The diagnostic value of the soluble IL-2 receptor in the tuberculous pleurisy and its comparison with adonosine deaminase

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The role of SIL-2R in diagnosis of tuberculous pleurisy was investigated and compared with adenosine deaminase (ADA) levels. Fifteen patients with tuberculous pleurisy and fifteen patients with non-tubeculous pleurisy were included in the study. The levels of sIL-2R in pleural fluid were significantly higher in tuberculosis group (p<0.001). When a cut-off level was accepted as 2000 pgj/ml to distinguish tuberculous and non-tuberculous pleurisises, sensitivity and specifity were 80% and 80% respectively. ADA levels also were higher in tubercolosis group)p<0.001). A cut-off level as 30 U/l distinguished tuberculous from non-tuberculous pleurisies with a sensitivity of 86. 6% and a specifity of 93%. In coclusion, slL-2R levels can be diagnostic for tuberculous pleurisies but its sensitivity and specifity is lower than ADA levels. [Turk J Med Res 1995; 13(3): 119-121]

Key **Words:** Tuberculosis, Pleurisy, IL-2R, Adenosine deaminase

It is not always easy to clarify the reason of the etiology of pleural liquids. Despite all biochemical and histopathological diagnostic methods, in 15-25% of pleurisy etiology cannot be established (1).

An important part of exudative pleural fluids in our country are due to tuberculosis. As spontaneous remission can be seen in tuberculous pleurisy, a pleural thickening and a restrictive breathing defect dependent on it may also develop. Furthermore, in the following 5 years there is the risk of lung tuberculosis development in the rates of 25-60% (2).

In spite of all bacteriological methods today, there are some difficulties in the diagnosis of tuberculous pleurisy, Therefore, there are many studies focused on diagnostic enzymes or indicators. The adenosine deaminase (ADA) is used for this aim an enzyme that takes part in the purine catabolism and is made of T lymphocytes and plays role in monocyte growth. The high ADA levels in tuberculous pleurisies is accepted to be diagnostic (3).

The soluble interleukin-2 receptor (sIL-2R) is T lymphocytes and is present at the secreted of membranes lymphocyte and monocytes. The ratio of T4 lymphocytes increases in tuberculous pleurisies. Like the ADA, it was shown that the sIL-2R level is high in tuberculous pleurisies (4).

In this study, the diagnostic value of the sIL-2R was evaluated in comparison to ADA in the diagnosis of tuberculous pleurisy.

MATERIALS AND METHODS

Of the 30 patients included to the study, 15 patients had tuberculosis and the other 15 had a pleural liquid due non-tuberculous reasons.

The tuberculous pleurisy diagnosis was set by determining a tuberculous granulation tissue in the pleura biopsy. The diagnosis in patients with malign pleural liquid was set by a pleura pin biopsy, histologically with a thoracoscopic biopsy and cytologically by determining malign cells in the liquid. Decortication was applied to one patient who had a chronic nonspecific pleurit diagnosis histopathologically at the end of a pleura biopsy. By the examination of decortication material, the same diagnosis was established.

The two events where a pleural liquid due congestive heart insufficiency was established were diagnosed clinically and radiologically. The transude property of the liquid supported the diagnosis.

The liquid and blood samples of the patients were taken at the same time. ADA and SIL-2R levels in pleural liquids and isochronically taken serum

Received: April 19,1994 **Accepted:** March 24,1995

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samples were measured. Pleural liquid and blood samples were saved at -20°C till the measurement was made.

The pleural liquid and serum ADA level were measured by the Guisti method by applying to the Berthelot reaction. The color at the end of this reaction was evaluated spectrophometrically. The SIL-2R level was measured by the ELISA method. Serum or pleural liquids were put twice into reaction with SIL-2R antibodies and read spectrophometrically at 490 nm.

For a statistical analysis the student-t test was applied and for the SIL-2R and ADA levels in the pleural liquid sensitivity and specifity were calculated.

