

PREVALENCE, INCIDENCE AND RESOLUTION OF ABSCESSSES AND SINUSES IN PATIENTS WITH TUBERCULOSIS OF SPINE : 5-YEAR RESULTS OF PATIENTS TREATED WITH SHORT-COURSE CHEMOTHERAPY WITH OR WITHOUT SURGERY IN MADRAS

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Summary. A controlled clinical study comparing 6 or 9 months of ambulatory chemotherapy alone with radical surgery plus 6 months of chemotherapy was undertaken in patients with spinal tuberculosis in Madras.

The prevalence of sinuses and/or clinically evident abscesses was 49 (19%) of 253 patients, with significantly higher proportions in patients with lumbar or lumbo-sacral lesions. The incidence of lesions appearing after the start of chemotherapy was 32 (16%) of 204 patients. By five years, all had resolved. The resolution of the lesions was significantly faster and the incidence significantly lower in the radical surgery group than in the two ambulatory series.

Mediastinal abscesses were observed on radiographs in 66 (66%) of 100 patients with thoracic or thoraco-lumbar lesions. By five years, the lesions had disappeared in all except two patients and the disappearance was significantly faster in the radical surgery group than in the two ambulatory series.

There was no recurrence of these lesions during a period of five years.

undertaken in patients with spinal tuberculosis to compare 6 or 9 months of ambulatory out-patient chemotherapy (Isoniazid and Rifampicin daily) with radical surgery plus 6 months of the same chemotherapy.¹⁰ This report presents the prevalence, incidence and resolution of sinuses and/or clinically evident abscesses and mediastinal abscesses during a period of 5 years in these patients.

Material and Methods

Eligibility criteria : Patients with clinically and radiographically active spinal tuberculosis, involving any vertebral body from the first thoracic to first sacral inclusive, were eligible for admission to the study provided they did not have paralysis (of lower limbs) severe enough to prevent them from walking across a room (about 6 metres), and had not received previous anti-tuberculosis chemotherapy for 12 months or more. Patients were admitted from 6 participating hospitals in Madras.

Pre-treatment investigations : The investigations included : (a) complete clinical (including neurological) examination, (b) antero-posterior (AP) and lateral radiographs of the whole spine, (c) examination by culture of 2 specimens of pus from any abscess or sinus, if present, and (d) sensitivity tests to Isoniazid and Rifampicin of positive cultures. Details of other investigations have been given in an earlier report.¹⁰

Introduction

Abscesses and sinuses (besides spinal cord involvement) are common complications of spinal tuberculosis. Abscesses can be either clinically evident or only radiographically visible, and the former may co-exist with sinuses.¹⁻⁹ In Madras, a controlled clinical study was

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Allocation of treatment : Patients were allocated at random to one of the following 3 series.

1. Rad 6 : Radical anterior resection with bone grafting plus Isoniazid and Rifampicin in one dose daily for 6 months.
2. Amb 6 : Ambulatory treatment with Isoniazid and Rifampicin in one dose daily for 6 months.
3. Amb 9 : Ambulatory treatment with Isoniazid and Rifampicin in one dose daily for 9 months.

The dosages were based on patients' body-weights, and were 5-7 mg/kg body weight for Isoniazid and 10-15 mg/kg for Rifampicin. In the Rad 6 series, surgery was undertaken within one month of the start of chemotherapy.

Administration of anti-tuberculosis drugs : For all in-patients and for outpatients aged less than 5 years, every dose of drugs was administered under the direct supervision of a staff member. Out-patients aged 5 years or more attended the clinic twice-weekly and at each attendance, the dose for that day was administered under direct supervision, and the medicament (2 or 3 doses) supplied for self-administration (of administration by the parent) for the days until the next visit.

Assessment of progress : Progress was assessed monthly until the end of chemotherapy, then every 3 months until 30 months, then at 6-monthly intervals until 5 years. The assessments included : (1) clinical (including neurological) examination, (2) AP and lateral radiographs of the vertebrae involved, and (3) bacteriological

examination by smear and culture of pus from any sinus or abscess.

