STUDY OF IMMUNOGLOBULIN A, ALPHA -1- ANTITRYPSIN & CERULOPLASMIN IN CASES OF BENIGN AND MALIGNANT PLEURAL EFFUSION

THESIS

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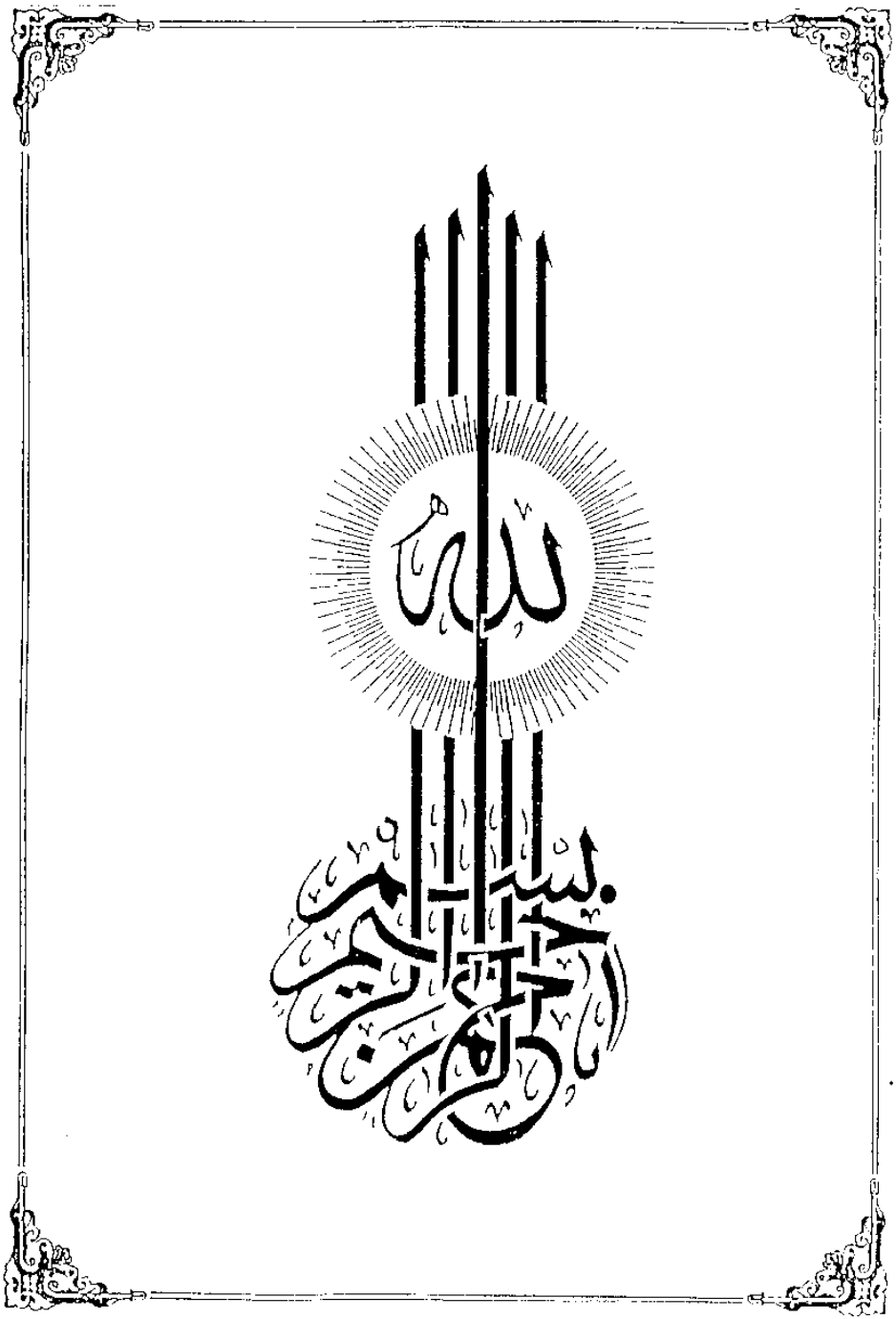

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The pleural effusion stands frequently as a difficult problem for many physicians , that has to be solved especially with the advent of modern techniques for diagnosis.

