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Original article

CD4:CD8 Ratio: A Valuable Diagnostic Parameter for Pulmonary Sarcoidosis

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SUMMARY

Sarcoidosis is a multi-organ disease and is characterized by sarcoidal noncaseating granuloma comprised of T-helper/inducer (CD4+) lymphocytes and scant cytotoxic (CD8+) T-lymphocytes. CD4+:CD8+ T-cell elevated ratio is a characteristic diagnostic parameter for sarcoidosis. This is the first report from Iran evaluating the CD4:CD8 ratio capability in differentiating pulmonary sarcoidosis from other interstitial lung diseases (ILDs) on a large cohort.

Fifty pulmonary sarcoidosis patients and 50 non-sarcoidosis interstitial lung diseases (nsILDs) patients were included in the current study. Bronchoalveolar lavage (BAL) was performed using flexible fiberoptic bronchoscopy and flow cytometer.

Non-sarcoidosis group was established by 50 components that were classified into eight subgroups. Fifty-two per cent of sarcoidosis patients and 62% of non-sarcoidosis interstitial lung disease patients had normal spirometric results. The CD4/CD8 ratio was significantly higher in sarcoidosis than in non-sarcoidosis interstitial lung diseases ($p < 0.001$). The CD4/CD8 ratio was found to be > 3.5 in 33.3%, 2.5–3.5 in 7.1%, 1.5–2.5 in 20.2% and < 1.5 in 39.4% of the entire study population. The best cut off point was 1.1 with the sensitivity of 92% and

specificity of 80% for distinguishing sarcoidosis from other interstitial lung diseases.

Performing bronchoalveolar lavage as the safe and rapid first step confirms the diagnosis of sarcoidosis in 92% of cases (current study sensitivity). Hence, performing an invasive procedure was required in a few patients only.

Bronchoalveolar lavage flow cytometry in the assessment of clinical and radiological findings supplies an appropriate diagnostic adjunct for discriminating sarcoidosis from non-sarcoidosis interstitial lung diseases.

Key words: **sarcoidosis, bronchoalveolar lavage, lymphocyte, CD4+:CD8+ ratio, flow cytometry**

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INTRODUCTION

Sarcoidosis is a multi-organ, tuberculosis-like disease and is characterized by a noncaseating granuloma, with the lung being the main involved organ (1-3). Sarcoidal multiple noncaseating granulomas (MNG) are comprised of mononuclear cells, epithelioid cells and T-helper/inducer (CD4+) lymphocytes with scant cytotoxic T-lymphocytes (CD8+) all over the periphery (4, 5).

Lung granulomatous inflammation is caused by an invasion of mononuclear cells against the alveoli and the host declined immunological response to a steady unidentified antigen presented by macrophages to T lymphocytes (6, 7). Generally, T cells operate in two ways: identifying an antigen and the amplification of the positional cellular and humoral response (7). The adjacency of operative CD4+ (helper/inducer) T helper1-like lymphocytes and alveolar macrophages was indicated as alveolitis (8). By contrast, CD8 alveolitis is considered a relatively rare incident in sarcoidosis, due to infrequent excess of CD8 T-lymphocytes (9, 10). Generally, the proportion of T cells accounts for 20-60% of the total cell count. CD4+:CD8+ T-cell ratio > 3-5:1 versus a ratio of 2:1 in healthy subjects is a characteristic diagnostic parameter for pulmonary sarcoidosis (9, 11). So far, numerous studies have indicated that CD4+:CD8+ ratio is inappropriate for discriminating sarcoidosis from other interstitial lung diseases (ILDs) (11).

Typically, clinical granulomas proved through transbronchial lung biopsy with radiological findings are the prior diagnostic reports for sarcoidosis (3). Studies on immunopathogenesis of interstitial lung disorder have investigated bronchoalveolar lavage (BAL), which reflects the clinical characteristic of the distal part of the lung (10). BAL is a noninvasive and safe method and is today presented as a standard method in the diagnosis of inflammatory lung disorders such as sarcoidosis. Furthermore, fiberoptic bronchoscopy (FOB) supplies BAL samples, covering a large area of the lungs and is associated with no morbidity compared to ranges 0.1–0.2% in transbronchial lung biopsy and 1.8–21% in open lung biopsy (3).