RESULTS

Of the 15 patients in the tuberculous pleurisy group, 5 were female and 10 were male. The average age was 30.86±3.2 (range: 19-65). There were 5 female and 10 male patients in the non-tuberculous group and the average age was 57.13±1.98 (range: 42-68).While 3 of the patients in this group had benign diseases, others had malign diseases. Four of the malignant diseases were mesothelioma, 4 we'r adenocarcinoma, 3 were small cell lung cancer and 1 was breast cancer metastasis.

The sIL 2R levels in the pleural fluid showed significant Increase with respect to the serum in the tuberculous group. The ADA levels in the pleural fluid were also significantly high.

While the sIL-2R levels in the pleural fluid were also significantly high with respect to the serum, there was no difference among the ADA levels in the non-tuberculous group.

The sIL-2R levels of pleural fluid in tuberculous group were significantly higher than that of the non-tuberculous group ($p<0.01$). The pleural fluid ADA levels were significantly higher in the tuberculous group ($p<0.01$) (Table 1).

When 20.000 pg/ml was accepted to be the cut-off value for the sIL-2R level in the pleural fluid, the sensitivity was calculated to be 80% and the specifity to be 80%, too. If this cut-off value was 30 U/L for the pleural fluid ADA, then the sensitivity was 86.6% and the specifity 93.3%.

DISCUSSION

The T lymphocyte level in the tuberculous pleural fluid is higher than it is in the peripheral blood. The CD4+ iymphocytes are forming the predominant fraction (4). In the bronchoalveolar lavage (BAL) fluid the T cell population and the CD4+ CD8+ ratios increased, too (5). The T4 lymphocyte increase is responsible for the increase in IL-2 and IFN-gamma levels in tuberculous pleurisies (5-9).

The IL-2 is self-effective, that is, it is an autocrin sytokin. The IL-2 effect provides the T cell develop-

Table 1. Properties of tuberculous and non-tuberculous patient groups

Properties	Tbc	Non-Tbc
Age	30.86+3.2	57.13+3.2*
SIL-2Rp (pg/ml)	21730+1423 (18900-24654)	14465+1375** (6300-21882)
SIL-2P.S (pg/ml)	9572+1161.7 (3528-17640)	6528.6+1214.9 (441-189000)
ADAp (IU/L)	74.16+10.01 (15.7-138.1)	12.64+1.6** (3.3-30)
ADAs (IU/L)	26.42+2.3 (4.5-55.7)	16.36+1* (11.2-25.8)

SIL-2Rs: Soluble interleucin-2 serum level
SIL-2Rp: Soluble interleucin-2 pleural liquid level
ADAs: Adenosin deaminas serum level
ADAp: Adenosin deaminas pleural liquid level
*p<0.05
**p<0.001

Table 2. Soluble interleucin-2R and ADA levels

	Tuberculosis		Non-Tuberculosis	
	SIL-2Rp	SIL-2RS	SIL-2Rp	SIL-2Rs
1.	2100	17640	9660	2520
2.	21000	6930	8400	4620
3.	18900	9030	18480	5040
4.	21000	3780	6300	1260
5.	19100	5544	13230	6342
6.	24654	12936	15288	18900
7.	19278	4998	19950	10878
8.	22848	11256	20706	10854
9.	21126	7014	15036	4232
10.	24486	14868	17034	3402
11.	23814	15732	21882	5124
12.	23982	3528	21084	10374
13.	24066	13188	12852	441
14.	20412	9576	10152	7350
15.	20286	7560	6972	6592

	Tuberculosis		Non-tuberculosis	
	ADAp	ADAs	ADAp	ADAs
1.	60.8	19.5	10	11.2
2.	15.7	19.1	8.6	13
3.	50	6.2	17.3	19.5
4.	62.7	52.7	8.1	15.4
5.	83.8	19.2	18.8	11.2
6.	102.8	20.1	7.6	17.7
7.	101.8	25.8	10	11.2
8.	134.4	55.7	11.3	25.8
9.	130.5	50.8	14.4	17.7
10.	138.1	47.2	30	12.5
11.	56.3	20.9	13.9	16.4
12.	40	19.7	13	16.8
13.	66.6	24.5	12	16.3
14.	28.5	4.5	11.3	20.8
15.	40.5	10.5	3.3	20

SIL-2R pg/ml
ADA IU/L

ment, growth and the IL-2 receptor increase. SIL-2R is at the lymphocyte surface.