Bacteriological examination : Bacteriological examinations (smear, culture, sensitivity and identification tests) were undertaken by standard techniques¹¹ using additional media for culture of pus specimens.¹²⁻¹⁴ The following definitions of drug resistance were used:

Isoniazid : growth of 20 colonies or more on 0.2 mg/l or a higher concentration.

Rifampicin : growth of 20 colonies or more on 64 mg/l or a higher concentration.

Results

Study population : In all, 304 (10 Rad 6, 101 Amb 6, 103 Amb 9) patients were admitted to the study. For various reasons, 51 patients were excluded from analysis. The details of exclusions for 44 patients during the first 3 years were given in a previous report;¹⁰ during the 3-5 year period of follow-up, 7 other patients (1 Rad 6, 2 Amb 6, 4 Amb 9) were excluded-2 were lost to follow-up and 5 died of non-tuberculous causes. After these exclusions, there remained 253 patients (84 Rad 6, 81 Amb 6, 88 Amb 9) in the analysis.

Condition on admission : The patients who had sinuses and/or clinically evident abscesses on admission and the patients who did not have sinuses and/or abscesses on admission were broadly similar with respect to sex, radiographic activity, vertebral body loss and number of vertebrae involved. but of the 63 patients aged 9 years or less, 5 (8%) had abscess and/or sinus, as compared with 44 (23%) with abscess/sinus

Table 1. Prevalence and resolution of sinuses and/or clinically evident abscesses

Treatment series	Total patients	No. of patients with sinuses and/or clinically evident abscesses initially		Resolution (by months)						
		No.	%	1	2	3	6	9	12	60
Rad 6	84	16	19	7	14	14	15	16	16	16
Amb 6	81	20	25	3	7	13	17	20	20	20
Amb 9	88	13	15	1	4	7	11	12	12	13
Total	253	49	19	11	25	34	43	48	48	49

among the 190 patients aged more than 9 years ($p = 0.01$).

Prevalence of sinuses and/or clinically evident abscesses (present on admission) : The proportions of patients with sinuses and/or clinically evident abscesses on admission (Figures 1 & 2) were similar in the three series, being 16 (19%) of the 84 Rad 6, 20 (25%) of the 81 Amb 6 and 13 (15%) of the 88 Amb 9 patients (Table 1). In all, 49 (19%) of 253 patients had this lesion on admission; 38 (11 Rad 6, 17 Amb 6, 10 Amb 9) had clinically evident abscess only, 6 (1 Rad 6, 2 Amb 6, 3 Amb 9) had sinus only and 5 (4 Rad 6, 1 Amb 6) had both.

Resolution of sinuses and/or clinically evident

abscesses : The resolution of sinuses and/or clinically evident abscesses is shown in Table 1. An abscess or sinus has been considered as resolved only if this assessment was made at two or more consecutive scheduled examinations. The speed of resolution was similar for abscesses and sinuses and, therefore, the results have been amalgamated.

The sinuses and/or clinically evident abscesses had resolved by the first month in 7 of the 16 Rad 6 patients, by 2 months in a total of 14 and by 6 months in 15. In contrast, in the Amb 6 and Amb 9 series combined, resolution occurred in 4 of the 33 patients by 1 month, 11 by 2 months, 29 by the end of chemotherapy and in a



Fig. 1. External abscess in the right inguinal region



Fig. 2. A sinogram showing the sinus-tract from the sinus to the abscess

Table 2. Incidence and resolution of sinuses and/or clinically evident abscesses

Treatment series	Total patients at risk	No. of patients with sinuses and/or clinically evident abscesses appearing during treatment		Onset (months)		Resolution (months)	
				1-6/9*	7/10-60**	1-6/9*	7/10-60**
				No.	%		
Rad 6	68	5	7	5	0	4	1
Amb 6	61	12	20	9	3	7	5
Amb 9	75	15	20	15	0	12	3
Total	204	32	16	29	3	23	9

* Treatment phase

** Follow-up phase

total of 32 patients by 9 months. In the remaining patient (Amb 9), the abscess had resolved by 3 months; 2 sinuses were evident at 9 months but both had resolved by 21 months. The resolution was faster in the Rad series than in the 2 ambulatory series, the difference being statistically significant ($p = 0.04$ at 1 month, $p < 0.001$ at 2 months).

