Clinical patterns of cutaneous tuberculosis at King Fahad Hospital of the University in Al-Khobar, Saudi Arabia over 13 years

Iqbal A. Bukhari, *MBBS, FD (KFU).*

Cutaneous tuberculosis is commonly seen in developing countries, and its incidence is increasing in developed countries, including the United States, and some European countries. In 2005, WHO estimated the incidence of tuberculosis in the Kingdom of Saudi Arabia to be 41.4 per 100,000 per year.[1] Cutaneous tuberculosis is classified into 3 main clinical types. The first type is cutaneous inoculation with *Mycobacterium tuberculosis (M. tuberculosis)* producing a wart-like lesion containing few organisms (paucibacillary), called tuberculosis verrucosa cutis, and it occurs in the presence of a high level of immunity. The other extreme of this form is when there is low immunity producing a solitary ulcer, which contains many organisms (multibacillary) called tuberculous chancre. The second type is produced by direct spread to the skin from a contiguous structure. It is most commonly represented by scrofuloderma, which is a paucibacillary form arising secondary to lymph node tuberculosis in the neck. It presents with a purplish, and infiltrated plaque over the lymph nodes with ulceration, and it occurs when the level of immunity is high. The other extreme of this is orificial tuberculosis, which presents with ulcers around the perianal region, and it occurs when the level of immunity is low. The final form is caused by dissemination to the skin following spread through the blood stream with the presence of poor host immunity represented by miliary tuberculosis, which is multibacillary presenting with widely distributed papules, and pustules over the skin. But, when the level of immunity is high, the clinical form is called lupus vulgaris, which is a solitary plaque often on the face and neck.[2] Cutaneous tuberculosis is a challenge for dermatologists in developing countries since patients can not afford the costly medicines with a lack of rapid diagnostic procedures making the problem difficult to control. The objective of this study was to present our clinical experience with cutaneous tuberculosis in our Dermatology Department of King Fahad Hospital of the University in Al-Khobar, Saudi Arabia between January 1995 to December 2007.

This prospective study was conducted from January 1995 to December 2007 in the outpatient clinic of the Dermatology Department of King Fahad Hospital of the University in Al-Khobar, which is a tertiary care referral hospital in the Eastern region of Saudi Arabia. All suspected cases of cutaneous tuberculosis or enlarged cervical lymph nodes were collected. Informed patient's consent was received from all study participants. Patients were carefully examined, and systemically evaluated. The Bacille Calmette-Guerin (BCG) scar was reported if present. Laboratory tests including complete blood count, liver function, renal function tests, urine analysis, stool analysis, culture of abscess content, chest x-ray, and purified protein derivative test (PPD) were carried out. Skin punch biopsy was carried out for patients with skin lesions, while lymph node biopsy was carried out for patients with cervical lymphadenopathy by the surgeon. Biopsy samples were fixed in 10% formalin for the hematoxylin-eosin and Ziehl-Neelsen staining. The final diagnosis of tuberculosis was assessed mainly on a clinical and histopathological basis. Antituberculous treatment was started for all the patients, which consisted of isoniazid, rifampicin, ethambutol, and pyrazinamide, with the addition of pyridoxine supplement to all the patients. The local committee of biomedical ethics approved this study. There were 7 cases of tuberculosis that were seen either as new cases or as consultations from other departments to our Dermatology Clinic at King Fahad Hospital of the University during the 13 year period. Their ages ranged from 16 years to 63 years. All were females. Four were Saudis, 2 Indonesians, and one Filipino. The duration of the lesions ranged between 1.5 months to 4 years. The clinical types were 2 cases of miliary tuberculosis, one case of lupus vulgaris, one case of tuberculosis verrucosa cutis, one case of tuberculous abscess with soft tissue tuberculosis, and 2 cases of tuberculous lymphadenopathy.

