STUDIES ON THE INCIDENCE OF CYTOMEGALOVIRUS IN ENDEMIC HEPATOSPLENOMEGALY

Thesis

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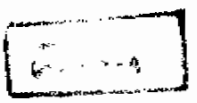
Tropical Medicine



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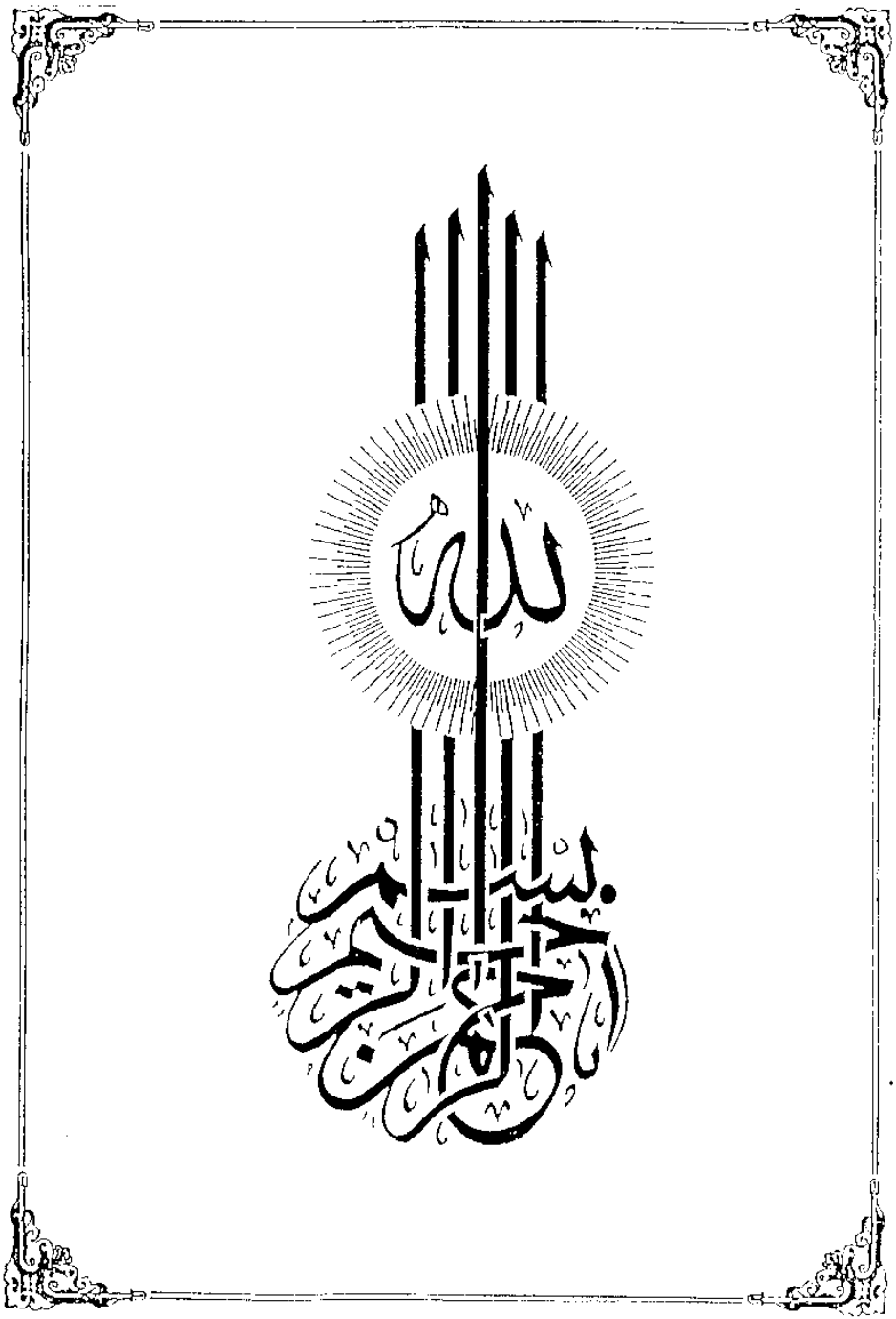

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Introduction:

Infection with cytomegalovirus (C.M.V) was found to be common in immunodeficiency syndromes with high morbidity and mortality. The population at greater risk for C.M.V. infection and diseases are those undergoing transplantation and those with malignancies receiving chemotherapy especially persons with reticuloendothelial cancer. Other debilitating conditions and homosexual men have also been associated with increase incidence of C.M.V. infection (Ho, 1982 and Drew et al., 1981). Because of the frequency of C.M.V. with AIDS up to 100%, C.M.V. was originally thought by some authors to be the etiologic agent(Siegal et al., 1981).

A lot of work has been done on depressed cell mediated immunity in endemic hepatosplenomegaly (Gastle et al., 1984, Fledmeier et al., 1985 and Masoud et al., 1986), hence the incidence of cytomegalovirus could be increased in this syndrome.

Aim of the Work:

The aim of this work was to study the incidence of cytomegalovirus in endemic hepatosplenomegalic paitents.

REVIEW OF LITERATURE

CYTOMEGALOVIRUS INFECTION

Definition:

Cytmegalovirus (CMV) is aubiquitous agent that usually produces either inapparent illness or an infectious mononucleosis syndrome in infected adults. However, it can cause severe or even fatal disease in the immunocompromised patient, noenate, or fetus. (Starr et al., 1979).