None had additional chemotherapy or surgery. Further, there was no recurrence of the lesions during the 5-year period.

In 9 of the 16 Rad 6 series patients, the sinuses and/or clinically evident abscesses resolved without aspiration or incision compared with 8 of the 33 patients in the two ambulatory series. In the other 7 patients in the Rad series, 1 or more aspirations of abscesses were performed. In the ambulatory series, 20 patients (11 Amb 6, 9 Amb 9) had 1 or more aspirations of abscesses and in the remaining 5 (3 Amb 6, 2 Amb 9) the abscesses were incised.

Incidence of sinuses and/or clinically evident abscesses observed after the start of chemotherapy: The incidence and resolution of sinuses and/or clinically evident abscesses observed for the first time after start of treatment is presented in Table 2. Of 204 patients (68 Rad 6, 61 Amb 6, 75 Amb 9) who did not have a sinus and/or clinically evident abscess on admission, 32 (5 Rad 6, 12

Amb 6, 15 Amb 9; 16%) developed the lesions, 29 (5 Rad 6, 9 Amb 6, 15 Amb 9) during the treatment phase and 3 (all Amb 6) in the follow-up phase. The incidence was 7% of 68 in the Rad 6, and 20% of 136 in the two ambulatory series, the difference being significant ($p = 0.03$). Of these 32 patients, 25 (3 Rad 6, 11 Amb 6, 11 Amb 9) developed clinically evident abscesses alone, 3 (2 Rad 6, 1 Amb 6) had sinuses alone and 4 (all Amb 9) developed both. The lesions had resolved in 23 (4 Rad 6, 7 Amb 6, 12 Amb 9) by the end of treatment and in the remaining 9 (1 Rad 6, 5 Amb 6, 3 Amb 9) by 60 months.

In the vast majority, namely 28 (4 Rad 6, 9 Amb 6, 15 Amb 9) patients, the lesions had resolved without additional surgery or chemotherapy and the remaining 4 needed additional chemotherapy and/or surgery (For details, please see pp. 156-157).

Of the 32 with incidence, aspiration was done in 24 (2 Rad 6, 8 Amb 6, 14 Amb 9), incision in 1 (Rad 6) and both in 1 (Amb 9). No recurrence of the lesions was observed during the 5-year period.

Prevalence, incidence and resolution of sinuses and/or clinically evident abscesses : The overall prevalence, incidence and resolution of sinuses and/or clinically evident abscesses from admission till 60 months is presented in Table 3.

Table 3. Prevalence, incidence and resolution of sinuses and/or clinically evident abscesses

Treatment series	Total patients	No. of patients with sinuses and/or clinically evident abscesses during 5 years		Resolution on allocated treatment		Resolution after additional		
						Surgery only	Chemo-therapy only	Surgery & chemo-therapy
		No. (a)	%	No.	% of (a)			
Rad 6	84	21	25	20	95	1	0	0
Amb 6	81	32	40	29	91	0	2	1
Amb 9	88	28	32	28	100	0	0	0
Total	253	81	32	77	95	1	2	1

Of the 253 patients, 81 (32%) patients (21 Rad 6, 32 Amb 6, 28 Amb 9) had sinuses and/or clinically evident abscesses and the lesions resolved on the allocated treatment in 20 of the 21 Rad 6 patients, in 29 of the 32 Amb 6 and in all 28 of the Amb 9 patients, that is, in a total of 77 (95%) of the 81 patients. In the remaining 4 patients, one (Rad 6) developed persistent post-operative sinus at the site of surgery and the graft was removed in the 33rd month; the sinus was observed last at the 42nd month. One patient (Amb 6) developed an abscess during treatment which persisted till the end of treatment; additional chemotherapy was given and the abscess resolved by 9 months. The other 2 patients (both Amb 6) developed abscesses during follow-up; both had additional chemotherapy - one for clinically active disease at the end of treatment in whom the abscess resolved by 18 months, and the other for persisting paraparesis for whom excision of a diseased rib also was done in the 10th month and the abscess subsided by 12 months.