Regardless of the underlying disease, pleural fluid contains all the major protein fractions present in the serum and probably originated from it. It was, thus thought that fractionation of proteins of different pleural fluids, and its comparison with those of serum might throw further light on possible aetolgenesis of pleural effusion (Salem et al, 1967 and Watkins, 1958) .

The present study deals with estimation of Immunoglobulin A, Alpha-1- antitrypsin and ceruloplasmin in the serum and pleural effusion in cases of benign and malignant pleural effusion and the aim of this study is to use these variations as markers which may help in differentiation of the aetiology of different cases of pleural effusion.

IMMUNOGLOBULINS

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Immunoglobulins are glycoproteins composed of 82-96% polypeptides and 4-18% Carbohydrate (Andrews and Copora ,1980) . The name of immunoglobulin was given by Hermous in 1959. They are mediators of humoral or antibody-mediated immunity , they are present in the blood stream, tissues and exocrine secretions or attached to cell surface.

These immunoglobulins are synthesized by plasma cells and to a lesser extent by circulating lymphocytes, lymphoid plasma cells and reticulum cells. All of them originate from B lymphocytes (Stiehem and Fulginite, 1980) .

All immunoglobulins have the same chemical structure of two types of polypeptide chains light and heavy chains (Eisen , 1974) .

The light chains are common to all immunoglobulin classes, Kappa (K) and Lambda (L) .While the heavy chain pair is different in each immunoglobulin class named gamma (γ) , alpha (α) , delta (δ) ar episilon (E) (Andrews and Copora, 1980).

Porter (1959) was able to fractionate the immunoglobulin molecule into fragments , one reacts with the antigen and called antigen binding fraction or "fab" and the other is a crystallizable fraction or "fc". This fraction is necessary for a number of effector functions including complement fixation, cell binding and placental transport.

Immunoglobulins are classified into 5 major classes IgG, IgA,IgM,IgD and IgE. The last one makes less than 1% of the total body immunoglobulins (Fedunburg et al ,19 78) These classes are defined by presence of specific heavy chain: gamma, alpha, M, delta and episilon. Each class of heavy chains may combine with either Koppa or lambda chains. Most of these classes have been divided into subclasses as of IgA (A1 and A2) two subclasses of IgM (M1 and M2) have also been identified (Natvig and Kunkel, 1973) .

Immunoglobulin destruction occurs in the cells of the reticulo-endothelial system particularly in the liver and in gastro-intestinal tract. As much as 40% of the immunoglobulins may be broken down within the intestinal lumen. Small quantity of immunoglobulins are also lost via the Kidney (Stiehem and Fulginite, 1980) .

Immunoglobulin A:-

IgA constitutes 13% of normal serum immunoglobulins . It is present in the plasma but its highest concentration is found in secretions (mucous, colostrum, tears, saliva, sweat etc) and it is an important factor in preventing infection of mucous membrane of respiratory and gastrointestinal tract (Tomäsi and Grey 1972) . Its molecular weight is 160,000 dultons, IgA contains a wide variety of antibodies which include antitoxins, antibacterial, agglutinins , isoagglutinins and skin senstizing antibodies. Two subclasses of IgA (A1 and A2) were detected (Richard , 1972) . T Helper function is required for both primary and secondary IgA responses (Benner et al., 1974) . Most of IgA in exocrine secretions appears to be locally synthesized in plasma cells in submucosa or regional lymph nodes. The primary form of serum IgA is the H2 h2 monomer while in secretion the predominant form is the dimer (Andrews and Copora,1980) .

IgA has a short half life with an average 5-8 days (Woldmann, 1969) . Patient with selective IgA deficiency have an increased frequency of infections

especially in respiratory system , of allergies, gastro-intestinal infections , autoimmune diseases and inward tendency to malignancies (Howowitz and Hong, 1977) .