Immunoperoxidase staining as the standard method for lymphocyte subtyping is time-consuming and depends on the operator's experience (12). In contrast, flow cytometry method, which is an alternative method, permits rapid analysis of lymphocyte subtypes such as CD4+: CD8+ ratio.

AIMS

Several surveys have been carried out worldwide, analyzing the role of the CD4+:CD8+ ratio since the 1980s, with diverse results. In contrast, only a small population of pulmonary sarcoidosis patients was previously studied among Iranian patients (10).

In order to study the clinical efficiency of the CD4+:CD8+ ratio for discriminating pulmonary sarcoidosis from nsILDs, the current cross-sectional study was conducted among a large cohort of interstitial lung diseases patients.

MATERIAL AND METHODS

STUDY DESIGN

This retrospective cross-sectional study was conducted at the Masih Daneshvari Hospital, Tehran. The current research study complied with the declaration of Helsinki and was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences. Intervention surgical procedures were health care services provided to patients and the study method was not designed for clinical research purposes. Written informed consents were signed by patients and patient privacy was observed during the study.

STUDY POPULATION

During the study period 2015-2016, 720 respiratory patients underwent both transbronchial lung biopsy and FOB. Sixty-seven patients were excluded regarding the technical drawback in BAL procedure. In total, 102 sarcoidosis and ILDs medically suspected patients who underwent flow cytometry were eligible for the current study. Transbronchial lung biopsies were analyzed meeting global criteria (3). Therefore, there were 50 patients with histopathologically confirmed pulmonary sarcoidosis and 52 patients were non-sarcoidosis ILDs proved. In general, 50 pulmonary sarcoidosis patients were included in the study as an experiment group, and to eliminate deficiencies of two unequal groups' comparison, 50 non-sarcoidosis ILDs (nsILDs) patients were included blindly as the control group. All the patients were newly diagnosed and none of them was previously steroid-treated at the time of BAL sampling. Moreover, nsILDs were classified as tuberculosis (TB), interstitial pulmonary fibrosis, connective tissue ILD (CT-ILD), idiopathic pulmonary fibrosis (IPs), adenocarcinoma, malignancy, unclassified interstitial fibrosis and atypical interstitial lung diseases. Study variables were compared between the two groups and also eight subgroups.

PRIMARY AND DEMOGRAPHIC DATA

Demographic data, such as age, gender, smoking status and medical records such as C-reactive protein (CRP) serological results, erythrocyte sedimentation rate (ESR) results, pulmonary function test results and histopathology results of transbronchial lung biopsies were recorded. Global guidelines were utilized in determining normality of parameters (13, 14).

Pulmonary function tests (PFT) representing forced expiratory volume in the 1st second (FEV1), forced vital capacity (FVC) and the FEV1/FVC were measured using spirometer (Spirolab II, Italy) according to the European Respiratory Society guideline (13).

BAL

A flexible fiberoptic bronchoscope (Olympus BF1T; Tokyo, Japan) was used for BAL performance, according to the previous guideline (14). After premedication with Lidocaine, the bronchoscopy processed transorally in the right middle lobe adjoining the segmental bronchi. Three aliquots of 50 ml sterile isotonic saline were aspirated into the lungs and immediately pulled into 3 sterile polycarbonate tubes. BAL analysis was performed on all three aliquots and the results were presented as the average number of the three experiments. BAL fluid was centrifuged at 300 – 400 XG for 15 minutes and the sediment was re-suspended in 2 ml of phosphate-buffered saline.

