Role of Interleukin-1 in Patients with Pott's's Spine

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Abstract: *Background: Pott's spine is caused by Mycobacterium tuberculosis, a slow growing gram-positive, acid-fast bacillus which becomes lodged in the bone via Batson's venous plexus and lymphatic from primarily infected lung, lymph nodes, mediastinum and viscera, forming granulomatous inflammation and caseation necrosis. IL-1 plays many different roles, from mediating the immune response to infection[6] to regulating vascular permeability and angiogenesis. But there is paucity of studies evaluating the relationship of Pots spine and interleukin 1, hence we have undertaken this study with the aim to assess the relationship between Interleukin-1 levels in patient with Pott's's spine. Aims & Objectives: To estimate the serum Interleukin 1 level in patients with Pott's's spine & determine its relationship with Pott's's spine. Methods: Present study was prospective in nature conducted among 37 patients of Pots spine. All patients fulfilling inclusion criteria and exclusion criteria were taken up for the study. Study was carried out over a period of 1.5 years. Serum Interleukin levels & CRP levels were assessed. Results: Majority of the patients was in the age group of 46-60 years and most of them were male. In this study, none of the cases had normal (0.1-5 pg/ml) interleukin 1 level while majority i.e. 16 (43.24%) of the cases had interleukin 1 level of 100.1-200 pg/ml. Mean interleukin 1 level in our cases was 165.49 + 89.54 pg/ml. Conclusion: High interleukin-1 level consistent with the better response to chemotherapy.*

Keywords: interleukin-1 level, Pots spine, Mycobacterium tuberculosis, CRP.

1. Introduction

Tuberculous spondylodiscitis (Pott's spine) is caused by Mycobacterium tuberculosis, a slow growing gram-positive, acid-fast bacillus which becomes lodged in the bone via Batson's venous plexus and lymphatic from primarily infected lung, lymph nodes, mediastinum and viscera, forming granulomatous inflammation and caseation necrosis.[1] It is the most gorm of skeletal tuberculosis. It is a serious form of extra pulmonary TB which if left untreated can be fatal.[2] The treatment of it can be chemotherapy alone or surgery in addition to chemotherapy.

Thoracolumbar region is the most commonly affected site while the cervical and sacrum regions are less commonly involved. Usually more than one vertebra is affected because of its segmental arterial distribution and subligamentous spread of the disease. The bacilli reach the disc space causing disc destruction, spreads to adjacent vertebral bodies leading to vertebral collapse, anterior wedging, characteristic kyphotic angulation (Gibbus deformity), which may compress the spinal cord and nerve roots producing functional impairment.[1,3,4]

Magnetic resonance imaging (MRI) makes the early diagnosis of spinal TB easier and a considerable number of patients with spinal TB are diagnosed earlier and treated more effectively before significant neurological deficits develop. However, patients can still present late with considerable spine deformity.[5] IL-1 plays many different roles, from mediating the immune response to infection[6] to regulating vascular permeability and angiogenesis.[7] Deregulated IL-1 responses have been associated with the development and progression of cancer[8] and also with autoimmune diseases such as rheumatoid arthritis.[9] But there is paucity of studies evaluating the relationship of Pots spine and interleukin 1, hence we have undertaken this study with the aim to assess the relationship between Interleukin-1 levels in patient with Pott's's spine.

Objectives
To estimate the serum Interleukin 1 level in patients with Pott's's spine & determine its relationship with Pott's's spine.

2. Materials and Methods

This was a facility based cross sectional observational study, protocol of which was approved by the Institutional Ethical committee of the medical college and is consistent with all the ethical standards. Written informed consent was taken from all study subjects.

