Case 16

A 29-year-old Thai male from Bangkok

Chief complaint: Progressive multiple violaceous nodules on face, trunk, extremities and oral mucosa for 2 weeks.

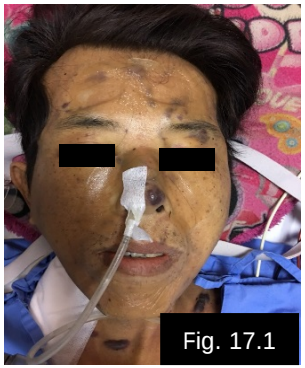

Fig. 17.1

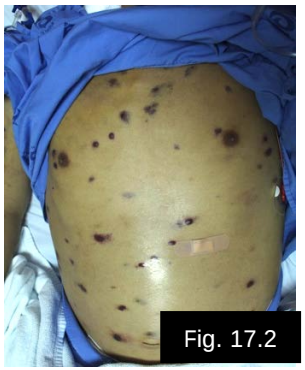

Fig. 17.2

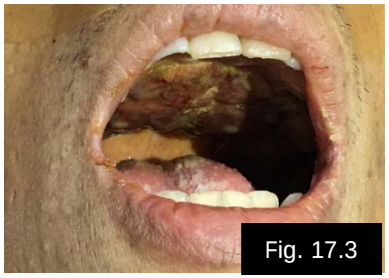

Fig. 17.3

Present illness:

The patient was diagnosed with AIDs and smear negative pulmonary tuberculosis on June 2018 presented with chronic cough. He had received anti TB drug (IRZE) treatment since first diagnosed and antiretroviral therapy (HAART regimen; TDF/3TC/EFV) was initiated 2 weeks later. The disease was stable for 3 weeks.

One month after initiation of HAART, the patient began to subsequently experience progressively severe dyspnea and abrupt onset of multiple violaceous papulonodular skin lesions. He was admitted to another hospital for 2 weeks and then transferred to our hospital due to worsening of the rash and progressive dyspnea.

Past history: Underlying disease: AIDs, smear negative pulmonary TB, late latent syphilis (complete treatment)

Physical examination:

- General appearance: A Thai male, co-operative, mark dyspnea
- HEENT: Moderate pale conjunctivae, icteric sclerae, oral thrush
- Heart: Normal S1S2, no murmur
- Lung: Coarse crepitation both lung
- Abdomen: Soft, not tender, abdominal distension, hepatosplenomegaly
- Lymph node: Cervical lymph node enlargement size 1*1 cm matted axillary lymphadenopathy size 4*2 cm
- Extremities: Pitting edema 3+
- NS: No facial palsy, motor power grade V all extremities
- PR: Melena

Dermatological examination (Fig. 17.1, 17.2, 17.3):

- Multiple violaceous papulonodules and thin plaques on face, trunk and extremities
- Erythematous plaque with yellowish slough on hard palate

Histopathology: (S18-028562, chest wall) (Fig.17.4)

- Proliferation of atypical spindle cells, numerous erythrocytes, admixed with some plasma cells. Atypical vascular channels with jagged border are noted and dissect between collagen bundles.
- Special stain (AFB, Fite, Brown & Brenn, GMS, PAS): negative
- Tissue C/S for Aerobe, TB, fungus: negative
- Tissue PCR for TB, 16s, 18s: negative

Immunohistochemistry

- HHV-8 nuclear staining: positive

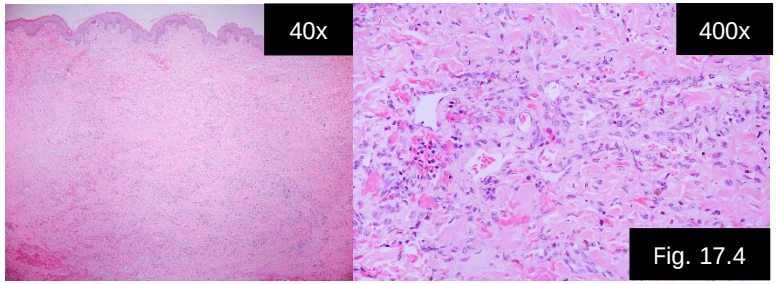

Fig. 17.4

Laboratory investigations:

- CBC: Hb 7.2 g/dL, Hct 21.3%, Plt 70,000 /mm^3, WBC 8,800 /mm^3 (N79%, L11%, M 6%, Band 2%, myelocyte 2%)
- CD4: 8 cell/ul (1%)
- Liver function test: AST/ALT 55/12 U/L, ALP/GGT 411/815 U/L, TB/DB 5.4/4.7 mg/dL
- BUN/Cr: 73/2.92 mg/dl
- U/S abdomen: A large infiltrative hyperechoic lesions with multiple small hyperechoic nodules involving periportal areas of both hepatic lobes
- Bronchoscopy: Infiltrative dark red patch from vocal cord to bilateral main bronchus and tertiary bronchus
- Bronchoalveolar lavage (BAL):
    - G/S, AFB, mAFB, GMS: negative
    - C/S for aerobe, TB, fungus: negative
    - PCR for TB, 16s, 18s: negative