There were no signs suggestive of systemic involvement in any patient besides the presenting lesion. The BCG scar was confirmed in 2 patients. Purified Protein Derivative test was positive in 4 patients, negative in one, and not carried out in 2 patients. The clinical details of each patient are shown in **(Table 1)**. There was no patient with tuberculosis cutis orificialis or tuberculous chancre, and no patient had the possibility of active foci of tuberculosis in the lungs suggested by the normal plain chest x-ray. There was one case with lumbar area and anterior chest wall soft tissue tuberculosis with abscess formation. Histopathologically, skin biopsies showed granulomas, either tuberculous with caseation or tuberculoid with no caseation. Sections from miliary tuberculosis showed tuberculoid granulomas with epithelioid cells, multinucleate Langhans giant cells, and other inflammatory cells. Sections from the lupus vulgaris patient showed tuberculoid granulomas with lymphocytes, epithelioid cells, and multinucleated Langhans giant cells with other inflammatory cells as lymphocytes, and plasma cells. Sections from lupus verrucosa cutis were hyperkeratotic, acanthotic,

Table 1 - Patients clinical and histopathological details.

Parameters	Patient number						
	1	2	3	4	5	6	7
Age (years)	16	35	63	32	33	47	32
Gender	F	F	F	F	F	F	F
Nationality	Saudi	Indonesian	Saudi	Filipino	Saudi	Saudi	Indonesian
Duration of lesion	4 years	1.5 years	2 months	2 months	1.5 months	2 months	2 months
Morphology	Papules, pustules, nodules	Erythematous papules, pustules, nodules	Bilateral erythematous plaques	Verrucous dry hyperpigmented raised plaque	Deep abscess of 3 cm in diameter	none	none
Clinical type	Miliary tuberculosis	Miliary tuberculosis	Lupus vulgaris	Tuberculosis verrucosa cutis	Tuberculous abscess	Tuberculous lymphadenopathy	Tuberculous lymphadenopathy
Site	Upper and lower limbs	Trunk, upper and lower limbs	Both cheeks	Dorsum of left foot	Abscess in the upper anterior chest wall and lumbar area	Bilateral cervical and right axillary lymphadenopathy	Left cervical lymphadenopathy
Systemic involvement	No	No	No	No	Tuberculosis of anterior chest wall and soft tissue tuberculosis of lumbar area	No	No
Lymphadenopathy	No	No	No	No	Left cervical	Bilateral cervical and right axillary	Left cervical
Any significant lab test	None	None	None	None	Culture of abscess aspirate +ve for Mycobacteria tuberculosis	None	None
Biopsy H&E	Tuberculoid granuloma	Tuberculoid granuloma	Tuberculoid granuloma	Tuberculoid granuloma	Cancelled	Lymph node biopsy Positive for tuberculous granuloma	Lymph node biopsy Positive for tuberculous granuloma
ZN stain	Negative	Negative	Negative	Negative	-	Negative	Negative
PPD results	Positive 20 mm with blister	Positive	Positive	Not carried out	Negative	Not carried out	Positive
BCG scar	Detected	Not detected	Not detected	Not detected	Detected	Not detected	Not detected

HE - hematoxylin-eosin, ZN - Ziehl-Neelsen, PPD - Purified Protein Derivative, BCG - Bacille Calmette-Guerin

papillomatous, and pseudoepitheliomatous with epithelioid cells, and giant cells. While lymph node biopsies showed typical tuberculous caseating granulomas, we could not locate acid-fast bacilli with ZN stain in all sections. Polymerase chain reaction (PCR) was not carried out since it was not available.

There is considerable variability in the clinical presentation of cutaneous tuberculosis depending on factors such as sensitization and immune reactivity of the host, route of infection, and pathogenicity of the infecting mycobacterial strain. In our study, we reported 7 cases of tuberculosis of which 4 were purely cutaneous. The age of the patients was mainly in the second, and fourth decades, and all the patients were females with good standard of living conditions in the city. A possible explanation is that females are expected to seek medical advice later than males due to their commitment to care for their families and housework. In a study carried out in Pakistan,[3] 90% of cutaneous tuberculosis occurred in poor farmers' families, children aged between 2 and 6 years, and those who are immunologically deficient. The nationality of our patients was mainly Saudi, but non-Saudis also contributed to this problem since they are coming from poor Asian countries where the disease is prevalent. Although we have seen different types of cutaneous tuberculosis; military tuberculosis, lupus vulgaris, and tuberculosis verrucosa cutis, we were not able to comment on the most predominant clinical type due to the small number of cases. Reports from the Western countries, and Hong Kong have shown