Sinuses and/or clinically evident abscesses on admission in relation to the level of the spinal lesions : The distribution of the prevalence of sinuses and/or clinically evident abscesses in relation to the initial level of vertebral involvement is shown in Table 4. Of the 93 patients who had a spinal lesion in the thoracic region, 11 (12%) had an abscess or sinus; the corresponding figures were 7 (21%) in the

thoraco-lumbar region and 31 (25%) in the lumbar region (26 lumbar, 5 lumbo-sacral). Thus, the prevalence of abscess and/or sinus was significantly more in patients with lumbar or lumbo-sacral lesions ($p = 0.05$).

Mediastinal abscess shadows on admission without sinuses and/or clinically evident abscesses at any time : The disappearance of mediastinal abscess shadows radiologically evident on admission, which were never manifest externally, was studied by an independent assessor. The allocated regimens of these patients had not been

Table 4. Prevalence of sinuses and/or clinically evident abscesses in relation to the initial level of the spinal lesion

Initial level of spinal lesion	Total patients	Patients with sinuses and/or clinically evident abscesses	
		No.	%
Thoracic	93	11	12
Thoraco-lumbar	34	7	21
Lumbar	109	26	25
Lumbo-sacral	17	5	
Total	253	49	19

Table 5. Prevalence of mediastinal abscesses without sinus and/or clinically evident abscess at any time, and their resolution

Treatment series	Total pts.*	Patients with mediastinal abscess	Resolution by (months)								Not resolved
			1	2	3	6/9	12	18	24	60	
Rad 6	34	21	8	13	13	15	19	20	21	21	0
Amb 6	31	21	1	6	6	9	16	17	19	21	0
Amb 9	35	24	0	5	5	15	19	20	21	22	2
Total	No. 100**	66	9	24	24	39	54	57	61	64	2
	% 100	66	14+	36	36	59	82	86	92	97	3

* Excluding patients with lumbar or lumbo-sacral lesions

** Excluding 27 patients with sinuses and/or clinically evident abscesses at any time

+ This and subsequent percentages are based on the total patients with mediastinal abscess initially.

modified by surgery or additional chemotherapy based on the radiographic findings. A total of 66 (66%) (21 Rad 6, 21 Amb 6, 24 Amb 9) patients had a radiographically visible mediastinal abscess on admission (Table 5). Considering the 21 Rad 6 patients, the mediastinal abscess disappeared by 1 month in 8, by 2 months in 13, by 6 months in 15, by 18 months in 20 and by 24 months in all. In the 45 (21 Amb 6, 24 Amb 9) ambulatory patients, the lesions were not seen by 1 month in 1, by 2 months in 11, by 6/9 months in 24, by 18 months in 37, by 24 months in 40 and by 60 months in 43 patients. Of the remaining 2 patients (both Amb 9), one had a persistent abscess shadow which had calcified; the other had a persistent abscess shadow, even though he had decompression surgery for worsening of paraparesis in the 2nd month. The mediastinal abscesses had disappeared more rapidly in the Rad 6 series than in the combined Amb series, the difference being statistically significant ($p < 0.001$ at 1 month; $p < 0.01$ at 2 and 3 months). In all, the mediastinal abscess disappeared during the treatment phase in 39 (15 Rad 6, 9 Amb 6, 15 Amb 9) patients, during the follow-up period without any intervention in 25 (6 Rad 6, 12 Amb 6, 7 Amb 9) patients and did not resolve in 2 Amb 9 patients even by 60 months.

No information is available on the incidence of mediastinal abscess.