Patients with back pain with features of Pott's's spine such as pain, numbness, loss of sensation, loss of power, loss of tone or bowel/bladder involvement & willing to participate in the study were included. All consecutive patients fulfilling inclusion and exclusion criteria were taken up for the study until the required sample size was fulfilled. Sampling method used was universal. Study was carried out over a period of 1.5 years from December 2020 to June 2022. Exclusion criteria were Patients with diagnosed neurological dysfunction such as stroke leading to monoparesis/ monoplegia/ paraparesis/ paraplegia/ quadriparesis/ quadriplegia, peripheral neuropathies, Guillain-barre syndrome or ataxia. Patients with traumatic cervical spine injury, patients with congenital spine

deformities, spinal tumours, patients with fractures in upper limb and known psychological dysfunction.

Detailed history regarding onset and progression of symptoms, history of trauma was taken. Detail neurological examination was done following which X-ray lumbar spine AP and LATERAL view and MRI spine with whole spine screening was carried out. Degree of the spinal cord compression was classified into one off our groups:

Level 0 – no pressure on thecal sac
Level 1 – mild compression on thecal sac
Level 2 – the degree of thecal sac compression is <1/3 Level 3 – the degree of thecal sac compression is >1/3

Then all the patients were subjected to lab investigations such as random blood sugar level, Interleukin 1 levels [normal range:0-5 pg/ml], CBC, RFTs, LFTs, Sr. electrolytes. Results of Interleukin 1 levels were compared statistically with severity of neurological impairment.

A. Batirel et al [10] in their study titled, the course of spinal tuberculosis (Pott's disease): results of the multinational, multicentre Backbone-2 study, found that the most common presenting feature amongst spinal TB cases was paraspinal abscesses in 69%, considering this proportion, at 95% confidence interval and 15% allowable error, the sample size came out to be 37. Sample size was calculated with the formula n = [DEFF*Np(1-p)]/ [(d2/Z21- α/2*(N-1) +p*(1-p)], using Epi info version 3.0

Data was collected in pre-structured proforma (Annexure I-case record sheet) which was pilot tested and after ensuring it's validity. Quantitative data was then tested by Mean and Standard Deviation, difference between more than two means tested by 'ANOVA' test. P value <0.05 was considered significant.

3. Results

In the current study, majority 17 (46.95%) of the cases were from the age group of 46-60 years followed by 12 (32.43%) from the age group of >60 years and least i.e. 08 (21.62%) from the age group of 31-45 years. Mean age of the patients was 54 ± 11 years with the range being 33-74 years. Male predominance was seen in the current study with 83.78% males & 16.22% females. Most, 22 (59.46%) of the cases affected side was right while in 14 (37.84%) was left side and bilateral in 01 (2.7%) case. Most commonly affected spinal level was lumbar in 14 (37.84%) cases followed by thoracic in 16 (43.24%) and least affected was cervical in 07 (18.92%). (Table 1)

Table 1: Distribution of patients according to baseline characteristics

	Baseline characteristic	Frequency (no.)	Percentage (%)
Age groups	31-45	08	21.62
	46-60	17	45.95
	>60	12	32.43
Gender	Male	31	83.78
	Female	06	16.22
Laterality	Left	14	37.84
	Right	22	59.46
	Bilateral	01	2.7
	Cervical	07	18.92
Level of spine affected	Thoracic	16	43.24
	Lumbar	14	37.84