high prevalence rates of lupus vulgaris.[4] None of our patients had any signs suggestive of pulmonary or extrapulmonary tuberculosis supported by the negative laboratory results. However, this does not explain the occurrence of miliary tuberculosis, and lupus vulgaris in our patients. In fact, all investigations for tuberculosis including chest x-ray are not a 100% conclusive, which means missing a focus is possible. In a Turkish study,[5] the association between cutaneous involvement with tuberculous lymphadenitis was much stronger than with pulmonary infection (44% versus 3%). Further, we did not find any of the tuberculid reactions, which are immunologically mediated such as erythema nodosum, erythema induratum, lichen scrofulosorum, and papulonecrotic tuberculid. To complete our diagnosis, detection of mycobacterium bacilli in the tissue, caseating necrosis in the HE sections, and positive culture was important. In our specimens, we were able to see the tuberculoid and tuberculous granulomas with caseating necrosis, but we were not able to find the acid fast bacilli in all the sections. In fact, most cutaneous tuberculosis lesions contain few bacilli and many studies reported that ZN staining was negative in their cutaneous tuberculosis specimens. Intradermal test with PPD does not distinguish active and previous tuberculosis infections even in normal persons due to previous exposure to the BCG vaccination. So, it does not indicate active tuberculosis except with other diagnostic findings.

In our study, PPD was positive in only 3 patients but the clinical, and histopathogical observations confirmed the diagnosis. Positive culture is the single most important method for the definite diagnosis of mycobacterial infection, which was positive in the abscess fluid of one patient with soft tissue tuberculosis. However, amplification of mycobacterial DNA using PCR permits rapid detection of *M. tuberculosis* complex DNA in formalin-fixed, paraffin-embedded tissue samples from different lesions of cutaneous tuberculosis. This procedure may be complicated by several sources of technical errors and difficulties affecting the results. Besides, it is costly, which makes it not practical in the laboratories of developing countries. In our study, we could not do it since it was not available. Another important issue in tuberculosis is the multidrug-resistance. The reasons for the rise in resistance are complex, and include the use of inadequately supervised treatment regimens, overcrowding, and predisposing underlying diseases. In our patients, we found only one case whose Mycobacteria bacillus was resistant to isoniazid. So, rushed accurate diagnosis, early supervised treatment, and proper knowledge of the country trends should be undertaken to prevent the problem of resistance and spread. Finally, Saudi Arabia has implemented a national antituberculosis screening program since the year 1989, which aimed at discovering new cases of active tuberculosis, and providing free treatment for them. Over the past few years, this program has proven its efficacy at reducing this chronic infection.

In conclusion, this study reports the occurrence of different clinical forms of cutaneous tuberculosis in a tertiary care hospital in the Eastern part of Saudi Arabia. Although the country is striving to control this communicable chronic infection, it is still a prevalent disease in certain remote areas. These untreated chronic cases account for the ongoing reported occurrence of different forms of the disease. However, further reports from other regions of Saudi Arabia are needed to document the true incidence, risk factors, and common clinical types for better approach of the problem.

Received 1st December 2008. Accepted 9th February 2009.

From the Department of Dermatology, King Faisal University and King Fahad Hospital of University, Dammam, Kingdom of Saudi Arabia. Address correspondence and reprint requests to: Dr. Iqbal A. Bukhari, Associate Professor and Consultant Dermatologist, Dermatology Department, King Faisal University and King Fahad Hospital of University, PO Box 40189, Al-Khobar 31952, Kingdom of Saudi Arabia. Tel. +966 (3) 8957886. E-mail: consultant@dermatologyclinics.net

References

1. WHO. The World Health Report. Geneva (Switzerland): ***World Health Organization*** 2007.
2. Hay RJ. Cutaneous infection with Mycobacterium tuberculosis: how has this altered with the changing epidemiology of tuberculosis? ***Curr Opin Infect Dis*** 2005; 18: 93-95.
3. Bhutto AM, Solangi A, Khaskhely NM, Arakaki H, Nonaka S. Clinical and epidemiological observations of cutaneous tuberculosis in Larkana, Pakistan ***Int J Dermatol*** 2002; 41: 159-165.
4. Chong LY, Lo KK. Cutaneous tuberculosis in Hong Kong: a 10-year retrospective study. ***Int J Dermatol*** 1995; 34: 26-29.
5. Kivanç-Altunay I, Baysal Z, Ekmekçi TR, Köslü A. Incidence of cutaneous tuberculosis in patients with organ tuberculosis. ***Int J Dermatol*** 2003; 42: 197-200.