Bacteriology of pus from abscesses and sinuses

(both aspirated and at surgery) : Of the 49 (16 Rad 6, 20 Amb 6, 13 Amb 9) patients with sinuses and/or clinically evident abscesses on admission, aspiration or incision was done in 32 (7 Rad 6, 14 Amb 6, 11 Amb 9) patients; the specimens were examined bacteriologically and the culture was positive for *M. Tuberculosis* in 18 (56%) patients. Pus was collected during surgery from 13 Rad 6 patients, of which 4 were positive by culture including one from a patient for whom the aspirated pus also yielded *M. tuberculosis* on culture. These 13 patients included the 7 (Rad 6) who had aspiration also. In the remaining 3 Rad 6 patients, pus was neither aspirated nor collected during surgery. Thus, bacteriological examination of the pus was undertaken in 38 (13 Rad 6, 14 Amb 6, 11 Amb 9) of the 49 patients and culture was positive in 21 (55% - 7 Rad 6, 8 Amb 6, 6 Amb 9) patients; all were sensitive to Rifampicin and Isoniazid.

Prevalence, incidence and resolution of sinuses and/or clinically evident abscesses in patients who were excluded from the analysis : Among 51 patients excluded from the analysis, 19 were either found to have no evidence of active tuberculosis or were withdrawn from the study as unsuitable for surgery; 1 patient who had an abscess on admission died 12 days after starting treatment. Of the remaining 31 (6 Rad 6, 13 Amb 6, 12 Amb 9) patients 8 (2 Rad 6, 3 Amb 6, 3 Amb 9) had a sinus and/or clinically evident abscess on admission; 6 had an abscess alone and

2 had both abscess and sinus. The sinus and/or clinically evident abscess resolved by the end of chemotherapy in six (2 in each series) and by 21 months in the other 2 (1 Amb 6, 1 Amb 9) patients. There was no recurrence of the lesions during the 5-year period, and none developed an abscess or sinus during treatment or in the follow-up phase.

Discussion

Sinuses and/or clinically evident abscesses and mediastinal abscess (besides spinal cord involvement). are common complications of spinal tuberculosis. The present report gives 5-year findings of these two complications, encountered during an investigation of short-course chemotherapy in the treatment of spinal tuberculosis.

Unlike in pulmonary tuberculosis, bacteriological confirmation of tuberculosis in extra-pulmonary forms, which are paucibacillary, is difficult. However, with the introduction of selective and multiple media, the culture positivity rates are high.¹²⁻¹⁴ In the present study, pus obtained from sinus and/or clinically evident abscess present on admission, by aspiration or incision, was examined in 32, of which 18 (56%) were culture positive. This result compares favourably with the culture positivity rate of 40% obtained by examination of aspirated pus in British Medical Research Council studies.^{15,16}

The prevalence of sinus and/or clinically evident abscess was 49 (19%) of 253 patients in this study. This is similar to the prevalence of 22% observed among 587 patients in Masan, Pusan, Bulawayo and Hong Kong.^{1-4,9}

The incidence of sinus and/or clinically evident abscess was not influenced by the kind of chemotherapy given; it was 27 (20%) of 136 patients receiving 6 or 9 months of daily Isoniazid plus Rifampicin (present study) and 59 (22%) of 273 patients treated with 18 months of daily Isoniazid plus PAS, with or without an initial Streptomycin supplement¹⁻³ in Masan, Pusan and Bulawayo. Considering the role of surgery, in the present study the incidence was 5 (7%) of 68 in the Rad 6 series treated with 6 months of daily Isoniazid and Rifampicin plus modified Hong Kong surgery and 9% of 44 Hong Kong patients treated with a regimen similar to the present Rad

6, excepting that the duration of chemotherapy was either 6 or 9 months,⁹ as compared with 27 (20%) of 136 in the Amb 6 and Amb 9 series combined in the present study ($p = 0.03$). A similar difference has been reported in studies with 18 months of daily Isoniazid plus PAS; the incidence was only 2% of 142 patients who had chemotherapy plus surgery (i.e. debridement or radical operation) as compared with 22% of 273 patients who had chemotherapy alone.¹⁻⁴ These findings indicate that surgery substantially reduced the incidence of sinuses and/or clinically evident abscesses.