FLOW CYTOMETRIC ANALYSIS

BAL suspension was stained with pairs of Phycoerythrin (PE) and Phycoerythrin-Cyanin (PC) conjugated antibodies CD4- PC5, CD8-PE (Becton-Dickinson, USA) and incubated for 30 minutes at room temperature. Accordingly, negative controls were obtained using isotype-matched antibodies. Consequently, BAL fluid cells were analyzed using FACSCalibur flow cytometry (Becton-Dickinson, Mountain View, California, USA) and data were recorded for 15,000 cells in each tube.

STATISTICAL ANALYSIS

Statistical Package for the Social Sciences (SPSS) (ver. 22.0; SPSS Inc. Chicago, IL, USA) software was

used for statistical analyses. Continuous variables were expressed as frequency and percentage, mean (± standard deviation) or median (minimum-maximum). Categorical variables were expressed as frequencies and percentages. Different parameter correlations were determined by Spearman´s rank correlation coefficient.

Between-group comparisons of continuous variables (such as CD4+:CD8+ ratio) were evaluated using nonparametric Mann-Whitney U test. Otherwise, the Chi - square test was used to evaluate between-group comparisons of categorical variables. Differences in the mean were calculated by Student's t-test and the Kruskal-Wallis test, using a p-value of < 0.05 for significant value. Receiver operator characteristic (ROC) curve provided the best cut-off value.

RESULTS

VARIABLES STATUS AND MEASURES

Kolmogorov-Smirnov test indicated normal distribution in age variable only. Hence, parametric tests were used for analyzing the age variable.

DEMOGRAPHICS ANALYSIS

One hundred patients were included in the current study. According to the histopathological criteria, the patients were divided into sarcoidosis or non-sarcoidosis ILDs groups (2, 3).

Fifty individuals (50%) constituted sarcoidosis group and non-sarcoidosis group involved 50 patients that were further classified into eight subgroups. Interstitial pulmonary fibrosis (10%), CT-ILDs (8%), idiopathic pulmonary fibrosis (7%), tuberculosis (5%), adenocarcinoma (5%), malignancy (4%), atypical interstitial lung disease (4%) and unclassified fibrosis (7%) were classifications of nsILDs subgroups.

Overall, sarcoidosis group was comprised of 14 men and 36 women with a mean (± sd) of 44.76 ± 7.36 years. Twenty-seven men and 23 women with 49.04 ± 13.09 years of age were involved in non-sarcoidosis ILDs. Two groups were not age-matched (p = 0.008, v = 0.264). The highest average age among non-sarcoidosis group belonged to atypical interstitial lung diseases group (53.5 ± 23.30 yrs.). Male subjects prevailed in the nsILDs group (54% versus 28%), and interstitial pulmonary fibrosis was the most common nsILDs disorder in male patients (10%). Conversely, female sex showed a significantly higher proportion in sarcoidosis than non-sarcoidosis group, i.e. 69% versus 45%, respectively.

Smokers made up 12% of sarcoidosis group and 13% of the nsILDs group. Interstitial pulmonary fibrosis group contained most smokers among nsILDs (3%). Accordingly, the smoking rate was 4.06 ± 7.62 pack/year in sarcoidosis group versus 8.4 ± 14.99 pack/year in sarcoidosis group. Tuberculosis group provided the highest smoking rate among nsILDs (15.2 ± 22.21).

CLINICAL ANALYSIS

The ESR counts in sarcoidosis and nsILDs were detected as 23.84 ± 11.69 versus 29.42 ± 18.63 mm/hour respectively, as both showed more than the normal range results. Nevertheless, T-test defined that differences in two main groups due to ESR did not reach significance level (p = 0.322).

CRP level was higher than the normal range in both sarcoidosis and nsILDs groups: 6.48 ± 11.22 versus 17.9 ± 25.29 mg.dL-1 respectively. CRP level was determined to be significantly higher in the nsILDs group, compared to the sarcoidosis group (p = 0.002).