Diagnosis: Immune reconstitution inflammatory syndrome associated with Kaposi sarcoma (pulmonary, intestine, liver, cutaneous & mucosa)

Treatment:

- Systemic CMT: paclitaxel (80 mg/m^2) 140 mg
- Continue anti-retroviral drug

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Discussion:

Kaposi sarcoma (KS) was first described by Hungarian dermatologist, Moritz Kaposi, in 1872.[1] It is one of the most common malignancy in human immunodeficiency virus (HIV) patient. KS is characterized by spindle cell proliferation, abnormal neoangiogenesis, inflammation, and edema.[2]

The exact pathogenesis of Kaposi sarcoma is not fully understood. Most study suggested Kaposi sarcoma – associated herpesvirus (KSHV) infection, especially HHV-8, promotes angiogenesis and inflammation through an autocrine and paracrine mechanism.[2,3]

There are four different types of KS.[4] The classic type mainly occur in elderly people of Mediterranean and eastern European. People typically have lesions on the lower extremities and have good prognosis.[1,4,5]The endemic African type occur in people living in Equatorial Africa. This type is more aggressive in children. KS due to iatrogenic immunosuppression is generally clinically similar to classic KS. Stopping the immunosuppressive drug often make lesion decrease or disappear. And lastly, AIDs-related KS most commonly affect HIV-infected patients with a low CD4 count, especially < 100 cell/cubic millimeters and high viral load count of > 10,000 copies/mL.[6] Clinical feature of KS in HIV patients are variable, some patient affect only single lesion, others involve whole skin, mucous membrane, lymph node and internal organs such as stomach, gut, lung or liver.

Our patient had a disseminated form of KS which involved the skin, mucosa, pulmonary and GI tract. The rapid progression in this patient could be explained by an Immune reconstitution inflammatory syndrome (IRIS)-related process. IRIS is a condition of inflammatory disorder associated with paradoxical worsening of pre-exciting infection or neoplasm such as Kaposi's sarcoma following the

initiation of highly active antiretroviral therapy (HAART).[7] KS-IRIS was diagnosed in patients receiving HAART regimen with a reduction of at least 1 log10 of HIV-1 RNA and/or an increase of > 50 cells/cubic millimeters or > two fold rise in baseline CD4+ cell count with an abrupt clinical worsening of previously existing KS (paradoxical IRIS KS) or new development unknown KS (unmasking IRIS KS) within the first 6 month after the initiation of HAART.[6,9] The supportive evidence of IRIS-KS in our patient was the temporal relation between rapid clinical progression of KS after initiation of HAART regimen.

Regarding treatment, HAART should be combined with cytotoxic chemotherapy in patients with rapidly progressive disease or with visceral disease or lymphedema. The most common recommended chemotherapy is pegylated liposomal doxorubicin hydrochloride (230 mg/m2 body surface), which used every 2 or 3 weeks in 6-8 cycles with 80% complete remission rate. Another drug is paclitaxel (100 mg/m2 or 135 mg/m2 body surface), which used every 2 weeks or every 3 weeks respectively and has shown similar response rate.[2]

Although IRIS-related KS represents only a fraction of the IRIS cases, it can be a life-threatening situation. Paclitaxel and HAART were given in our patient, however his condition progressively deteriorated and he died within 3 days after receiving chemotherapy with good supportive care.

References:

1. Cheng CH, Hsu YH. Immune reconstitution inflammatory syndrome-associated disseminated Kaposi's sarcoma in a patient infected with human immunodeficiency virus: Report of an autopsy case. Ci Ji Yi Xue Za Zhi.2017;29:41–5
2. Hoffmann C, Sabranski M, Esser S: HIV-Associated Kaposi's Sarcoma. Oncol Res Treat.2017;40:94-8
3. Schneider, Johann W, and Dirk P Dittmer. “Diagnosis and Treatment of Kaposi Sarcoma.” Am J Clin Dermatol.2017;18:529-39
4. Curtiss P, Strazzulla LC, Friedman-Kien AE. An Update on Kaposi's Sarcoma: Epidemiology, Pathogenesis and Treatment. Dermatol Ther.2016;6:465–470
5. Bulent Cetin, Bilge Aktas, Oznur Bal et al. Classic Kaposi's sarcoma: A review of 156 cases, Dermatologica Sinica, 2018;36:185-9
6. Andy Sing Ong Tang, Yeon Chiat The et al, Disseminated AIDS-related Kaposi’s sarcoma, Oxford Medical Case Reports: 2018;12,452-4
7. Letang E, Lewis JJ, Bower M et al. Immune reconstitution inflammatory syndrome associated with Kaposi sarcoma: higher incidence and mortality in Africa than in the UK. AIDS.2013; 19:1603-13
8. Mehta S, Garg A, Gupta LK, Mittal A, Khare AK, Kuldeep CM. Kaposi's sarcoma as a presenting manifestation of HIV. Indian J Sex Transm Dis AIDS.2011;32:108–10.
9. Volkow P, Cesarman-Maus G, Garciadiego-Fossas P, Rojas-Marin E et al. Clinical characteristics, predictors of immune reconstitution inflammatory syndrome and long-term prognosis in patients with Kaposi sarcoma. AIDS Res Ther.2017;14:30.