CELL MARKERS QUANTITATION IN PLEURAL EFFUSION

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BY

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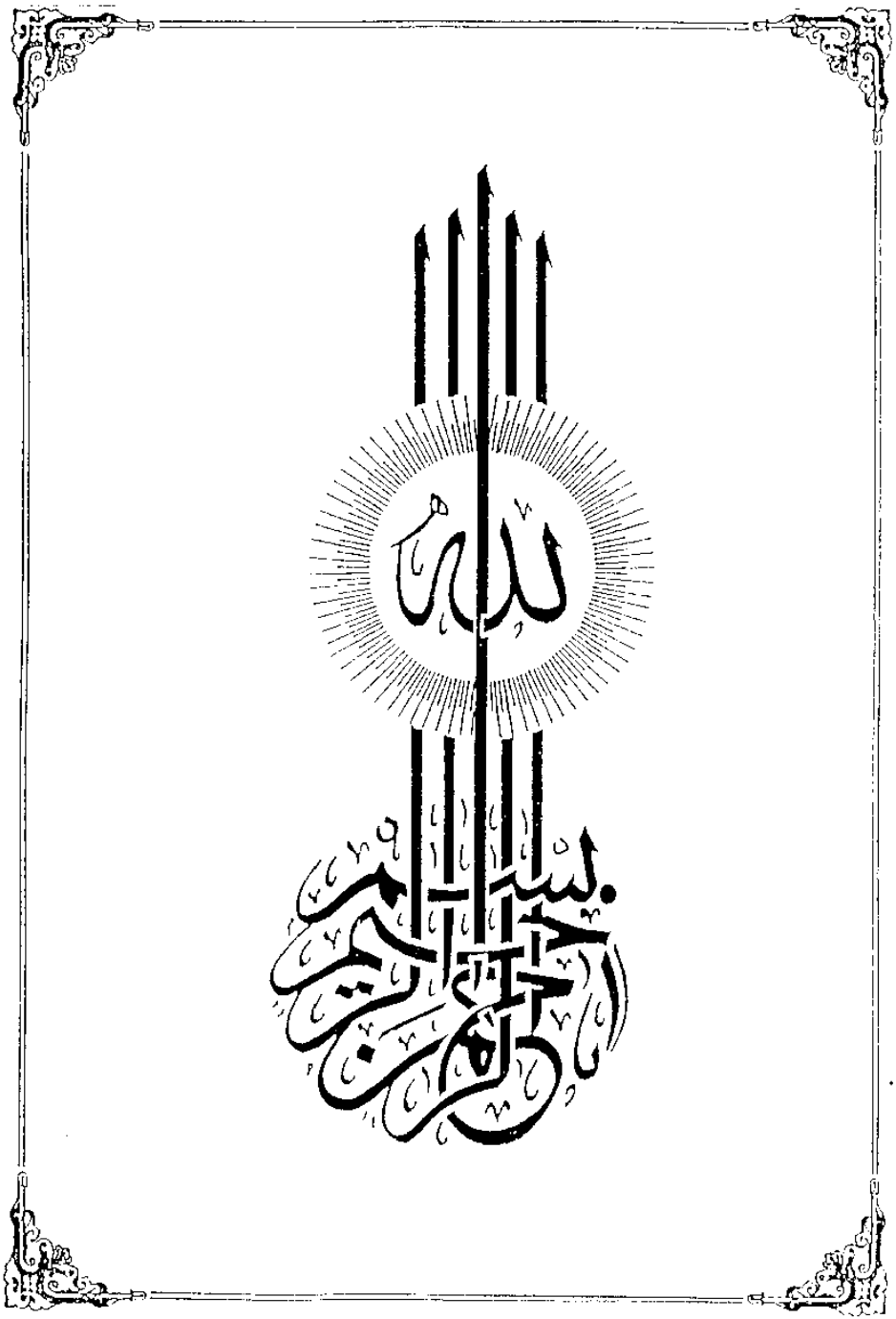

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CONTENTS

Page

ACKNOWLEDGEMENT..... i

INTRODUCTION AND AIM OF WORK..... 1

REVIEW OF LITERATURE..... 2

MATERIAL AND METHODS.....113

RESULTS.....129

DISCUSSION.....193

SUMMARY AND CONCLUSION.....207

REFERENCES.....210

ARABIC SUMMARY..... -

INTRODUCTION AND AIM OF THE WORK

The pleural effusion stands frequently as a difficult problem for many physicians, that has to be solved especially with the advent of modern techniques for diagnosis.