PULMONARY TEST

The FEV1 value in two sarcoidosis and nsILDs groups were identified as insignificantly associated (75.53 ± 17.92, 77.9 ± 9.49. p = 0.710). The highest FEV1 value was obtained from the CT-ILD group among nsILDs. FVC was significantly higher in the sarcoidosis group compared to the nsILDs group (103.14 ± 14.74, 94.4 ± 11.96. p = 0.001).

Fifty-two per cent of sarcoidosis patients showed the normal spirometric sequel, while 62% of nsILDs patients represented normal spirometric results with an insignificant discrimination (p = 0.313). CT-ILD group showed the highest normal pattern value (14%) among nsILDs and displayed a significant segregation in comparison with sarcoidosis group. However, the restrictive spirometric pattern was evaluated in 16% of sarcoidosis group and 34% of the nsILDs group. Thirty-two per cent and 4% of case and control groups showed an obstructive spirometric pattern, respectively. In addition, the chi-square test revealed no significant differentiation between the two main groups, in restrictive and obstructive patterns (p = 0.208, p = 0.364).

BALF LYMPHOCYTE SUBSETS

One of the results was excluded in order to be in the abnormal range. The CD4 value was estimated at 57.98 ± 2.31 in sarcoidosis group versus 31.29 ± 10.07 in

nsILDs group. CD8 amount was determined as 23.19 ± 16.81 versus 22.74±13.08. In sarcoid patients, CD4+: CD8+ ratio mean was 3.41 ± 1.63. Also, 1.74 ± 0.95 was specified in nsILDs group. As expected, CD4+:CD8+ ratio was significantly higher in sarcoidosis than in non-sarcoidosis group ($p < 0.001$), although the highest CD4+:CD8+ ratio in the nsILDs group was observed in the malignancy patients with 2.91 ± 1.58, this level was still significantly lower than in the sarcoidosis group ($p < 0.05$).

The CD4+:CD8+ ratio was found to be > 3.5 in 33.3% of the study population (Table 1). The CD4/CD8 ratio remained in the range 2.5-3.5 in 7.1% of subjects. Moreover, in 20.2% of patients, the CD4+:CD8+ ratio was in the range of 1.5-2.5, while in 39.4% it was less than 1.5. The CD4+: CD8+ ratio was higher than 3.5 in 33 (33.3%) subjects, of whom 28 (84.8%) were sarcoid patients.

Although the two groups differed significantly in value ($p < 0.001$), 6.1% of malignancy patients of the second group showed that CD4+:CD8+ ratio was higher than 3.5. With regard to the age of patients, the CD4+:CD8+ ratio was significantly higher in subjects aged more than 50 years ($p = 0.01$). In twenty-seven (27%) subjects, who were aged more than 50 years, the CD4/CD8 ratio was higher than 3.5.

The best cut off value of the CD4+:CD8+ ratio for the diagnosis of the sarcoidosis was assessed through the ROC curve analysis (Figure 1). 1.1 cut off point was the best cut off point with the sensitivity of 92% and specificity of 80%. An increased CD4+:CD8+ ratio cut off value resulted in increased specificity, but also decreased sensitivity. At the time of establishing the diagnosis of sarcoidosis, the cutoff point of 3.5 showed high specificity and low sensitivity (96% and 38% respectively).

Table 1: **CD4/CD8 ratio in bronchoalveolar fluid of sarcoidosis and non-sarcoidosis subjects**

