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ORIGINAL ARTICLE

Role of interleukin-6 in diagnosis of pleural effusion

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KEYWORDS

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Abstract *Objectives:* To determine the level of interleukin-6 (IL-6) in both serum and pleural fluid in order to evaluate the diagnostic utility of IL-6 in differentiation between different types of pleural effusion.

Background: Pleural effusion is a relatively common clinical condition. It is often diagnostic dilemma for the physician. Interleukin-6 (IL-6) has multiple functions on various cells and tissues. It is often used as a marker for systemic activation of pro-inflammatory cytokines.

Methods: This study was conducted on 40 patients of pleural effusion, they were selected from Al-Mahalla Chest Hospital in the period between October 2012 and May 2013. All patients were subjected to detailed clinical history, thorough clinical examination, plain chest-X-ray (postero-anterior and lateral views), blood sample for: Complete blood picture (CBC), erythrocyte sedimentation rate (ESR), liver functions, renal functions and serum and pleural fluid (LDH, protein and IL-6) by ELISA.

Results: Serum and effusion IL-6 could differentiate between exudate transudate as it increased in exudate than transudate. In the present study there was higher concentration of IL-6 in the serum and pleural effusion of parapneumonic effusion than malignant and tuberculous exudative pleural effusion and higher concentration in malignant than tuberculous effusion.

Conclusion: Effusion IL-6 could be used to differentiate between exudate and transudate and serum IL-6 could be used as an alternative non invasive method for differentiation between exudates and transudate as there was a significant positive correlation between serum IL-6 and effusion IL-6.

Introduction

Pleural effusion occurs in a great variety of abnormalities. Even exhaustive diagnostic tests fail to reveal the etiology in about 20 percent of the cases [1]. Distinguishing an exudate

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from transudate is the initial step determining the cause of pleural effusion. Pleural fluid is enriched in proteins, inflammatory cells, and mediators [2]. Cytokines-producing cells and cytokines have been reported in pleural effusion from patients with malignant diseases, tuberculosis and empyema [3]. Tuberculous pleurisy (TBP) is a common cause of pleural effusion in areas with high disease prevalence, the diagnosis of TBP represents largely an immunological reaction in which a repertoire of cytokines is involved in pathogenesis. These include especially interleukin (IL) IL-22, IL-6, IL-8, tumor necrosis factor-alpha (TNF-α), and interferon gamma (INF-γ) [4]. The pleiotropic cytokine interleukin-6 (IL-6) is a major marker of systemic response to inflammatory process and is involved in the regulation of a variety of cellular responses [5].

Aim of the study

The aim of this work is to determine the level of interleukin-6 (IL-6) in both serum and pleural fluid in order to evaluate the diagnostic utility of IL-6 in differentiation between different types of pleural effusion.

Methods

A written consent was obtained from all subjects prior to inclusion and the regional ethics committee of the Menoufia University hospital approved the study. The study was conducted in Al-Mahalla chest hospital during the period between October 2012 and May 2013. The study involved forty patients with pleural effusion; their ages ranged from 25 to 75 years. 15 were females and 25 were males.

Study subjects were divided into two groups: Group I: included 15 cases with transudative pleural effusion, and classified into Group Ia: 6 cases with transudative pleural effusions due to liver cell failure. Group Ib: 6 cases with transudative pleural effusions due to heart failure. Group Ic: 2 cases with transudative pleural effusions due to combined heart and liver cell failure. Their ages ranged from 54 to 65 years And 1 case due to renal failure. Group II: This group included 25 cases with exudative pleural effusion. This group was subdivided into: Group IIa: 4 cases with exudative tuberculous effusions, 1 male and 3 females. Group IIb: 6 cases with exudative parapneumonic pleural effusions, 5 cases were males and 1 female. Group IIc: 10 cases with exudative malignant pleural effusions, 8 cases were males and 2 females. 2 cases were with exudative collagen pleural effusions. 1 case was with exudative effusion due to pulmonary embolism. 1 case was with exudative pleural effusions due to cholecystectomy operation. 1 case was with exudative pleural effusion due to Meig's syndrome.

All subjects were subjected to: detailed clinical history, thorough clinical examination, plain chest-X-ray, blood sample for: CBC, ESR, liver functions, renal functions, serum and pleural effusion (LDH, protein and serum and IL-6).

Results

There was a statistically highly significant difference between patients with transudative and exudative pleural effusion as regards pleural fluid protein, serum LDH, pleural fluid LDH and pleural fluid IL-6 ($P \leqslant 0.001$), and a non statistically significant difference between both groups as regards serum protein ($P > 0.05$), and significant difference between the two groups as regards serum IL-6 (as shown in Table 1).

This study showed a statistically significant increase in serum and effusion LDH and highly significant increase in effusion IL-6 in patients with transudative effusion due to liver cell failure, and also showed a statistically significant increase in serum and effusion LDH in patients with transudative effusion due to heart failure in comparison with liver cell failure, while no statistically significant difference in serum and effusion LDH and effusion IL-6 in patients with transudative effusion due to combined liver cell failure and heart failure (as shown in Table 2).

This study showed that patients with parapneumonic effusion had statistically significantly higher pleural fluid LDH and IL-6 levels than non parapneumonic effusion while serum pleural fluid protein and serum LDH didn't differ between both groups (as shown in Table 3).

There was a highly significant difference between malignant and parapneumonic exudative pleural fluid as regards effusion LDH, there was a significant difference between tuberculous and parapneumonic exudative pleural effusion as regards serum IL-6, there was a significant difference between malignant and parapneumonic exudative pleural fluid as regards effusion IL-6 and there is a highly significant difference between TB and parapneumonic exudative pleural effusion as regards effusion IL-6 (as shown in Table 4).

There was a significant positive correlation between serum IL-6 and pleural fluid protein and (serum and effusion) LDH. And there was a significant positive correlation between

Table 1 Comparison between patients with transudative effusion and patients with exudative effusion as regards serum and effusion protein (g/dl), LDH (u/dl) and IL-6 (u/ml).

	Transudate (n = 15)		Exudate (n = 25)		T-test	
	Range	Mean ± SD	Range	Mean ± SD	T	P-value
Serum protein (g/dl)	5.9–8.1	6.665 ± 0.661	6–7	6.5 ± 0.4	0.8	0.4
Pleural fluid protein (g/dl)	1.2–4.1	2.3 ± 0.9	3–4.7	3.8 ± 0.45	7.03	0.000**
Serum LDH (u/dl)	87–319	199.33 ± 87.15	163–625	461.8–126.1	−76	0.000**
Pleural fluid LDH (u/dl)	109–552	318.3 ± 139.9	315–1405	884.1 ± 276.3	−7.4	0.000**
Serum IL-6 (pg/ml)	19–37	26.9 ± 5.7	14.2–190	106.6 ± 53.9	−5.7	0.03*
Pleural fluid IL-6 (pg/ml)	91–530	254.1 ± 136.4	91–1900	863.9 ± 526.2	−4.4	0.000**

* Means significant.
** Means highly significant.