Pleural effusion is an important and common clinical finding. In some diseases, this represents the initial or the only presentation and its presence can alter the prognosis and the treatment of the concomitant disease. Pleural effusion can accompany many diseases at some stage of their evolution, however the etiology of the effusions is often obscure and various diagnostic procedures may be required in order to find their causes, cases in which an etiology could not be found are not uncommon.

Lately , several tumour markers such as carcinoembryonic antigen (CEA) and α -fetoprotein(AFP), β_2 microglobulin (β_2M) and α_1- acid glycoprotein (AGP) had been ascribed to be useful aids in diagnosis of malignant pleural fluids.

AIM OF THE WORK

Measurement of the concentration of CEA, AFP ,AGP and β_2 m both in pleural fluid and in the serum as a diagnostic tools in the differentiation between malignant and non-malignant pleural effusions.

REVIEW OF LITERATURE

CLASSIFICATION OF PLEURAL EFFUSION:

It is convenient and clinically useful to classify pleural effusion as transudates and exudates (Paddock,1940). A pleural fluid containing protein of 3 gm /100 ml or more and specific gravity of 1016 or more has classically been as an exudate. Transudates have a lower protein level and specific gravity(Paddock,1941). In one series, 8% of exudate and 15% of transudates were misclassified (Carr and Power,1958).

In 1972 Light and associates reported a new set of criteria that have proved to be more sensitive: A ratio of pleural fluid to serum protein of 0.5 or more. A pleural fluid lactate dehydrogenase(LDH) content of 200 IU or more. A ratio of pleural fluid to serum LDH of 0.6 or more. A pleural fluid red blood cell count of 100,000 cells/mm^3 or more. Using these criteria, exudative pleural fluids will be diagnosed accuratelly in more than 70% of patients if any one of these criteria is present, and in more than 90% of two or more of these criteria are found (Light et al., 1972).

PRINCIPAL CAUSES OF TRANSUDATES

1) Congestive heart failure:

It is by far the commonest cause of pleural effusion, the effusion is most likely to occur when there is both systemic and pulmonary venous hypertension. In this situation, fluid formation by the systemic pleural capillaries is increased, absorption by pulmonary pleural capillaries is decreased and lymphatic drainge is impeded by the systemic venous hypertension. Absorption of pleural fluid by the viscral pleural capillaries in the presence of normal pulmonary venous pressure may explain the low incidence of pleural effusions in patients with right heart failure due to chronic obstructive lung disease. The fluid is typically clear, straw colored and a transudate, with the total leukocyte count being less than $1000/mm^3$ and the differential revealing mainly lymphocytes (Light,1963). In one series, 88% of the effusion were bilateral, 8.3% were right sided and 3.8% were left sided (Race et al., 1957).

2) Cirrhosis of the liver:

It is associated with pleural effusion only when ascites is present. The most likely cause for these effusion is transfere of the fluid from the peritoneal cavity to the pleural cavity via defects in the diaphragm or via diaphragmatic lymphatic channels. Other contributing factor are hypoproteinemia and azygous vein hypertension. The fluid is a transudate, and the leukocyte count is usually less than

500/mm^3. The fluid is blood tinged because of associated hypoprothrombinemia. (Huber and Hass,1969). The predominance of pleural fluid on the right may be explained by the fact that the lymphatic network on the right side of the diaphragm is more extensive than that on the left (Petty,1975).

3) Constrictive pericarditis:

Pleural effusion results from the combined effect of congestive heart failure and hypoproteinamia due to liver damage from congestive heart failure. Gross congestive failure with a radiographically small heart should suggest the diagnosis. Calcification of the pericardium in a lateral view may be present (Crofton and Douglas,1981).

4) Nephrotic syndrome:

Mechanism of pleural effusion in nephrotic syndrome is diminution of plasma osmotic pressure. The fluid is commonly located in infrapulmonic space (Trevina and Vich,1958).

5) Acute glomerunephritis:

The effusion observed in children with acute glomerunephritis were usually associated with cardiomegaly and pulmonary edema and were usually a mainfestation of fluid overload (Kirkpartick and Fleisher,1964).