			Group									Total
			Sarcoidosis	Interstitial pulmonary fibrosis	CT-ILDs	Idiopathic pulmonary fibrosis	Tuberculosis	Adenocarcinoma	Malignancy	Atypical interstitial lung disease	unclassified fibrosis	
CD4/CD8	CD4/CD8 1.50 and less	Count	8	7	5	4	1	3	1	3	7	39
		% within CD4.CD8.1	20.5%	17.9%	12.8%	10.3%	2.6%	7.7%	2.6%	7.7%	17.9%	100.0%
		% within $new1	16.0%	70.0%	62.5%	66.7%	20.0%	60.0%	25.0%	75.0%	100.0%	
		% of Total	8.1%	7.1%	5.1%	4.0%	1.0%	3.0%	1.0%	3.0%	7.1%	39.4%
	1.51 - 2.50	Count	9	2	2	1	3	1	1	1	0	20
		% within CD4.CD8.1	45.0%	10.0%	10.0%	5.0%	15.0%	5.0%	5.0%	5.0%	0.0%	100.0%
		% within $new1	18.0%	20.0%	25.0%	16.7%	60.0%	20.0%	25.0%	25.0%	0.0%	
		% of Total	9.1%	2.0%	2.0%	1.0%	3.0%	1.0%	1.0%	1.0%	0.0%	20.2%
	2.51 - 3.50	Count	5	0	0	1	0	1	0	0	0	7
		% within CD4.CD8.1	71.4%	0.0%	0.0%	14.3%	0.0%	14.3%	0.0%	0.0%	0.0%	100.0%
		% within $new1	10.0%	0.0%	0.0%	16.7%	0.0%	20.0%	0.0%	0.0%	0.0%	
		% of Total	5.1%	0.0%	0.0%	1.0%	0.0%	1.0%	0.0%	0.0%	0.0%	7.1%
	3.51 and higher	Count	28	1	1	0	1	0	2	0	0	33
		% within CD4.CD8.1	84.8%	3.0%	3.0%	0.0%	3.0%	0.0%	6.1%	0.0%	0.0%	100.0%
		% within $new1	56.0%	10.0%	12.5%	0.0%	20.0%	0.0%	50.0%	0.0%	0.0%	
		% of Total	28.3%	1.0%	1.0%	0.0%	1.0%	0.0%	2.0%	0.0%	0.0%	33.3%
Total		Count	50	10	8	6	5	5	4	4	7	99
		% of Total	50.5%	10.1%	8.1%	6.1%	5.1%	5.1%	4.0%	4.0%	7.1%	100.0%

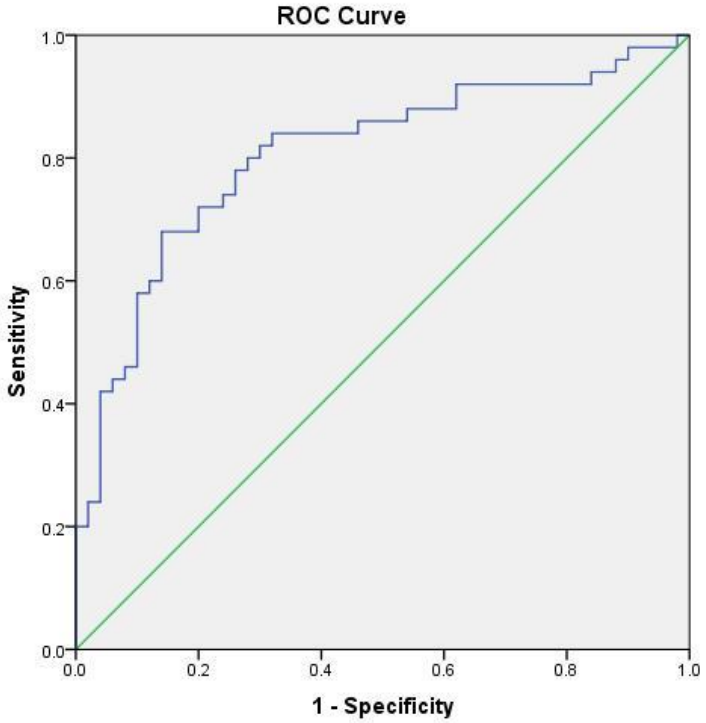

Figure 1. **Performance of CD4+: CD8+ ratios in BAL fluid discriminating sarcoidosis and nonsarcoidosis groups in receiver operator curve space.**

DISCUSSION

BAL fluid T lymphocytes CD4+:CD8+ ratio have been implicated as a diagnostic mean for interstitial lung diseases such as sarcoidosis (10, 15). So far, a few surveys have been carried out in Iran, relevant for the population with pulmonary diseases (10, 15). To the best of our knowledge, this is the first report from Iran, evaluating the CD4+:CD8+ ratio capability in distinguishing sarcoidosis from other interstitial lung diseases (ILDs) on a large cohort. The current study investigated 50 sarcoidosis patients and 50 non-sarcoidosis ILD patients.