Biology:

Cyotomegalovirus is a D.N.A. virus belonging to the herpes virus group that also include varicella, herpes zoster, herpes simplex virus and Epstein-Bar virus (E.B.V.). There are a number of different strains of C.M.V. All have specific characteristics including a strong propensity for cell association and lability (fresh material is needed for isolation), a tendency to remain latent, and possibly, a potential for malignancy (Bhumbra and Nankervis 1983).

Epidemiology:

Cytomegalovirus was originally discovered by

Jesionek who described enlarged cells with inclusion in an infant in 1904 (Gold and Nankervis, 1982). In 1920 Goodpasture coined the term "cytomegalia" to describe the swollen cell which a viral cause was postulated. In 1932 Farber and Wolbach noted inclusions in salivary glands of 14% out of 183 autopsied infants. Finally in 1956 Smith isolated C.M.V. (Gold and Nankervis, 1982).

Cytomegalovirus infection has worldwide distribution, with higher infection rates occurring in third world countries where crowding and poor living conditions coexist. Approximately 50% of women in the childbearing period are seropositive (Krech and Tobin 1981). Congenital cytomegalovirus infection, as diagnosed by isolation of virus from neonates, is found in approximately 1% of all populations around the world. (Hanshaw, 1971). Only a small proportion about 5% of infected babies are affected severely enough to exhibit symptoms of birth, but long-term pediatric surveillence of apparently unaffected neonates has shown that many about 10% to 15% will subsequently develop abnormalities of hearing or intellectual function (Reynolds et al., 1974). It is the most common infectious cause of

congenital deafness and mental retardation (Reynolds et al., 1974).

Mode of Transmission:

In newborns it is usually acquired congenitally or during passage through the birth canal (Gold and Nankervis, 1982). In children, particularly those in day care centers droplet is a major mode of transmission (Pass et al., 1982). In adults transmission include droplet, fecal-oral route, blood transfusion. There is direct relationship between occurrence of C.M.V. infection and the number of unites of blood transfusion (Yeager et al.,1981).

It can also transmitted by sexual contact (Lang et al., 1974).

Pathology:

As its name implies, the formation of giant cells is the essential feature of the pathology of C.M.V. disease. These cells may measure between20 and 40 u in diameter, and they are characterized by the presence of intranuclear and intracytoplasmic inclusion bodies. In the neonatal form of the disease

these inclusion bodies are found almost in any tissue of the body i.e. diffuse form: in the salivary glands, in the liver, lung, kidney, pancreas, thyroid, in the brain and meninges, in the bone marrow, heart, spleen and in the eye (Weller and Hanshaw, 1962). In some organs there may be infiltration of the interstitial tissue with mononuclear cells: subacute mononuclear pneumonitis and interstitial nephritis are common and hepatic necrosis may be found on liver biopsy. In the brain there may be signs of meningoencephalitis (Weller and Hanshaw, 1962). The disease is usually fatal in the neonatal form, but congenitally infected infants may show few or no signs but later show evidence of severe damage such as microcephaly and mental retardation (Pass et al., 1980).

Analysis of T Lymphocyte Subsets in Cytomegalovirus Mononucleosis:

Recent studies suggest that a delicate balance exists between helper and suppressor T lymphocytes in the maintenance of immune homeostasis (Reinherz and Schiossman, 1980). Cytomegalovirus can cause a mononucleosis syndrome either spontaneously (community-

acquired) or in patients who have received multiple blood transfusions (K emola et al., 1969). This syndrome is characterized by malaize, fever, and peripheral blood lymphocytosis with atypical lymphocytes (K emola et al., 1969).

Previously shown that patients with cytomegalo-virus-mononucleosis developed a hyporesponsiveness to certain minogens (Rinaldo et al., 1980). Recently Carney et al., (1981) have determined that the peripheral blood helper/suppressor ratio is reversed with lympho-cyte hyporesponsiveness during C.M.V. mononucleosis. With relative increase in cytotoxic-suppressor (OKT8) and a decrease in helper lymphocytes (OKT4). Whether these altered ratio in the peripheral blood reflect similar changes at other tissue sites is unclear. However convalescence is associated with a gradual increase in peripheral blood helper/suppressor ratio and a more rapid return of lymphocyte responsiveness.

It is unclear how C.M.V infection results in increaed suppressor T lymphocytes and decrease helper T lymphocytes. Direct C.M.V. infection of normal T-lymphocytes has not been observed (Rinaldo et al., 1978).

Clinical Manifestations of C.M.V.:

I- Congenital Infection:

Up to 2% of all infants born in the United States have congenital C.M.V. infection at birth. Only about 10% of these have significant sequelae, but others may have little damage such as hearing deficit (Hanshaw, 1971).

Studies of cell mediated immunity in C.M.V.-infected mothers and infants have indicated that such immunity tends to be depressed in both groups, more so in those have symptoms. This finding may help to explain why only certain infants are affected more than others (Starr, et al 1979). Another characteristic that may be afactor in neonatal damage is the timing of the primary maternal infection during pregnancy. The later such infection occurs, the greater possibility that the infant will have congenital infection. However, damage appear to result only when maternal infection occurs in the first or second trimester (Nankervis et al., 1974). Also another characteristic that may predispose to damage is the strain of C.M.V. involved. Some strains may be virulent than others. (Bhumbra and Nankervis 1983). Symptomatic congential infection