

BACTERIOLOGICAL STUDY OF RENAL TUBERCULOSIS IN THE PUNJAB AREA

Pages with reference to book, From 137 To 141

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Abstract

Microbiological investigations were carried out on suspects of renal tuberculosis reporting to Urology Department of Tuberculosis Research Unit of Mayo Hospital, Lahore. Out of 520 cases investigated, 94 had some clinical indication along with urine positive for acid fast bacteria by smear or culture. Most of the positive cases were in the range of 20-40 years age belonging to average and well-to-do socio-economic class. Out of 65 positive cultures, 14 were found to be mycobacteria other than *M. tuberculosis* (MOTT), mostly schotochromo-gens. About 30.5% of isolated tubercle bacilli were found to have some degree of resistance against at least one of the seven tested anti-tuberculous drugs. Bacteriologically positive renal tuberculosis cases, in contrast to pulmonary cases, were found to have significantly depressed tuberculin sensitivity. Overall 18.6% were found tuberculin negative. It is also interesting to note that 28.6% showed blood sedimentation rate within normal limits. The most common symptom observed in these cases was pyurea with or without haematuria. In 9.7% cases there was no present indication or past history of haematuria or pyuria (JPMA 30:138, 1980).

Introduction

Genito-urinary tuberculosis continues to be a significant problem all over the world. In the recent years the incidence of renal tuberculosis has been reported from many countries to be on the decline, (Brothwick, 1970; Petkovic et al., 1969) while other workers, like Shabad from Russia, reported that its incidence had not declined but probably increased in the last two decades (Shabad, 1975). In Pakistan the incidence of renal tuberculosis is not known. However, incidence of pulmonary tuberculosis is reported to be as high as 4.6%, while other extra-pulmonary infections are also quite frequent (Report of Tuberculosis Survey, 1962; Siddiqi, 1973). With this much prevalence of tuberculosis in general, it was expected that the incidence of urologic tuberculosis should also be high. This study was initiated to find out the incidence of renal tuberculous infection as well as the general pattern of bacteriological findings in this infection in a selected group of patients. In this paper laboratory investigations on bacteriologically positive cases are reported, including type of mycobacteria involved and their drug susceptibility. Further comparison has also been made with mycobacteria isolated from pulmonary tuberculosis.

Material and Methods

All suspected cases reporting to Urology Department of Mayo Hospital and Tuberculosis Research Centre of Pakistan Medical Research Council were investigated from the beginning of 1972 to the end of 1976. The selection was made according to the clinical judgement depending on the patients history of symptoms, and other laboratory findings. About 1000 urine specimens of 520 patients suspected of renal tuberculosis were processed during this period for acid fast bacterial (AFB) smear and culture. Complete history of each case was recorded, tuberculin test was performed using 5TU of tuberculin (supplied by CDC, Atlanta, Georgia, USA), chest X-ray and intravenous urogram (I.V.P.) was obtained as well as urine and blood were examined for routine investigations. Some of the patients could not be

investigated fully because of lack of facilities and poor cooperation from the patients.

For bacteriology, full morning first specimen was collected in a sterile bottle. The urine was processed by concentration method for AFB smear and culture within two to three hours of collection (Centre for Disease Control (CDC), 1975). Lowenstein Jensen (LJ) medium was used for culture. All the inoculated tubes were incubated at 37°C and were checked weekly for a maximum of 7-8 weeks. Any AFB growth obtained was further tested for identification according to procedures laid down by the U.S. Public Health Service and CDC.

Drug susceptibility was performed in drug containing LJ medium following proportion method (Canetti et al., 1969). Critical proportion for resistance was taken at 1% in Isoniazid, PAS, Ethambutol and Rifampicin while in case of Streptomycin, Ethionamide and Thiacetazone any growth more than 10% of the control was taken as a resistant one.

Results

In general a majority of bacteriologically proven cases of renal tuberculosis were within the age of 20-40 years with 54.2% males (Table 1).

Table I: Age and Sex Distribution of Bacteriologically Positive Cases of Renal Tuberculosis.

	0 — 10		11 — 20		21 — 30		31 — 40		41 — 50		50 — +		Total	
	M	F	M	F	M	F	M	F	M	F	M	F	M	F
Culture positive	2	0	4	9	13	8	15	7	2	1	4	0	40	25
Only smear positive	0	1	0	6	8	7	2	2	0	1	1	1	11	18
Total	2	1	4	15	21	15	17	9	2	2	5	1	51	43

Strikingly, a majority of these cases were from good to average socio-economic groups. Only about one third of the 94 patients were those who could be considered to be from a poor economic class.

Out of 520 patients, 94 (18.1%) were found to be positive by smear and/or culture. Smear positivity was found to be very low and among culture positive cases, many of them were smear negative (Table II).

