STUDY OF ESOPHAGEAL MOTILITY IN SCLERODERMA PATIENTS

THESIS

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BY

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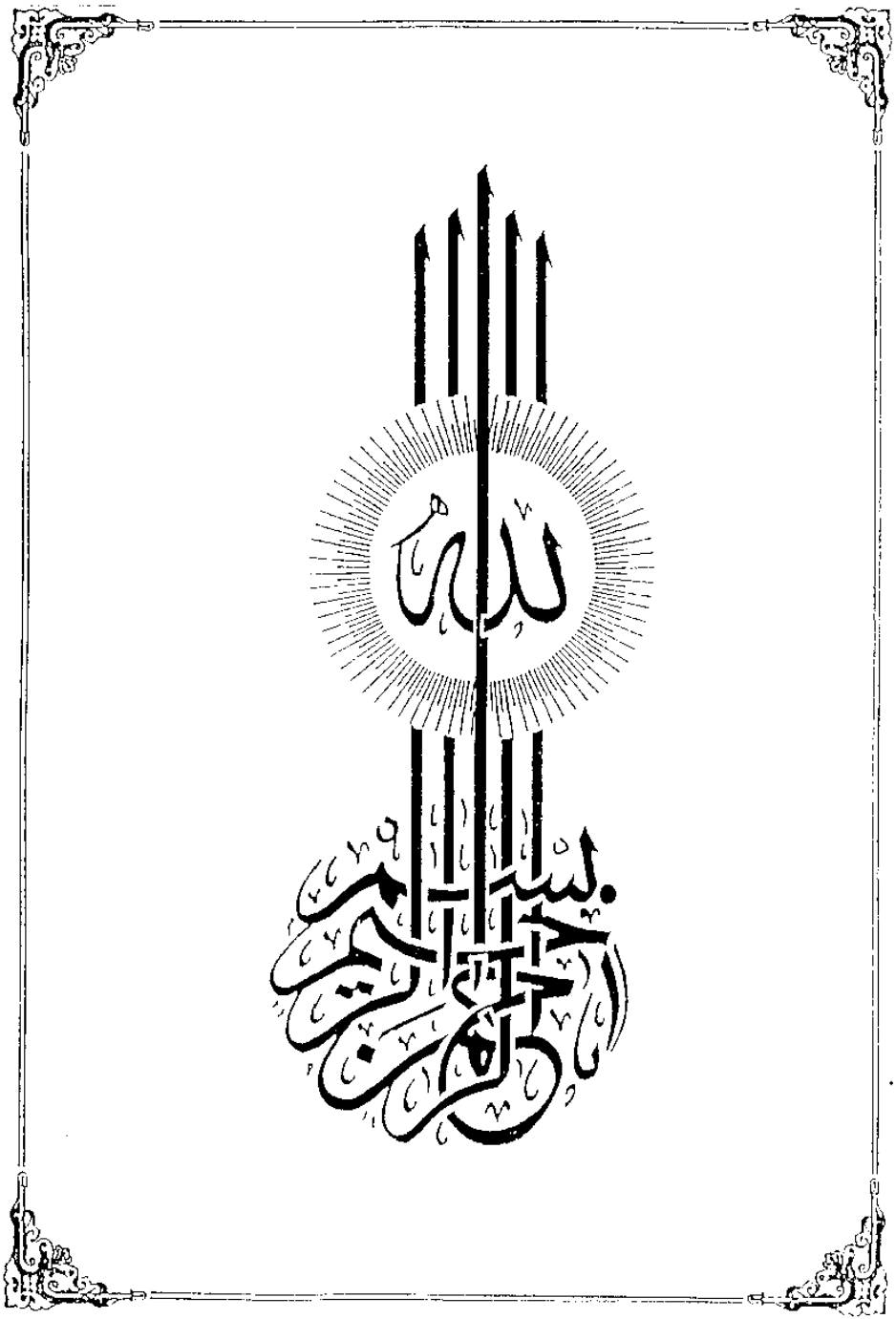

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INTRODUCTION AND AIM OF THE WORK

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Most patients with progressive systemic sclerosis (Scleroderma) show esophageal involvement in the natural history of the disease. These patients frequently complain of dysphagia which is commonly ascribed to alternations in the esophageal motor activity.

The aim of the work is to study esophageal motility pattern in patients with progressive systemic sclerosis and to report any change from the normal pattern. Thirty subjects will be studied. Ten normal subjects, twinty patients with progressive systemic sclerosis. Esophageal motility will be studied by using the proximal electormagnetic transducer system with the use of open tip., tilumen continuously water perfused catheter system with mechanical syringe pump and to correlate between the clinical data and laboratory investigation of the patients togehter with the manometric finding in a trial to establish early diagnosis of seleroderma.

REVIEW OF LITERATURE

SCLERODERMA

Scleroderma is a complex connective tissue disease of unknown cause, in which the development of fibrosis is predominant in the skin and in various organs in systemic sclerosis (Rowell, 1986).

The First detailed description of Scleroderma like disease came from Curizio (1754), in Naples, Italy, who reported Lesions and hardness of the skin in young women. the name of sclroderma was introduced much later, and only in this country, intensive involvement of other organs has been realized. This has been reviewed extensively in the last decade (Krieg and Meurer 1988).

