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SERUM ELECTROPHORETIC PATTERN IN OSTEOARTICULAR TUBERCULOSIS

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A serum electrophoretic study was carried out in 37 established osteoarticular tuberculosis cases. The result of this study has been analysed according to severity and chronicity and also after treatment, including certain streptomycin-resistant cases. It has been observed that there was a decrease in albumin and an increase in $Alpha_2$ and gamma-globulin fractions of serum protein as the disease became more advanced and chronic in nature. The administration of known antitubercular drugs reverses this phenomenon. The resistant cases revealed an increase in gamma-globulin fraction at almost the same level as observed in the untreated cases.

Key words: tuberculosis; serum electrophoresis

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In spite of a good regimen of chemotherapy, tubercular infection may persist in some osteoarticular lesions for a number of months (Debaumont 1966). This raises the question that it might be developing resistance to the standard antitubercular therapy. However, there are no parameters available by which one can exclude those cases that are acquiring resistance to streptomycin therapy. Moreover, there are very few criteria through which the effectiveness of any therapeutic trial can be assessed.

It is a well-established phenomenon that patients with tuberculosis invariably become hypoproteinaemic due to undernourishment. Under the circumstances, variations in different fractions of protein are known to occur both quantitatively and qualitatively, and these conditions are referred to as paraproteinaemia and disproteinaemia, respectively. This alteration of different protein fractions has been demonstrated in various other diseases such as Kala azar, nephrotic syndrome and pulmonary tuberculosis (Narsimha & Sadasivudu 1964). However, no reports are available where the protein fractions in skeletal tubercular cases have been studied.

PATIENTS AND METHOD

We studied 57 cases; 20 were normal, and 37 were suffering from osteoarticular tuberculosis. Out of the 37 cases of osteoarticular tuberculosis, there were five with neurological complications (e.g. tingling sensation in the lower limb, paraplegia, loss of urinary bladder control etc.). Twenty-one were male and 16 were female. All cases were in different age groups ranging from 14 to 45 years. The diagnosis was established by:

(1) Clinical examination.

(2) Radiological examination of the local lesion both anteroposteriorly and laterally.

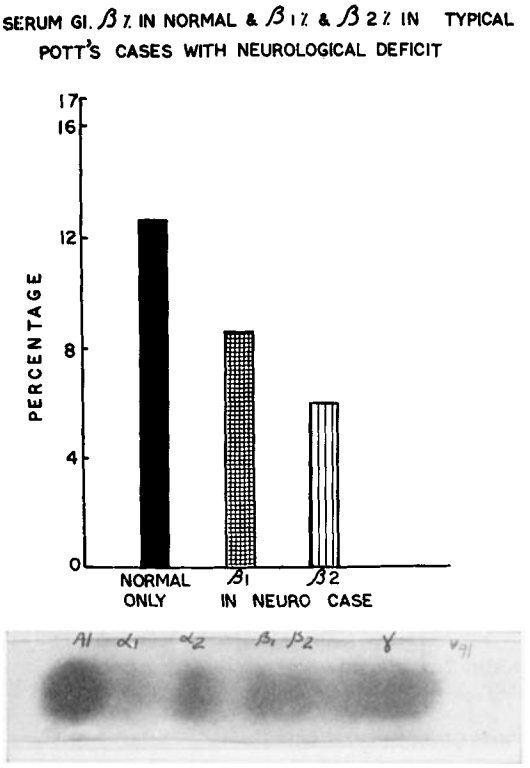

Figure 1. The extra Beta$_2$ band in serum electrophoretic strip in the cases of Pott's spine with neurological complications.

(3) Mantoux test.
(4) Erythrocyte sedimentation rate.

Then a blood sample was taken from each patient for serum electrophoretic study. After fixation and staining of the filter-paper strips, each fraction of protein was eluded by calorimetric readings for quantitative estimation.

The levels of Albumin, Alpha$_1$, Alpha$_2$, Beta and Gamma fractions of serum protein were analysed according to the severity and chronicity of the disease. The electrophoretic analysis of protein was repeated after two and four months of the standard regimen of antitubercular treatment. For analysis according to chronicity the cases were divided into three main groups:

(a) Those having the lesion for up to six months.
(b) Seven months to one year.
(c) More than one year.