Table II: AFB Smear and Culture Results of Urine From 520 Suspects of Renal Tuberculosis

	<i>M. tuber- culosis</i>	<i>MOTT</i>	<i>Uniden- tified</i>	<i>Total</i>
Culture positive Smear positive	13	5	1	19
Culture positive Smear negative	36	9	1	46
Culture negative Smear positive	—	—	—	29
Total	49	14	2	94

On further typing of the isolated mycobacteria, majority of the isolates were found to be *Mycobacterium tuberculosis*. However, 14 out of 65 positive cultures (21.5%) were identified as mycobacteria other than *M. tuberculosis* (MOTT) belonging to Runyons' group II, III and IV. *M. bovis* and group I photochromogens were not isolated (Table III).

Table III: Identification of Mycobacteria Other Than *M. tuberculosis* Isolated from Urine Samples According to Runyon's Grouping

1—Group I Photochromogens	0
2—Group II Schotochromogens	7
3—Group III Non chromogens	2
4—Group IV Fast Growers	4
5—Unidentified	1
Total	14

Drug susceptibility results of isolated *M. tuberculosis* showed that 30.6% have had some degree of resistance to at least one of the seven drugs tested (Table IV).

Table IV: Drug Sensitivity of *M. tuberculosis* Isolated from Renal Tuberculosis Cases

<i>Sensitivity pattern</i>	<i>No.</i>	<i>%</i>
Sensitive to all the drugs	34	69.4
Resistant to Isoniazid only	1	2.0
Resistant to Streptomycin only	6	12.2
Resistant to Isoniazid as well as Streptomycin	4	8.2
Resistant to Isoniazid, PAS and Streptomycin	4	8.2
Resistant to Ethionamide	0	0
Resistant to Ethambutol	0	0
Resistant to Thiacetazone	0	0
Resistant to Rifampicin	0	0
Total:	49	100

Isoniazid, 0.2 mcg/ml of LJ medium; Streptomycin, 4.0 mcg/ml; PAS, 0.5 mcg/ml; Ethionamide, 20 mcg/ml; Ethambutol, 2.0 mcg/ml; Thiacetazone, 2.0 mcg/ml; Rifampicin, 40.0 mcg/ml.

Streptomycin resistance was found to be the highest. Overall 14.2% were found resistant to only one, 8.2% to two drugs and 8.2% to three drugs.

So far as other laboratory investigations are concerned, 43 culture positive cases were checked for tuberculin sensitivity and 35 (81.4%) were found positive to 5 TU, showing 10 mm or more induration (Table V).

Table V: Tuberculin Sensitivity in Bacteriological Positive Renal Tuberculosis Cases.

	<i>Positive</i>	<i>Negative</i>	<i>Total</i>
Culture positive	28	5	33
Smear positive	7	3	10
Total:	35 (81.4%)	8 (18.6%)	43

5 tuberculin units/test. Tuberculin supplied by CDC, Atlanta, Georgia, USA.
Positive, 10 mm or more induration.

Results of blood sedimentation rate (ESR) showed that despite proven tuberculous infection 25 out of 56 investigated (44.7%) showed blood sedimentation rate within 20 mm fall after first hour (Table VI).

Table VI: Blood Sedimentation Rate in Renal Tuberculosis Cases

	<i>ESR in mm first hour*</i>					<i>Total</i>
	<i>No. of Cases</i>					
	0—10	11—20	21—30	31—40	40+	
Culture positive	8	6	7	3	11	35
Only smear positive	8	3	3	3	4	21
Total	16 (28.6%)	9 (16.1%)	10 (17.8%)	6 (10.7%)	15 (27.8%)	56

*Westergren method.

Presence of frank or microscopic haematuria and pyuria has been analyzed in Table VII.

Table VII: Haematuria and Pyuria in Renal Tuberculosis Cases*

	<i>Haematuria + Pyuria</i>	<i>Haematuria only</i>	<i>Pyuria only</i>	<i>None</i>	<i>Total</i>
Culture positive	21	4	13	2	40
Only smear positive	12	5	1	4	22
Total	33 (53.2%)	9 (14.5%)	14 (22.6%)	6 (9.7%)	62

*Microscopic or macroscopic, present or past history.

More than half of the patients have had both haematuria and pyuria while 14.5% had only haematuria and 22.6% only pyuria, while a majority of these were culture negative for pyogenic infection. There were 9.7% cases who had neither pyuria or haematuria. However, pain and burning in micturition and other symptoms were present.