In our study, tuberculous patients and patients with a non-tuberculous pleural liquid were compared. The average age in the tuberculous group was significantly low. The reason why tuberculosis is still widespread in our country may be explained by the many malign diseases in the other groups.

Scollard and friends have showed that the TL's in the pleural liquids of patients with a tuberculous pleurisy which was excited by PPD were increasing and the lymphokines (Gamma-IFN, IL-1, IL-2) were much more secreted than they are secreted in the peripheria! blood. Furthermore, it was established that the soluble IL-2 receptor that shows high affinity to IL-2 is found to be in great amounts in the pleural liquid (10).

Ronchbach et al have found the SIL-2R level in the pleural liquid to be higher than the serum and have asserted that this increase showed the local cellular immunity (7).

The SIL-2R levels in our study which were obtained from tuberculous effusions were significantly higher than the ncn-tuberculous group ($p<0.001$). The sensitivity and specifities were found to be at the rates of 80% when the cut-off value was 20.000 pg/ml. Scollard et al have found the SIL-2R levels higher than the malign, parapneumonic and transudative liquids. Furthermore, the SIL-2R level in malign and parapneumonic liquids was higher than the transudes in their studies (10). In our study, the average SIL-2R level in malign pleural liquids was higher than transudes, too (15616+1456-9996, 3+765). But because of the low number of samples (12 malign, 3 transudative liquids) a statistical comparison could not be applied.

The SIL-2R level was found to be higher than the serum in the pleural liquid. This fact supports the idea that T lymphocytes in pleural liquids are Higher than the peripheral blood in tuberculosis.

Brown et al have asserted that, despite the optimal chemotherapy, tuberculosis is in counter relation with the prolonged activation of the immune system and have stated that in this infection, the SIL-2R level measurement could seperate the active immunity from the memorial immunity. As a result, they conclude that SIL-2R measurings could be useful in the diagnosis of the disease and the following of the immune response during the therapy (11).

Following intradermal PPD injection Scollard et al have investigated the IL-2R levels in induration and bullous. They essert that IL-2R plays an important role by speeding up the proliferative response which is dependent on the T cell and by clarifying invivo the immune function (10).

Statistically, the SIL-2R levels were significantly high as in the ADA levels in tuberculous pleurisy diagnosis. But in regard with the sensitivity and specifity, the ADA level gave better results.

As a result, the sensitivity and specifity of the SIL-2R level was not found to be as high as the ADA level although it is diagnostic for the tuberculous pleurisy.

Tüberküloz plörezisi tanısında soluble IL-2 reseptör düzeyinin tanısal değeri ve adenozin deaminaz ile karşılaştırılması

Tüberküloz plörezili hastaların plevra sıvısında Solübl ınterlökin-2 (SIL-2R) reseptör düzeylerinin tanısal değeri araştırılarak adenozin deaminaz (ADA) Düzeyleri ile karşılaştırıldı. Çalışmaya 15 tüberküloz plörezili ve 15 tüberküloz dışı plörezisi olan hasta alındı. Plevra sıvı SIL-2 düzeyleri tüberküloz grubunda diğer griptan anlaomlı olarak yüksek bulundu ($p<0.01$) Cut-off değeri 20000 pg£ml olarak alıondığında tüberküloz ve tüberküloz dışı plevral sıvı ayrımında sensitivite %80 ve spesifite %80 olarak hesaplandı. ADA düzeyleri de tüberküloz grubunda anlamlı olarak yüksekti ($p<0.001$). Cut-off değeri 30 U/L olarak alındığında ayrım için sensitivite %86.6 ve spesifite %93.3 olarak bulundu. Bu sonuçlara göre SIL-2r düzeyinin tüberküloz plörezilerde tanısal olabilmekle birlikte sensitivite ve spesifitesi ADA düzeyinden düşük bulundu. [TurkJMedRes 1995; 13(3): 119-121]

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