



Chitotriosidase – reliable test for sarcoidosis activity

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Abstract

BACKGROUND

Chitotriosidase is an enzyme secreted by activated macrophages able to catalyze the hydrolysis of both chitin and chitin-like substrates. Patients with sarcoidosis have elevated levels of chitotriosidase as the result of massive production of chitotriosidase by sarcoid macrophages. The aim of the study was to analyze serum chitotriosidase concentrations in patients with active vs. inactive sarcoidosis. We also wanted to compare the reliability of these results with serum angiotensin-converting enzyme (ACE) in sarcoidosis patients.



METHODS

53 biopsy positive sarcoidosis patients were enrolled in this study (39 female and 14 male) mean age 50.4 years. 37 patients had active and 16 patients had inactive sarcoidosis. Level of serum chitotriosidase and serum ACE were analyzed in relation to the clinical activity of sarcoidosis.

RESULTS

Considering the small investigated sample of our group of patients we performed discriminant analyses. Discriminant analysis showed that cut off for chitotriosidase in the group of patients with active diseases is highly statistically significant (Lambda=0.654; Chi square=21.417; Canonical Correlation=0.588 p<0.05) than in the group with inactive disease. The difference for serum ACE level was not statistically significant to coexist with the disease activity. (Lambda=0.896; Chi square=5.525; Canonical Correlation=0.322 p<0.05)

CONCLUSION

Although this data needs to be validated by further investigations, the observations made in this study seem to indicate that serum chitotriosidase concentrations may be a useful marker for monitoring sarcoidosis disease activity and prognosis.

Patients & Methods

This was a pilot study done with the help of Mr sci pharm. Sumarac Zorica, Biochemical laboratory, Clinical Center Serbia, Belgrade, who has been working for years on the same test in patients with Gaucher disease.

Sarcoidosis patients	53 biopsy positive sarcoidosis patients
Female	39
Male	14
Mean age	50.4 years
Active sarcoidosis: (symptoms, clinical signs, lung function, chest Xray)	37
Not active sarcoidosis	16

All sarcoidosis patients voluntarily joined the study. This small sample of patients is a part of a large group of 1600 sarcoidosis patients registered in Serbia.

The aim of the study was to analyze serum chitotriosidase concentrations in patients with active vs. inactive sarcoidosis. We also wanted to compare the reliability of these results with serum angiotensin-converting enzyme (ACE) in sarcoidosis patients.

Considering the small investigated sample of our group of patients we performed Discriminant analyses. Elevated serum chitotriosidase (according to the lab test value) was > 166 nmol/l/h and elevated serum ACE > 52 U/l

Conclusion



Although this data needs to be validated by further investigations, the observations made in this study seem to indicate that serum chitotriosidase concentrations may be useful marker for monitoring sarcoidosis disease activity and prognosis.

Literature:

- Grosso S, Margollicci MA, Bargagli E, et al: Serum levels of chitotriosidase as a marker of disease activity and clinical stage in sarcoidosis. Scand J Clin Lab Invest 2004; 64: 57–62.
- Korolenko TA, Zhanaeva SY, Falameeva OV, et al: Chitotriosidase as a marker of macrophage stimulation. Bull Exp Biol Med 2000; 130: 948–950.
- Dai H, Guzman J, Chen B, Costabel U: Production of soluble TNF receptor and TNF alpha by alveolar macrophages in sarcoidosis and extrinsic allergic alveolitis. Chest 2005; 127: 251–256
- Boot RG, Bussink AP, Verhoek M, et al: Marked differences in tissue-specific expression of chitinases in mouse and man. J Histochem Cytochem 2005; 53: 1283–1292.
- Aguilera B, Ghauharali-van der Vlugt K, Helmond MTJ, et al: Transglycosidase activity of chitotriosidase. J Biol Chem 2003; 278: 40911–40916
- Bargagli E, Maggiorelli C, Rottoli P: Human Chitotriosidase: A Potential New Marker of Sarcoidosis Severity. Respiration 2008; 76: 234–238

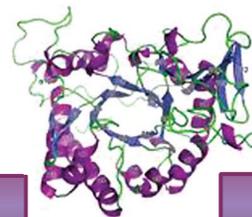
Results

Summary of Canonical Discriminant Functions (Serum Chitotriosidase)

Eigenvalues

Function	Eigenvalue	% of Variance	Cumulative %	Canonical Correlation
1	.528 ^a	100.0	100.0	.588

a. First 1 canonical discriminant functions were used in the analysis.