Similarly, these cases were also divided into three grades depending on the severity of the disease, i.e., Grades I, II and III.

RESULTS

Results of this study on 37 patients were analysed according to the grades and chronicity. In addition, the normal values of 20 individuals were compared with the normal values reported in the literature.

Serum electrophoretic pattern according to grades

It has been observed that there was a gradual decline in the level of serum albumin fraction as the disease advanced from Grade I to Grade III, in comparison with the normal values (Table 1). An

Table 1. Serum protein analysis according to grades.

Grade	Albumin %		Globulin							
			Alpha$_1$ %		Alpha$_2$ %		Beta %		Gamma %	
	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
I	37.12 49.71	44.92	3.55 7.52	5.60	8.09 11.78	10.43	12.72 19.24	16.24	20.29 26.16	22.81
II	36.10 51.07	43.35	4.74 9.30	6.65	7.93 15.32	11.63	10.17 17.51	14.47	20.46 26.27	23.90
III	24.05 46.39	30.58	1.41 7.27	4.90	8.89 22.2	14.38	10.08 20.00	10.34	21.22 48.90	29.80
Normal		52.87		5.19		9.04		12.64		20.26

Table 2. According to chronicity.

Chronicity	Albumin %		Globulin							
			$Alpha_1$ %		$Alpha_2$ %		Beta %		Gamma %	
	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
Up to 6 months	20.55 47.70	34.11	3.10 11.64	5.55	7.62 18.06	13.86	8.33 17.38	13.86	20.46 39.37	32.62
6 months to 1 year	25.33 51.31	43.25	2.72 7.51	4.98	7.31 22.20	12.70	10.50 19.25	14.31	19.31 29.33	24.86
1 to 2 years	24.05 47.94	33.90	2.74 7.27	4.74	9.59 15.15	11.31	10.77 20.00	14.43	30.29 48.71	35.73

estimate of the $Alpha_1$ fraction showed a gradual increase in Grade I and also in Grade II followed by a small decrease in Grade III, whereas the other globulin fraction, i.e., $Alpha_2$, revealed a gradual increase in the level as the disease advanced from Grade I to III. The gamma fraction of serum globulin showed an increase in the level as the disease advanced from Grade I to Grade III (Table 1).

Serum electrophoretic pattern according to chronicity

Analysis of the albumin-fraction of serum protein showed a decrease in the concentration as the disease became more and more chronic in nature. The $Alpha_1$ and $Alpha_2$ fractions of serum protein did not reveal much difference in comparison with the normal level. Similarly, the Beta fraction was on a higher level throughout the period with little change according to the chronicity. The most important observation made in connection with the chronicity was in the level of the gamma fraction of serum globulin. The level of gamma globulin increased as the disease became chronic in nature (Table 2).

Pott's spine with neurological complications

In this series we have included only those three paraplegic cases who had lost their control of the urinary bladder and anal sphincters. Significant observations made in all these cases were that there was an extra band of Beta fraction of serum globulin. This was labelled as $Beta_2$ fraction (Figure 1). The Beta fraction of serum protein also showed a much lower value in comparison with those cases of osteoarticular tuberculosis without neurological complications. However, the total value of Beta fraction ($Beta_1$ and $Beta_2$) in these cases was almost the same as in the uncomplicated cases. Also, the values of other protein fractions were almost the same as observed in the uncomplicated cases.

Effect of operation

The electrophoretic analysis of serum proteins in these paraplegic cases was repeated two months later after operative intervention. It was observed that the extra band of the $Beta_2$ fraction of globulin had disappeared without much change in the $Beta_1$ fraction. The albumin fraction increased to 51.64 per cent from a previous value of 47.19 per cent, whereas the gamma-globulin fraction of protein decreased from 25.65 per cent to 19.48 per cent two months after operation.