In the present study, most common complaint was back pain in 27 (72.97%) cases followed by fever in 15 (40.54%), difficulty in walking in 12 (32.43%), tingling & numbness in 10 (27.03%), weakness in 07 (18.925), neck spasm among 05 (13.51%), chills & weight loss in 04 (10.81%) each and night sweats in 02 (5.41%). (Chart 1) Chart 1. Presenting complaints wise distribution of cases.
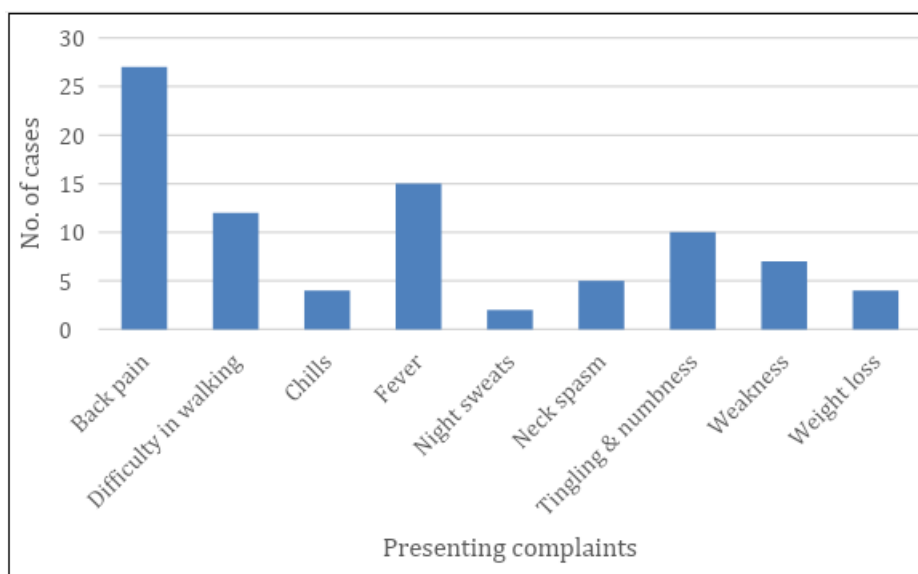
In this study, none of the cases had normal (0.1-5 pg/ml) interleukin 1 level while majority i.e. 16 (43.24%) of the cases had interleukin 1 level of 100.1-200 pg/ml followed by 200.1-300 pg/ml in 08 (21.62%) cases, 50.1-100 pg/ml among 07 (18.92%), and 5.1-50 pg/ml & 300.1-400 pg/ml in 03 (8.11%) each. Mean interleukin 1 level in our cases was 165.49 + 89.54 pg/ml. (Table 2)

Table 2: Distribution of patients according to interleukin 1 level

Interleukin 1 level (pg/ml)	Frequency	Percent
0.1-5 (Normal)	00	00
5.1-50	03	8.11
50.1-100	07	18.92
100.1-200	16	43.24
200.1-300	08	21.62
300.1-400	03	8.11
Total	37	100
Mean $\pm$ SD	165.49 $\pm$ 89.54	

In our study, most common diagnosis was thoracic pots spine in 16 (43.24%) cases followed by lumbar pots spine in 14 (37.84%) cases and cervical pots spine in 07 (18.92%). (Table 3)

Table 3: Distribution of patients according to diagnosis.

Diagnosis	Frequency	Percent
Cervical Pots spine	07	18.92
Thoracic Pots spine	16	43.24
Lumbar Pots spine	14	37.84
Total	37	100

On analysis of association of some baseline parameters of Pots spine cases with the Interleukin 1 level, we have found that significantly high Interleukin 1 level in young age group (31-45 years, p=0.03) which means better response to chemotherapy & good prognosis in young patients while low level in <60 years age group indicating poor prognosis; there was no significant association of Interleukin 1 level with gender (p=0.08); and there was significantly high Interleukin 1 level in cases with low CRP level while low Interleukin 1 level in cases with high CRP level (p=0.04). (Table 4)

Table 4: Association of some baseline parameters of Pots spine cases with the Interleukin 1 level.

Parameter		Interleukin 1 level (pg/ml) Mean $\pm$ SD	P
Age groups	31-45 (n=08)	213.6 $\pm$ 108.4	**0.03**
	46-60 (n=17)	154.6 $\pm$ 58.8	
	>60 (n=12)	116.5 $\pm$ 77.3	
Gender	Male (n=31)	176.6 $\pm$ 89.9	0.08
	Female (n=06)	108 $\pm$ 61.4	
CRP	Low (n=21)	185 $\pm$ 73.3	**0.004**
	High (n=16)	101.6 $\pm$ 96.1	

4. Discussion

The immunology of tuberculosis in humans is complex and not fully understood.