Summary of Canonical Discriminant Functions (serum ACE)

Eigenvalues

Function	Eigenvalue	% of Variance	Cumulative %	Canonical Correlation
1	.116 ^a	100.0	100.0	.322

a. First 1 canonical discriminant functions were used in the analysis.

Wilks' Lambda

Test of Function(s)	Wilks' Lambda	Chi-square	df	Sig.
1	.654	21.417	1	.000

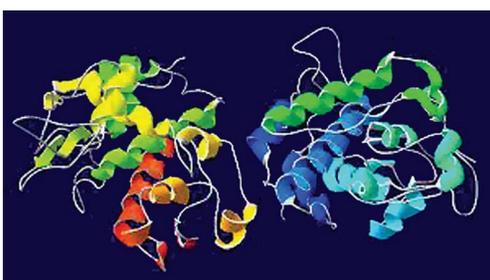
Discriminant analysis showed that elevated serum chitotriosidase in the group of patients with active diseases is highly statistically significant than in the group with inactive disease. (Lambda=0.654; Chi square=21.417; Canonical Correlation=0.588 p<0.05)

Wilks' Lambda

Test of Function(s)	Wilks' Lambda	Chi-square	df	Sig.
1	.896	5.525	1	.019

The difference for serum ACE levels were not statistically significant to coexist with the disease activity. (Lambda=0.896; Chi square=5.525; Canonical Correlation=0.322 p<0.05)

Introduction



Sarcoidosis is a multisystemic granulomatous disorder of unknown etiology. The unpredictable clinical course of the disease has prompted research into

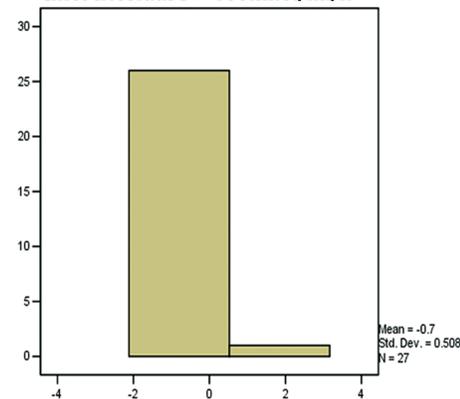
biomarkers useful for predicting outcome. Among the potential markers of sarcoidosis, a recently proposed indicator was chitotriosidase, a chitinase produced by activated macrophages. Chitotriosidase is involved in the defense against pathogens containing chitin. Increased concentrations of chitotriosidase have been observed in a number of lysosomal storage diseases including Gaucher disease and more recently also in sarcoidosis.

In 2004, significantly higher serum chitotriosidase activity was reported for the first time in sarcoidosis patients with respect to controls by Grosso and co workers. Chitotriosidase has been considered as serum marker of macrophage activation.

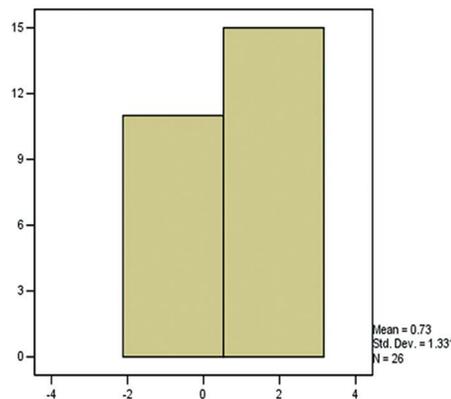
Enzyme activity was also found to be more elevated in active sarcoidosis than in patients with inactive sarcoidosis, and correlations with serum ACE concentrations and radiographic stages, were reported, suggesting that the enzyme could be a marker of disease severity.

Canonical Discriminant Function

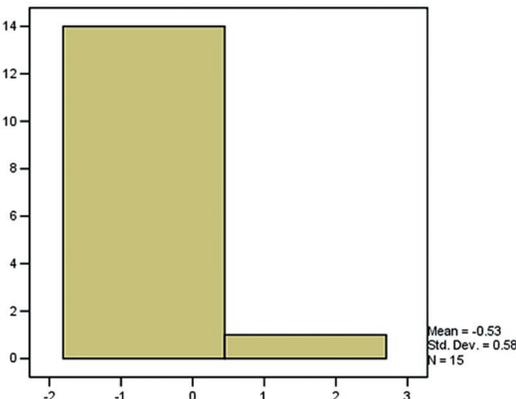
Chitotriosidase > 166nmol/ml/h



Chitotriosidase < 166nmol/ml/h



ACE > 52U/l



ACE < 52U/l