In the study, 59 women were involved in the study population, who constituted 72% of sarcoidosis and 46% of nsILDs patients. Our results confirm previous debates on sex parameter in sarcoidosis. As indicated earlier in different studies, sarcoidosis occurs predominantly in female population (16). Our findings were consistent with this fact.

The age of non-sarcoidosis patients with interstitial pulmonary fibrosis, as the most common disorder in nsILDs group showed a slightly significant elevation in contrast to the other nsILDs disorders (53.5 ± 23.30 yrs.).

Moreover, smoking status did not vary significantly between the two main groups ($p > 0.05$).

However, smoking rate was not significantly correlated in two main groups due to investigating the influence of smoking habits upon sarcoidosis.

CRP level was significantly lower in sarcoidosis group compared to the nsILDs group ($p = 0.002$). This finding was due to the fact that all the sarcoidosis patients were newly diagnosed and none of them was in the progressive stage. Generally, progressive sarcoidosis leads to the induction of CRP level, in contrast to stable and newly diagnosed sarcoidosis.

Ordinarily, increased lymphocytes usually activate Th cells, as seen in 90% of BAL of patients with sarcoidosis. CD4+ Th lymphocytes are an immune response regulator in the respiratory organ (11). The current study demonstrated a significantly higher CD4 value in sarcoidosis group versus nsILDs group ($p < 0.05$).

CD8 amount was defined equivalently in both groups. In contrast to our results, Jamaati performed a study on 14 sarcoidosis patients and revealed that CD8 value was insignificantly higher than in the non-sarcoidosis group (10). This may be explained due to the small study population size.

Taking the abovementioned into consideration, the CD4+:CD8+ ratio presents a significant distinctive value between sarcoidosis group and nsILDs group ($p < 0.001$). BAL fluid analysis in non-sarcoidosis ILD pati-

ents showed significantly elevated CD4+:CD8+ ratios in tuberculosis and malignancy subjects in comparison to other nsILDs. Non-sarcoidosis ILDs BAL fluid features demonstrated the significantly increased CD4+:CD8+ ratio in TB and malignancy patients. TB remains a serious public health concern and a major disease in Iranian population (17). The current study revealed that TB group showed significantly lower CD4+:CD8+ ratios than sarcoidosis patients. Therewith, TB and malignancy ratios showed the significantly increased CD4+:CD8+ ratio compared to other subgroups of non-sarcoidosis ILDs ($p < 0.005$).

Age parameter significantly correlated with the CD4+:CD8+ ratio. Furthermore, the CD4+:CD8+ ratio showed a significant correlation with age ($p = 0.01$). Eighty-one point eight per cent of subjects with the CD4+:CD8+ ratio exceeding 3.5 were more than 50 years old.

Two percent of the sarcoidosis population in the current study had the CD4+:CD8+ inversed ratio below 1.0. This finding is in agreement with the ratio below 1.0. shown by Kantrow et al., 12% range obtained by Jamaati et al. and 10.5% range and by Costabel et al (10, 18, 19). The lower inverse range may arise from the different patient collection followed by different designed methods.

The best cut off value of CD4+:CD8+ for the diagnosis of the sarcoidosis was assessed through the ROC curve analysis as 1.1 point with the sensitivity of 92% and a highly specific pattern (80%). This observation is in line with a previous study (16). Similarly, in a study on 27 sarcoidosis patients, a specificity of 89% was observed in distinguishing characteristic transbronchial biopsy in sarcoidosis (11). A population of 117 sarcoidosis patients studied by Costabe et al. demonstrated a sensitivity of 52% and specificity of 94% for the ratio exceeding 3.5 (19). A study involving 38 ocular sarcoidosis patients demonstrated that the CD4+:CD8+ ratio exceeding 3.5 shows a sensitivity of 100% and a specificity of 96.3% in the diagnosis of vitreous lymphocytes (16). Conversely, 86 sarcoidosis patients in another study showed a low sensitivity for the CD4:CD8 ratio (18). This contrasting result may be due to different study designs and studied population.

