary thoracic malignancy. In our case, the exudative nature of the fluid with 99% lymphocytic predominance initially steered suspicions toward tuberculosis, although the normal ADA levels (15 UI/L) and negative bacteriological assays disputed this hypothesis.

Furthermore, conventional diagnostic modalities show poor sensitivity for pleural KS. Pleural fluid cytology is almost always negative for malignant cells because KS is a vascular interstitial tumor rather than an epithelial malignancy shedding cells into the fluid. Blind percutaneous pleural biopsies routinely fail because they sample tissues at random, missing the specific vascular nodules scattered across the pleura. This diagnostic failure was clearly observed in our patient, where multiple blind biopsies and bronchoscopic samplings returned non-specific inflammatory results.

Ultimately, medical thoracoscopy proved to be the decisive diagnostic tool. It allowed direct, clear magnification and visualization of the pleural space, revealing the unmistakable macroscopic signatures of Kaposi's sarcoma: hypervascular, violaceous angiomatous nodules and a granular, "powdered" pleural surface. Most importantly, it enabled precise, targeted biopsies of these vascular lesions, avoiding sampling errors and providing the pathologist with adequate tissue architecture to confirm spindle cell proliferation and vascular slits.

4. Conclusion

Classic Kaposi's sarcoma can present with severe, life-threatening visceral complications, including massive exudative pleural effusions, even in the complete absence of HIV infection or iatrogenic immunosuppression. Clinicians must maintain a high index of suspicion and perform a thorough mucocutaneous examination—looking for long-standing indurated, violaceous plaques or lower limb lymphedema—in any elderly patient presenting with an unexplained exudative pleural effusion.

When cytological fluid analyses and blind percutaneous needle biopsies prove inconclusive, early recourse to medical thoracoscopy is vital. It represents the gold standard for directly visualizing characteristic angiomatous pleural lesions and obtaining definitive histopathological confirmation, thereby preventing critical diagnostic delays.

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Figure Legends :

Figure 1: Cutaneous manifestations of classic Kaposi's sarcoma. *Legend:* Confluent violaceous and purplish indurated plaques with bilateral lymphedema on the lower extremities of the 69-year-old patient.

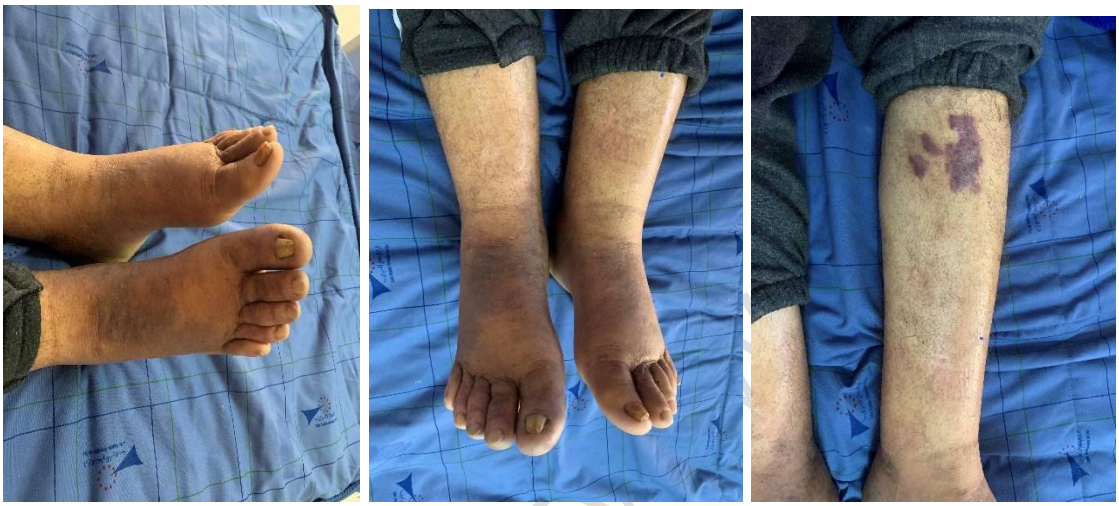

Figure 2: Dermoscopic evaluation of the lower limb skin lesions. *Legend:* Polarized dermoscopy showing characteristic "rainbow patterns" and multicolored shiny zones superimposed on a diffuse violaceous background, highly specific for Kaposi's sarcoma vascular proliferation.