INTRODUCTION
Cutaneous leishmaniasis (CL) caused by obligate intracellular protozoa of the genus *Leishmania* and transmitted by the sandfly, *Phlebotomus* in the Old World. CL is one of the four different forms of the disease; the other three being visceral leishmaniasis (or Kala-azar), mucocutaneous leishmaniasis and diffuse mucocutaneous leishmaniasis. The Province of Balochistan located in the western part of Pakistan, is one of the endemic areas for CL, where it is caused by *Leishmania tropica*. CL manifests as single or multiple papules, nodules or plaques, which are non-itchy, painless and with or without ulceration, usually over exposed areas of body. Once infected with CL the chances of re-infection by the same species of *Leishmania* are very unlikely, due to lifelong immunity.

We are reporting three cases of CL who were found to be suffering from co-existent HIV infection.

CASE REPORT
Case 1: A 40 years old male, married with 4 children, resident of Balochistan came through the OPD of Civil Hospital, Karachi, in February 2012, with black crusted lesions on his left hand later spreading to the rest of his body, for last one year. He attributed these lesions to the bite of a fly. There were no aggravating or relieving factors; he had difficulty in eating and swallowing. There were no associated features. There was no history of intravenous drug abuse, blood transfusion or previous surgery. He had sexual relations with other women when he lived in Dubai 9 years ago. He was admitted and treated in Quetta (Balochistan) for similar lesions. Recently, he had lost appreciable weight within a year.

On examination, he had ulcerated, indurate lesion on the left hand about 5 x 4 cms in diameter (Figure 1). He had black crusted lesions all over the body appearing erythematous at various places and annular. On his face, he had black raised maculopapular lesions, his nose had a saddleback appearance deviated to the right, with crusty debris filled nares, and similar crusted lesions on both lower limbs (Figure 2). He had deep ulcer on ventral aspect of his tongue with eroded lesions and a few vesicles, with white coating on his palate. His teeth were mostly black, with dry crusty lips. His genitals also had maculopapular lesions on the scrotum and corona sulcus. Other systemic examination was normal.

His Hb at the time of admission was 8.00 gm/dl, a TLC count of 2,600/ul, lymphocytes 06%, monocytes 08%. Suspecting leishmaniasis with syphilis, his biopsy was taken from multiple sites and his RPR and TPHA tests were done which were non-reactive. His biopsy revealed features compatible with cutaneous leishmaniasis, with no evidence of granuloma or malignancy. His HIV serology was positive. His CD4 count (15) revealed stage IV disease. He was started on meglumine antimoniate and antiretroviral therapy and his lesions began to improve.

His ultrasound of the abdomen showed liver with focal fatty infiltrates, the granulomatous obstruction causing increase in alkaline phosphatase. He was transfused 3 pints of packed cells. The patient improved gradually and decided to go home. He was advised to continue his ARV therapy and complete the course of 28 days of I/G meglumine antimoniate. He has not yet returned to the OPD.

Case 2: An 18 years old female, married for last one year with no issue, resident of Balochistan came to the OPD...
OPD with crusted, ulcerated lesions on both arms and forearms for last one year and fever for 3 days. Biopsy reported positive for cutaneous leishmaniasis. She improved on meglumine antimoniate and was discharged. After 5 months, she was readmitted with recurrence of lesions at the same site and similar morphology as previously. She had generalized weight loss, 7 kg in 5 months with diarrhea, 6 - 7 episodes in a day. Systemically, she was found to have hepatosplenomegaly, with left sided pleural effusion. Her initial work up for disseminated tuberculosis was done and turned out to be negative. Patient refused liver biopsy and pleural tap. At this time, HIV was suspected despite no prior history of multiple sexual partners, blood transfusions, or surgical procedures. She was found to be HIV positive on ELISA, with CD4 count of 20. ARV therapy was started with the consent of HIV and infectious disease control departments along with meglumine antimoniate. Patient responded well and her diarrhea subsided and the lesions healed. Her CD4 count, however, did not improve; she was discharged but she expired.

**Case 3:** A 25 years unmarried male patient, with multiple sexual partners, resident of province of Balochistan, admitted in medical ward with severe weight loss and diarrhea; with thick crusted lesion at the base of the nose. He was HIV positive with smear positive for leishmaniasis and CD4 count of 60. This patient was just given initial treatment but expired without further workup.

### DISCUSSION

Leishmaniasis is endemic in many parts of the world. In cases of leishmaniasis in adults, a very important co-factor for reactivation of the disease is a co-infection with Human Immunodeficiency Virus (HIV), which along with malnutrition is a very important source of worsening of leishmaniasis. In such patients, leishmaniasis appears with a decrease in immunity as HIV advances, with most of the patients having a CD4+ count of less than 200 cells/mm³. Individuals having visceral leishmaniasis (VL) and HIV co-infection experience a higher incidence of drug toxicities, increased number of relapses and a higher mortality. HIV-infected immunodeficiency patients with leishmaniasis usually show multiple disseminated and atypical cutaneous lesions, which exhibit poor response to the established treatment with frequent relapses. Data suggests an association of CL and HIV/AIDS from different countries in the last two decades. Currently, the standardized treatment of CL for immunocompetent patients is either intralesional or systemic antimonials, however, HIV-infected patients have also shown a good response to antimonials, and very rare reports of resistance, if any.

Both the diseases (leishmaniasis and HIV) infect and multiply in monocytes, and in the case of a co-infection, there is a mutual replication of both in host cells. In fact, a leishmaniasis infecting myeloid cells promotes HIV replication while HIV in turn, promotes an uptake of leishmaniasis by macrophages and amplifies parasitic replication in monocytes. In VL, clinical features (weight loss, fever, hepatosplenomegaly etc.) are similar in patients with a HIV co-infection and patients without such co-morbidity. However, there are a number of certain clinical features that are more specific to patients having a co-infection of leishmaniasis with HIV including atypical parasitic location, multiple relapses, and skin involvement (cutaneous leishmaniasis [CL]). Does not follow a particular pattern of appearance, and may become evident before or after the visceral lesions, occurring as a result of reactivation after a dormant infection or as a result of dissemination after a previous infection. CL shows a remarkable variety in appearance in a patient with HIV, and includes macules, papules, nodules or even ulcers.

In the Old World, CL is caused by *Leishmania tropica*, *Leishmania major*, *Leishmania infantum* and *Leishmania aethiopica*. Multiple scattered lesions over different areas of the body can be due to multiple bites of sandfly in an immuno-competent person, but are usually associated to an underlying deficiency in cellular immunity. These cases were having typical papulonodulo-ulcerative lesions of CL without systemic symptoms except one of the patients; they were diagnosed as cases of localized or disseminated CL which is endemic in this region. These patients responded to treatment satisfactorily but relapsed with lesions re-appearing at the same site; Hence, HIV infection was diagnosed and found to be positive. CL usually responds well to systemic or intralesional antimonials and relapses are uncommon in immuno-competent patients. In fact, even in co-infected patients, antimonal treatment is effective and resistance is very rarely reported. The co-infection causes complex immunological disturbances in the patients, both by HIV and *Leishmania*, which may be the reason of relapse in first 2 cases presented. This report indicates that CL may be the first manifestation of HIV infection, particularly in endemic areas.

Thus, to conclude, patients presenting with leishmaniasis and sudden onset of weight loss, with or without systemic symptoms, should be considered for HIV with leishmaniasis.
REFERENCES