The speed of resolution of sinuses and clinically evident abscesses with short-course or standard chemotherapy, with or without additional surgery, is also of interest. Of 86 patients treated with 18 months of daily Isoniazid plus PAS, the lesions resolved in 29 (34%) by 3 months, 46 (53%) by 6 months and 71 (83%) by 12 months.¹⁻³ In the present study, of 33 patients treated with 6 or 9 months of daily Isoniazid plus Rifampicin, the corresponding figures were 20 (61%), 28 (85%) and 32 (97%), respectively. This finding suggests that the resolution was faster in those treated with short-course chemotherapy (SCC) than in those treated with standard chemotherapy. Considering the 23 patients (Madras : 16; Hong Kong : 7) treated with radical surgery plus short-course chemotherapy (6 or 9 months of daily Isoniazid plus Rifampicin), the lesions resolved in 20 (87%) by 3 months and in 21 (91%) by 6 months.⁹ These proportions are higher than in those treated with ambulatory short-course chemotherapy, suggesting that surgery enhanced the speed of resolution further. In the patients treated with surgery (debridement or radical operation) plus 18 months of daily Isoniazid and PAS, the lesions resolved in 25 (71%) by 3 months, in 29 (83%) by 6 months and in 33 (94%) by 12 months^{3,4} these proportions are higher than in those treated with 18 months of daily Isoniazid plus PAS without surgery.¹⁻³ Thus the speed of resolution was greater when surgery was undertaken in addition to chemotherapy.

By 5 years, the lesions had resolved in all 81 (100%) patients treated with short-course chemotherapy of 6 or 9 months' duration with or without surgery (present study), as compared to 117 (92%) of 127 patients who were treated with

18 months of chemotherapy alone and in all 67 patients who were treated with surgery in addition to 18 months of chemotherapy.^{1,4}

Considering the disappearance of radiographically visible mediastinal abscesses present on admission, at the end of chemotherapy, that is at 6 or 9 months in the present study and the second study in Hong Kong, the abscesses had disappeared in 15 (71%) of 21 patients in the Rad series and in 24 (53%) of 45 patients in the combined Amb series in Madras and in 8 or 9 of 12 patients treated with radical surgery plus short-course chemotherapy in Hong Kong. This finding suggests that the disappearance of the abscesses was faster in patients treated with radical surgery in addition to short-course chemotherapy. In patients treated with 18 months of Isoniazid plus PAS (standard chemotherapy), the abscesses had disappeared in 69 (83%) of 83 patients at the end of treatment.¹⁻³ The corresponding figures for patients treated with additional debridement were 26 (81%) of 32³ and with additional radical surgery, 19 (86%) of 22⁴. This similarity suggests that surgery (debridement or radical) did not enhance the rate of resolution of mediastinal abscesses in patients treated with PAS and Isoniazid daily for 18 months. By 18 months, the lesions had disappeared in 95% in short-course chemotherapy series even though they did not receive any anti-tuberculosis drugs beyond 6 or 9 months. These proportions are similar to the 81-86% observed at the end of 18 months of Isoniazid plus PAS, with or without surgery (see above). Unlike the resolution of sinuses and/or clinically evident abscesses, the radiological disappearance of mediastinal lesion was *not* influenced by the kind of chemotherapy given.

It is concluded that clinical abscess/sinus and mediastinal abscess do not pose any special problems in management and respond well to short-course chemotherapy consisting of daily Isoniazid plus Rifampicin of 6 or 9 months duration. The resolution of sinuses and clinically evident abscesses was faster with short-course chemotherapy than with standard chemotherapy. When surgery was undertaken in addition, the resolution was faster irrespective of the type of chemotherapy. The incidence of sinuses and/or clinically evident abscesses was also significantly less in patients who underwent surgery. The resolution of mediastinal abscesses was also faster

in the surgical series. These findings are different from the conclusion reported in another paper, on 5-year findings in patients with spinal tuberculosis¹⁷ that, ambulatory chemotherapy with daily Isoniazid and Rifampicin for 6 or 9 months was highly effective in spinal tuberculosis and radical surgery did not enhance the efficacy of the 6-months regimen. However, by 5 years, the resolution of sinuses and/or clinically evident or mediastinal abscesses, was equal in both ambulatory and surgical series.

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