Discussion

It is being recommended that for AFB smear and culture studies in renal tuberculosis, only fresh morning specimens should be checked. Kenney et al (1960) pointed out that there was much higher contamination rate if 24 hours specimen is checked, besides the inconvenience of collecting and processing of 24 hour specimen. Our experience in this study confirms these findings. Generally smear positivity is lower in urine specimens due to lesser number of tubercle bacilli present in urine. It appears from these results that AFB culture is a more reliable diagnostic-test in case of renal tuberculosis as compared to AFB smear alone, since 46 out of 65 culture positive specimens were smear negative;. On the other hand 29 patients whose urine was smear positive-for AFB, did not yield a positive culture. Out of these 29 cases, 15 had repeatedly positive smear and at times with 1-10 AFB/oil immersion field. Most of these patients were not on anti-tuberculous therapy. In one case, who happened to be a lady doctor, 14 specimens were cultured before positive culture could be obtained (Batty type.) while smear was repeatedly positive. There could be many explanations for smear positive culture negative cases. Certain polypeptides and other factors have been isolated from normal(human urine having marked tuberculostatic activity even in low concentration (Tsuji et al. 1965). There is a possibility that these substances may interfere in the growth of mycobacteria on culture. Generally tuberculosis in Pakistan is considered to be a poor man's disease but in our series most of these cases were from well-to-do class (three doctors). Higher incidence of renal tuberculosis in well-to-do persons, especially from the medical profession has been reported by Lattimer (1965). It is quite possible that the tuberculostatic factor is in higher concentration in poor people, thus making them more resistant to renal tuberculous infection. Further investigation in this direction would be most fruitful.

Majority of the isolated cultures in this series were found to be *M. tuberculosis*. *M. bovis* has never been isolated from this area, although *M. bovis* infection in humans is well known in the West (Siddiqi, 1973, 1976; Bruce, 1970). Further more our animals are infected with *M. bovis* only and *M. tuberculosis* was not isolated from cattle which shows that cross infection between humans and cattle

does not occur in Pakistan (Siddiqi and Niaz, 1978; Niaz and Siddiqi, 1979).

The difference in the incidence of MOTT infection in pulmonary and extra-pulmonary sites is striking. In pulmonary tuberculosis, after processing about 10,000 specimens, it was found that MOTT infection was rare (Siddiqi, 1976). However, in renal tuberculosis 14 out of 65 cultures were found to be MOTT. At least in 3 cases MOTT were isolated repeatedly. MOTT of unknown aetiology has been isolated from healthy persons particularly in urine samples by various workers (Edwards and Palmer, 1959; Pellmen and Runyan, 1964). In this study only those cases were considered as infected by MOTT in whom the urine specimen gave rise to more than 8-10 colonies in different culture tubes and the patient had some other definite clinical indication of tuberculosis. Moreover, those mycobacteria whose parasitic nature is not known, like *M. Smegmatis* or *M. gordonae*, were disregarded as being contaminants. Among MOTT in renal infection, schotochromogens were the most common one. In other extra-pulmonary infections like lymph nodes, schotochromogens have also been found to be the main infecting mycobacteria in this area (Siddiqi, 1973; Siddiqi et al., 1974). Reports from India also indicate high incidence of MOTT infection, specially schotochromogens in urologic cases (Singh et al., 1975). Many workers have reported presence of acid fast MOTT bacteria in urine and their possible role in the disease process (Siddiqi et al., 1974; Koltz, 1970). In our series, majority of them have had some evidence, radiological or clinical, of presence of mycobacterial infection besides positive culture for MOTT. We feel that yield of more than 8-10 colonics of the potential pathogenic MOTT along with some clinical indication is enough supporting evidence for the presence of active disease.

In some of our bacteriologically positive cases IVP findings were within the normal range. We feel that generally these represented the early stages of the disease because there were some indications of tuberculous infection. It seems that at the early stage of renal tuberculous infection, specially in mycobacteroses due to MOTT it is difficult to diagnose the disease by routine radiological investigation. In such cases, AFB smear and culture is the best tool to help in the diagnosis.

Overall drug resistance seems to be higher among the isolates, of *M. tuberculosis* in our series. However, the extent of the drug resistance in pulmonary tuberculosis was observed to be much higher in this area. More than half of the pulmonary cases reporting to this hospital show some degree of resistance to at least one of the anti-tuberculous drugs (Siddiqi, 1976).

Other laboratory investigations were also sometimes misleading as shown in the case of blood sedimentation rate, tuberculin test and presence of haematuria and/or pyuria. Depressed tuberculin skin sensitivity was observed in many renal tuberculosis cases in the present series. Positive percentage as well as overall size of induration of tuberculin reaction was found lower as compared with pulmonary cases. Similar observation was also made in other extra-pulmonary infections (Siddiqi et al., 1974).

There is no apparent explanation for lower tissue mediated hyper-sensitivity in extra-pulmonary tuberculosis.

Further investigation, clinical and radiological findings, therapeutic and surgical treatment and follow up will be discussed in a separate report.

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