A previous study in Iran is in line with our results which demonstrated a sensitivity of 54% and specificity of 95% in the CD4+:CD8+ ratio higher than four, distinguishing sarcoidosis patients from TB and non-TB patients. In contrast, CD4+: CD8+ ratio in the current study established higher sensitivity and accuracy. Another study obtained the sensitivity and specificity of 76.4% and 79.4%, respectively, in BAL CD4+:CD8+ with a cut-off point of 1.34, whereas our study presented a better finding (20).

Finally, despite some limitations, the current study was conducted on a large cohort and patients were followed up until the disease was confirmed.

CONCLUSION

Performing BAL, as the safe first step, confirms the diagnosis of sarcoidosis in 92% of cases (current study sensitivity). Hence, only a few patients require undergoing an invasive procedure. BAL CD4+:CD8+ ratio with the lack of morbidity risk or the lethal complications provides a safe and rapid diagnostic technique for sarcoidosis. BAL flow cytometry in the assessment of clinical and radiological findings supplies an appropriate diagnostic adjunct for discriminating sarcoidosis from non-sarcoidosis ILDs.

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Odnos CD4:CD8: Značajan dijagnostički parameter kod plućne sarkoidoze

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SAŽETAK

Sarkoidoza je multiorganska bolest i karakteriše se pojavom sarkoidnog nekazeoznog granuloma koji se sastoji od T-helper/inducer (CD4+) limfocita i retkih citotoksičnih (CD8+) T- limfocita. Povećani odnos CD4+:CD8+ T ćelija karakterističan je dijagnostički parameter za sarkoidozu. Ovo je prvi izveštaj iz Irana u kome je analizirana vrednost odnosa CD4:CD8 u diferencijaciji plućne sarkoidoze od ostalih intersticijalnih bolesti na većoj grupi ispitanika.

U studiju je uključeno pedeset bolesnika sa plućnom sarkoidozom i 50 bolesnika sa nesarkoidnim intersticijalnim plućnim bolestima. Bronhoalveolarna lavaža urađena je pomoću fleksibilne fiberoptičke bronhoskopije i protočne citometrije.

Bolesnici koji nisu imali sarkoidozu bili su podeljeni u osam podgrupa. Pedeset i dva posto bolesnika sa sarkoidozom i 62% bolesnika sa nesarkoidnim intersticijalnim plućnim bolestima imalo je normalne spirometrijske rezultate.

CD4/CD8 odnos bio je značajno povećan kod bolesnika sa sarkoidozom za razliku od pacijenata koji su imali nesarkoidne intersticijalne plućne bolesti ($p < 0,001$). Odnos CD4/CD8 je kod 33,3% bolesnika bio > 3,5, kod 7,1% je iznosio 2,5-3,5, a kod 20,2% 1,5-2,5. Za razlikovanje sarkoidoze od ostalih intersticijalnih bolesti, najbolja granična vrednost je iznosila 1,1 sa senzitivnošću od 92% i specifičnošću od 80%.

Izvođenje bronhoalveolarne lavaže, kao sigurne i brze procedure, potvrdilo je dijagnozu sarkoidoze kod 92% ispitanika (senzitivnost naše studije). Izvođenje invazivne procedure bilo je neophodno kod samo nekoliko bolesnika.

Protočna citometrija bronhoalveolarne lavaže u proceni kliničkih i radioloških nalaza pomaže u razlikovanju sarkoidoze od nesarkoidnih intersticijalnih plućnih bolesti.

Ključne reči: **sarkoidoza, bronhoalveolarna lavaža, limfociti, CD4+:CD8+ odnos, protočna citometrija**