中文題目：肺腺癌併發卡波西氏肉瘤之個案報道

英文題目：A case Pulmonary Adenocarcinoma with Kaposi Sarcoma

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Abstract:

We report the case of a 57 year old HIV negative woman with a diagnosis of pulmonary adenocarcinoma and multiple metastases, who received several cycles of systemic chemotherapy. Subsequently, we detected progressively growing cutaneous lesions over bilateral distal lower extremities. Histology revealed a diagnosis for Kaposi Sarcoma. No specific treatment was given, and her malignancy was controlled with Gefitinib (Iressa). Gradual regressions of the cutaneous Kaposi sarcomas were observed. Immunosuppressoin contributed to the development of Kaposi sarcoma; withdrawal of immunosuppressive therapy led to regression of the Kaposi sarcoma.

Introduction:

Kaposi sarcoma (KS) is characterized by the abnormal proliferation of vascular and endothelial cells. First described in 1872 by Moritz Kaposi, this low grade vascular neoplasm is now classified into four variant types, including classic, endemic, immunosuppression or transplantation associated and AIDS-associated. The human herpesvirus 8 (HHV 8) is present in KS. Alteration of host immunity upon disease, or by means of therapy may cause the occurrence of KS.

Case Report:

A 57 year old female with type 2 diabetes mellitus, worked as a farmer and without history of smoking. She presented with dyspnea for one month, particularly on exertion. There were no symptoms of cough, hemoptysis, chest pain or weight loss. A left sided pleural effusion and an irregular mass detected over the left lung field on chest x-ray (Fig. 1). Sputum microbial studies including tuberculosis and acid fast stains were negative. Chest CT scans confirmed the irregular mass at the left upper lobe; pericardial effusions and mediastinal lymph nodes were also evident. Cytology for both pleural and pericardial effusions reported adenocarcinoma. Multiple bone metastases detected over multiple ribs, skull, thoracic spine and pelvic bone regions. She was diagnosed of pulmonary adenocarcinoma with metastases, cT2N3M1, stage IV. Subsequently, brain metastases manifested itself in the form of seizures and were documented on Brain CT. Four courses of Cisplatin and Docetaxel were administered

after which we maintained her cancer treatment primarily with oral Gefitinib (Iressa), a selective inhibitor of epidermal growth factor receptor (EGFR). During her hospitalization, we noted the occurrence of cutaneous lesions over her bilateral plantar feet. The blue-purplish pigmented nodules, one on each sole of her feet appear to be grossly identical; they were firm, rounded, well-defined, and mildly erythematous. On her left foot, the nodule was located on the medial edge of the sole, measured at about 1.5 cm in diameter (Fig.2). The nodule on her right sole was larger, measure at about 2.5 cm in diameter (Fig.3). Both lesions were not painful. An incisional biopsy was performed with the nodule on her left sole. Microscopically, it showed a picture of Kaposi's sarcoma (Fig. 4), with well-defined nodules of intersecting fascicles of spindle cells with numerous slit-like vascular spaces containing red blood cells. Hyaline globules were found inside and outside the spindle cells, highlighted by PAS stain. In immunohistochemical study, the neoplastic cells show positive for CD31 and HHV-8 (Fig. 5). According to the features, KS was diagnosed. Serology for the Human immunodeficiency virus was negative. There were no new developments of lesions. Gefitinib was used continuously and no other specific interventions were directed at her KS. The KS lesionsgradually formed ulcers and hardened before detaching to reveal new skin growth.

Discussion:

In 1969, the first case of immunosuppression KS was diagnosed in a renal transplant patient. It is now clear that KS may develop in organ-transplant recipients and in patients who are receiving immunosuppressive therapy. Cutaneous KS typically manifests as lesions of bluish-red colored, well demarcated, painless, dermal patch, maculae, plaques, or even nodules or tumor like in distal lower extremities. Histology shows spindle cell tumors, in combination with the proliferation of abnormal and leaky vessels, slit-like vascular clefts, and extravasated erythrocytes, as well as hemosiderins from older haemorrhages. Inflammatory infiltrates are also notable. HHV8 is also known as the Kaposi sarcoma-associated herpesvirus (KSHV). Virtually, all KS are thought to contain KSHV.

The virus infects endothelial cells, causing changes in its morphology, biochemistry and cellular process, including metabolism, gene expressions, cell cycles and ultimately, oncogenicity. KSHV infection is necessary but not the sole cause of KS. Other factors are crucial for KS development including HIV or drug induced immunosuppression. As with the presented case, immunosuppression was induced by systemic chemotherapy, and subsequently causing development of KS in her lower extremities. Immunosuppression KS is well known in organ transplants recipients, but sporadically reported in other medical condition or circumstances. Immunosuppressed

KS had been reported in chronic steroid usage, such as in SLE and bullous pemphigoid. In 1996 Kato *et al*., reported a 65-year-old Japanese woman with KS, similarly, the lesions occurred on the legs while she was treated for lung cancer. Steroids were used for control of inflammation. They reported that immunosuppression caused KS in that setting. KS treatment includes radiation and systemic therapy for advanced diseases. In many cases of immunosuppressed KS, lesions regress upon withdrawal, reduction or modification of immunosuppression. Our case reflects that withdrawal of immunosuppression has successfully caused the regression of KS; and Gefitinib might had a role in the process as a growth factor inhibitor. Recent researches led to the better understanding of the pathogenesis of KS and the KSHV. New therapeutics potentially target at inhibiting angiogensis and other growth factors.

Figure 1

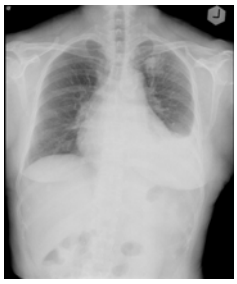

Figure 2

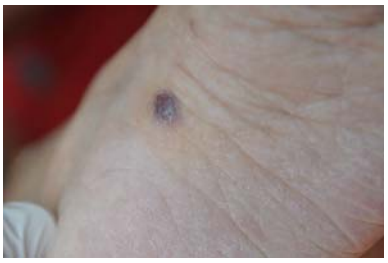

Figure 3

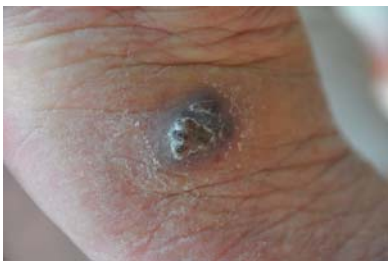

Figure 4

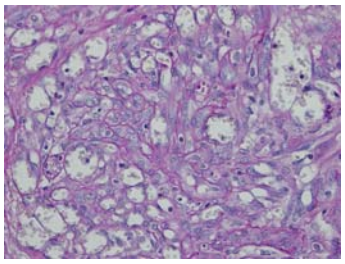

Figure 5