6) Myxoedema :

It may occasionally give rise to pleural effusion. The fluid is transudate and appears to be due to altered capillary permeability. The effusion disappears after treatment with thyroxine (Schewerson and Zaly ,1958).

7) Uramic patients treated with peritoneal dialysis:

In 1967, Edwards and Unger observed massive pleural effusion on the right side of uramic patients during peritoneal dialysis. The mechanism of this effusion appears to be due to increased intra-abdominal pressure, which stretches the diaphragm, resulting in leakage of fluid from the peritoneal to pleural cavity.

8) Meigs Syndrome:

In 1954, Meigs observed pleural effusion in patient with an ovarian neoplasm. This syndrome has the following criteria:

- Tumour must be benign and solid as fibroma.
- The tumour must be accompanied by ascitis.
- Pleural effusion must be present.
- Removal of the ovarian tumour must lead to clearing of the ascitis and the pleural effusion.

The effusion is usually on the right side but may be bilateral. The fluid is usually straw colored but may be blood tinged. There is usually a predominance of lymphocytes, a protein concentration of less than 3.5 gm/ 100 ml , a normal sugar value and negative cytopathological finding (Mokrohisky,1958).

PRINCIPAL CAUSES OF EXUDATES:

1. Parapneumonic pleural effusion:

Streptococcus pneumonia does not commonly cause a roengero-graphically demonstrable pleural effusion. When effusion do develop after several days of observation, they are often sterile with low leukocyte counts. Streptococcus pyogenes pneumonias are not frequent, they are unique, however, in that there is an extremely high incidence of associated parapneumonic effusions. (Welch, et al., 196). They suggested that streptococcal effusion may be due to the plugging of lymphatic vessels by purulent materials.

Klebsiella pneumoniae, usually occuring in alcoholics and diabetics, is characterized by involvement of the upper lobe, bulging of the interlobar fissure and cavitation. Pleural effusion complicates the disease in 5 to 35% of patients. The effusions are most commonly sterile and small (Reid et al., 1967).

Pseudomonal aernginosa pneumonias occur most commonly in patients with chronic pulmonary or cardiac diseases. There is high incidence of parapneumonic effusions in those patients. The pleural fluid appears to be thin with leukocyte counts of less than 20,000/mm^3 (Tilotson and Lerner, 1967).

Culture from blood or pleural fluid is more than isolation of gram-negative from sputum especially in patients who had already received chemotherapy (Fetzer et al.,1967).

Tilotson and Lerner(1968),also described an associated empyema with bacteroides pneumonia. The pleural fluid tends to be thick, foul smelling and frequently loculated. The diagnosis is suspected by Gram-strain and confirmed by anaerobic culture of pleural fluid.

Staphylococcus aureus pneumonias are frequently complicated by pleural effusions, 90% of infants and 15-20% of adults. These effusions often develops very rapidly (Steiles et al.,1970).

Escherichia coli pneumonia tends to occur in patients with diabetes, pyelonephrities and cardiac disease and generally follows bacteremias originating from infections of the gastro-intestinal or genitourinary tract. The pneumonias tend to be patchy and involve the lower lobe which is often complicated by empyema (Tilotson and Lerner,1969).

Haemophilus influenza is not a common of pneumonia in adults. Pure hamophilus pneumonia is said to be usually due to encapsulated strains especially type B and is rarely associated with parapneumonic effusions (Wallace et al.,1978).

Two stages in the evolution of parapneumonic effusions are recognized. In the exudative phase,there is rapid movement of fluid into the pleural space because of pleural inflammation. The fluid contains relatively few leukocytes.

In the fibropurulent stage, cellular debris, large numbers of neutrophils and fibrin accumulate. Loculation tends to occur during this stage. In the organizational stage, fibroblastic proliferation and collagen formation occur on both pleural surfaces, causing pleural fibrosis (Petty, 1975).

In post pneumonic effusions the fluid is amber or straw colured, possibly turbid and on microscopic examination, the predominant cell is neutrophil polymorph. The patient is nearly always having antibiotic treatment when the effusion develops and it is not common for the causal organism to be cultured from the fluid (Potts et al.,1976).

The pleural reaction which so frequently accompanies bacterial pneumonias may progress to pleural effusion and this complication should always be suspected if fever persists despite appropriate chemotherapy. Usually there will be recognizable preceeding features of pneumonia(Crofton and Douglas,1981).