Interleukin - 1A is an acute phase reactant which induces fever and sleep, activates resting T cells, is co-factor for haemopoietic growth factor, stimulates synthesis of interleukins-2, 3, and interleukin-2 receptors, tumour necrosis factor, gamma-interferon and activates macrophages.[11]

When effective chemotherapy is given to Pots spine cases, the inhibition of bacteria would allow a protective immune response to develop, which in turn would be beneficial for the ultimate cure. Elevation of interleukins promotes a TH-1 type response indicating a favourable trend. To the best of our knowledge, our study is first of such kind, conducted on Pots spine patients in which IL-1 A has been evaluated in

this way. Our observations reveal that in the study group, the IL-1 A levels were high indicating an activated immune system response, done on 37 cases of Pots spine to assess the relationship of interleukin 1 level with the disease, important findings of which are discussed below.

In the current study, majority (46.95%) of the cases were from the age group of 46-60 years followed by 32.43% from the age group of >60 years. Mean age of the patients was 54 $\pm$ 11 years. Male preponderance (83.78%) was seen in the present study. Majority (59.46%) cases had right side affected. Most commonly affected spinal level was lumbar (37.84%) followed by thoracic (43.24%) and cervical (18.92%). Similarly, A. Batirel et al[10] noted mean age of 51 $\pm$ 18 years & male majority (52%), Prasad Chandramouliswara Bodapati et al[12] noted 52.08% male cases of Pots spine, Elvina Karyadi et al[13] also noted male majority.

In the present study, back pain was commonest complaint (72.97%) followed by fever (40.54%), difficulty in walking (32.43%), tingling & numbness (27.03%), weakness (18.92%), neck spasm (13.51%), chills & weight loss (10.81% each) and night sweats (5.41%). This is in line with A. Batirel et al99 who noted majority of the Pots spine patients experienced back pain (83%) followed by other constitutional symptoms like fever, sweating, weight loss, loss of appetite, weakness, arthralgia etc. Prasad Chandramouliswara Bodapati et al[12] and Rejith Valsalan et al[14] also noted that most common complaint was back pain followed by weakness.

In this study, none of the cases had normal (0.1-5 pg/ml) interleukin 1 level while majority (43.24%) had interleukin 1 level of 100.1-200 pg/ml followed by 200.1-300 pg/ml (21.62%), 50.1-100 pg/ml (18.92%), and 5.1-50 pg/ml & 300.1-400 pg/ml (8.11% each). Mean interleukin 1 level in our cases was 165.49 $\pm$ 89.54 pg/ml. Consistently, Deepak Rosha et al[15] evaluated the relationship of interleukin 1 levels in 20 MDR-TB patients found that all the 10 cases who had a favorable response had elevated IL-1A levels (12-21.6 pg/ml) while in the 10 non-responders all were found to have IL-1A levels in the low normal range (1.2-2.3 pg/ml).

Santhuri Rambaran et al[16] studied the effect of inflammatory cytokines on culture conversion in TB and found that plasma expression of IL-6, IL-1RA, IP-10 and IL-1a were significantly associated with shorter time to culture conversion.

In our study, most common diagnosis was thoracic pots spine in 16 (43.24%) cases followed by lumbar pots spine in 14 (37.84%) cases and cervical pots spine in 07 (18.92%).

On analysis of association of some baseline parameters of Pots spine cases with the Interleukin 1 level, we have found that significantly high Interleukin 1 level in young age group (31-45 years, p=0.03) which means better response to chemotherapy & good prognosis in young patients while low level in >60 years age group indicating poor prognosis; there was no significant association of Interleukin 1 level with gender (p=0.08); and there was significantly high Interleukin 1 level in cases with low CRP level while low

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Interleukin 1 level in cases with high CRP level (p=0.04). This is in line with Mohammad Shameem et al[17] who had reported that serum-CRP levels were significantly higher in active tubercular patients as compared to control and are significantly correlated with disease severity in patients.

5. Conclusion

High Interleukin 1 level in young age group and patients with low CRP associated with better response to chemotherapy & good prognosis in Pots spine cases.

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