Effect of antitubercular treatment

Those cases treated with standard antitubercular therapy (Streptomycin 1 g,

Table 3. Serum protein analysis after antitubercular treatment

Treatment	Albumin %		Globulin							
			Alpha$_1$ %		Alpha$_2$ %		Beta %		Gamma %	
	Range	Mean	Range	Mean	Range	Mean	Range	Mean	Range	Mean
Before	28.05 43.02	34.88	3.58 7.93	5.41	7.85 17.68	12.77	8.75 15.68	12.11	29.65 39.37	34.83
After 2 months	35.12 51.27	42.07	1.66 9.92	4.74	7.96 15.28	11.67	5.35 15.93	11.03	21.17 34.32	30.50
After	46.36 54.84	47.70	4.03 7.27	5.65	11.29 15.15	11.22	12.10 20.00	16.05	17.74 21.21	19.38

Isonex 300 mg, and P.A.S. 6 g daily for two months) showed a gradual increase in the albumin fraction of serum protein at different intervals during follow-up. The Alpha$_1$ and Beta fractions of serum globulin did not reveal any significant change during treatment, whereas the Alpha$_2$ decreased in the subsequent follow-up. The gamma-globulin fraction which was higher before starting the treatment showed a rapid fall in concentration during treatment (Table 3).

Serum electrophoretic pattern in streptomycin-resistant cases

In this series we have included those cases who had full antitubercular treatment for two months or more, but had produced no beneficial effect. The electrophoretic study of serum protein in these cases revealed a decrease in the albumin fraction and a significant increase in the gamma-globulin fraction, which was almost at the same level as those who had no previous antitubercular treatment. Remaining fractions, i.e., Alpha$_1$, Alpha$_2$ and Beta did not show much difference.

DISCUSSION

Seibert et al. (1947) were probably the first to report the serum electrophoretic pattern in pulmonary tuberculosis cases. Their investigations showed an increase in Alpha$_2$ and gamma-globulin fractions in the early stage of tuberculosis. They have further pointed out that in chronic illness all the globulin fractions tend to be raised. Narsimha & Sadasivudu (1964) have also observed a high gamma globulin and a decrease in albumin fraction in pulmonary tuberculosis, which was confirmed by the work of Blokhin & Syromyatnikova (1964). However, none of these workers have studied the electrophoretic pattern at the various stages of skeletal tuberculosis nor have they correlated the response of antitubercular treatment.

The results of our study, when classified according to the grade and chronicity of osteoarticular tuberculosis cases, indicate that the Alpha$_2$ fraction of serum globulin increases gradually as the disease becomes more advanced and chronic in nature. The increase in serum gamma globulin corroborates the observation by Schaffner et al. (1953) who attributed the increase in gamma globulin to immunological factors. It suggests that as this disease becomes more and more advanced, there is more demand for antibody production in the body. Since the main function of the plasma proteins, particularly of the albumin fraction, is the maintenance of plasma-osmotic pressure, the decrease in the level of this fraction

in the serum suggests that it is probably due to undernourishment of the tissue in these cases. Our study also suggests that by measuring the albumin, $Alpha_2$ and gamma-globulin fractions of serum protein, the severity of the disease can be determined.

A similar observation was made in the cases of Pott's spine with neurological complications when an extra band of $Beta_2$ globulin was observed. This disappeared after compression was relieved. It is very difficult to interpret this extra $Beta_2$ fraction of serum protein at this stage, although it was a constant finding. However, it may be possible that this extra band is due to compression over the spinal cord.

Those skeletal tuberculosis cases treated with standard antitubercular therapy showed a fall in gamma-globulin fraction of serum protein after 2 to 4 months of treatment in comparison with the pretreatment value. Whereas the albumin fraction had a decreasing tendency in the early stages, it started increasing to reach a normal level after treatment. This confirms our findings that raised gamma-globulin and decreased albumin occurs in tubercular cases that have responded to the antitubercular treatment. Thus these values could be taken as one of the main quantitative criteria for assessing the effectiveness or the extent of the lesion and response to any antitubercular drugs.

Some of the established osteoarticular tuberculosis cases did not respond to the antitubercular treatment. In these cases gamma-globulin fraction was found to be raised even after treatment. These studies suggest that probably by measuring the albumin and gamma-globulin fraction of serum protein one may find out whether the disease is responding to antitubercular therapy, or becoming resistant to streptomycin, even in the early stages.

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