IgA Deficiency , Respiratory Infection and Asthma:-

There are some evidences for an association between respiratory disease including asthma and depressed IgA in the serum.

Koistinen (1975) found virtually no lower respiratory tract infection and a significant increase in uppper respiratory tract infection in blood donors with IgA deficiency. The finding might be misleading if subject with recurrent respiratory infection did not become blood donors .Several authors have suggested that there is an association between IgA deficiency and upper respiratory tract infection. There is a little evidence for an association between IgA deficiency and asthma. Buckley et al,(1968) found no patient with low or absent IgA in a pediatric series of 85 patients. Kaufmen and Hobbs (1970) found four patients with IgA deficiency out of 641 patients seen at dermatological clinic.

Moderate IgA deficiency and Respiratory tract diseases:

The lack of correlation between serum IgA and respiratory tract infection in childhood is puzzling. The most likely explanation is that the true correlate of resistance to recurrent respiratory tract infection is the ability to increase secretory IgA during and not the absolute level of serum IgA (Kibbutz and Silvien 1977) .

In adults the lack of correlation between infection and serum IgA may be due to studying patients with respiratory diseases due to smoking and other causes. In fact ,patients with recurrent attacks of bronchitis with normal health between attacks, who lack obvious causes of chest infection, have a raised incidence of moderately low serum IgA . These findings were not an artifact due to the selective referral of patients with depressed serum IgA (Buckely et al (1968) .

Allergic diseases and IgA deficiency:

Harrison et al (1976) described 25 infants mainly boys who presented with weight loss , vomiting and diarrhoea related to cow's milk,occult blood and reducing

substances (Sugars), were found in the stools. Nearly all the children had a family history of allergy and positive prick test. Forty percent of the infants had IgA below the normal for their ages.

However as the range of mortality includes undetected levels in their age group, these studies are difficult to interpret in the absence of concurrent controls for the level of serum IgA. Ostergaard (1977) Provided good evidance that moderately low serum IgA was associated with an increased severity of asthma, and increased incidence of asthma precipitated by infection .

Diabetes:-

Ambus et al (1977) found a raised incidence of diabetes in cases of IgA deficiency but the series is difficult to assess because the basis for selection is unknown,however Smith et al,(1978) found a raised incidence of IgA deficiency in juvenile but not in adult onset diabetes .

Secondary IgA Deficiency:-

IgA deficiency may be secondary to taking certain drugs in particular phenytoin . It may develop in patients with still's disease and ulcerative colitis. Its reversion to normal has been observed in a patient with systemic lupus erythematosus (Savilahti& Fikonen 1980) It has been reported following congenital rubella (South et al, 1975) . It may be the first immunoglobulin to be depressed in chronic lymphatic leukaemia. Somewhat low levels of IgA and IgM occur in lichen plannus(Stankler 1975) .

Drugs:-

Phenytoin is used to treat epilepsy and causes depression of lymphocytic count and frank lymphopenia when the blood levels are high (Brandt & Nilsson ,1976) Mackinney &Booker ,1972) .

Penicillamine depresses serum IgA. This probably explains the moderately low serum IgA seen in a few patients with Wilson's hepato-lenticular degeneration who were treated with penicillamine (Strick land & lew 1975) . Gold (Sodium aurothiomalte)is another drug

which may depress serum IgA (Stan worth et al, 1977).

IgA in lymphomas and lymphatic leukaemias:-

Studies on the immunological changes in lymphatic leukaemias and lymphomas were undertaken by different workers. No equivocal tumour specific markers have been identified in leukaemias and lymphomas(Bowman et al, 1980) . The result ofserum immunoglobulins are conflicting due to variation in methodology and patient selection. Massaud et al(1984) in a study of 48 untreated Hodjkin's disease found that the mean value IgA started to increase in the sera of advanced Hodjkin's disease.

Nasr et al, (1982) found that IgA level was increased in the serum of patient with acute lymphatic leukaemia.

IgA in lung cancer patients:-

Khalifa et al, (1983) carried on biochemical and immunological studies on 9 patients with lung cancer, They found that there was a significant increase in serum IgA& IgG.