CLASSIFICATION

Scleroderma is classified into (a) Circumscribed type or morphoea and (b) Systemic Scleroderma or progressive Systemic sclerosis (Lever and Schanmburg Lever, 1990). Krieg and Meurer (1988), classified scleroderma into: Localized scleroderma, Systemic Scleroderma which was classified into acroscleroderma, acroscleroderma with ascending sclerosis and diffuse scleroderma and the third type of scleroderma is the Overlap Syndromes (Fig I)

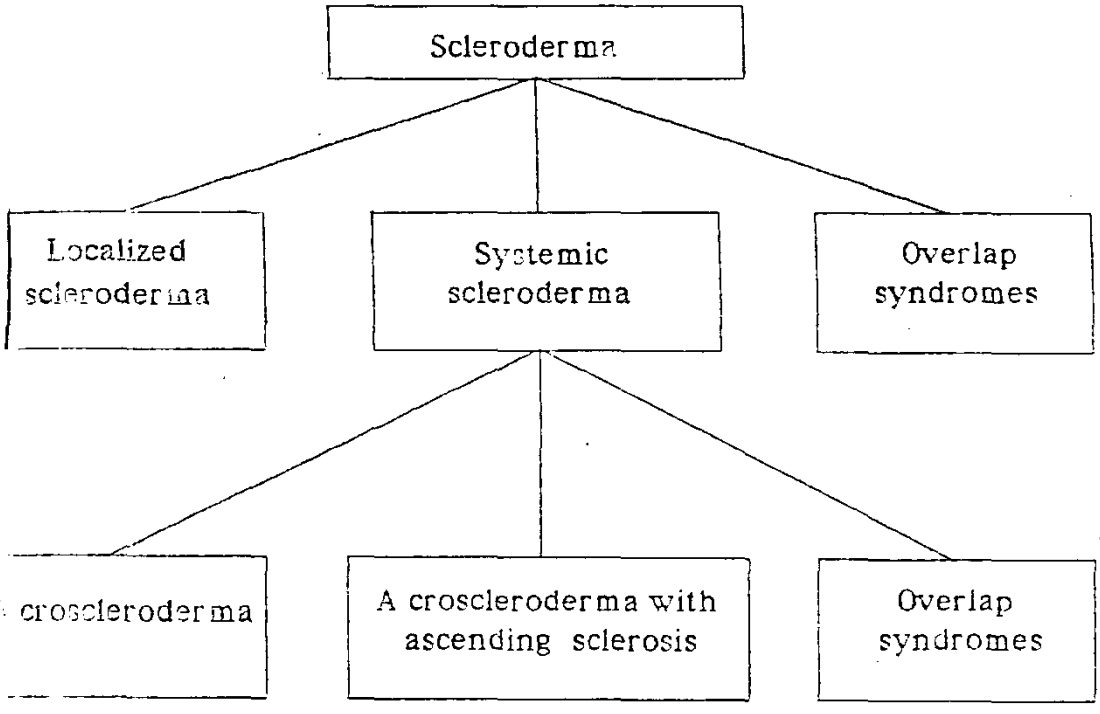

Fig. 1: The clinical spectrum of scleroderma

Krieg and Meurer , 1988

Fleischmajer and Lebwohl (1986), also classified scleroderma into a localized from and a systemic form. The Systemic Form was divided into two clinical subsets: The first is CREST Syndrome in which there is Calcinosis, Raynaud's phenomena Oesophageal involvement, Sclerodactyly and talangectasia. The second the diffuse form which is characterized by more skin involvement in the face, hands, arms, trunk and early pulmonary and Kidney disease.

Epidemiology of Scleroderma

The average annual incidence was 2.7 new patients per million population, with rates three times higher in Females than males for both whites and nigroes.

No Significant racial differences in incidence were observed. there ware few children cases compared with adult cases. Incidence increased with age.

No Socioeconomic Factors affecting Scleroderma incidence, no epidemiologic evidence of an infections agent contributing to the cause of Systemic scleroderma (Medsger and Masi, 1971).

HISTOPATHOLOGY OF SCLERODERMA

I- Histopathology of localized scleroderma

The different Types of morphoea can not be differentiated histopathologically. However, they differ in regards to severity and to their level of location in the skin. An early inflammatory and a late Sclerotic stage exist (Fleischmajor and nedwich, 1972).

In the early inflammatory stages, particularly at the violaceous border of the enlarging lesions, the reticular dermis shows thickened collagen bundles and a moderately severe inflammatory infiltrate predominantly by lymphocytes, between the collagen bundles and around the blood vessels. (Reed et al., 1973).

In addition to the lymphocytes, the inflammatory infiltrate also consists of plasma cells, histiocytic cells and macrophages (Fleischmajer and Nedwich, 1972). And also mast cells are present in the papillary dermis in the early stages of Scleroderma (NishiOka et al, 1987).

A much more pronounced inflammatory infiltrate than that seen in the dermis often involves the subcutaneous

fat and its upward projection towards the eccrine glands. the trabeculae subdividing the subcutaneous fat are thickened because of the presence of an inflammatory infiltrate and deposition of new collagen. Large areas of subcutaneous fat are replaced by newly formed collagen, which is composed of fine wavy fibers, rather than bundles and which stain only with haemaloxytin-eosin (Fleischmajer and Nedwich, 1972).

Vascular changes in the early inflammatory stage generally are mild both in the dermis and in the subcutaneous tissue. they may consist of endothelial swelling and Oedema of the walls of the vessels (O'leory et al., 1975).

In the late Sclerotic stage, the inflammatory infiltrate has disappeared almost completly except in some areas of the subcutis. The epidermis is normal. the collagen bundles in the reticular dermis often appear thickened and closely packed and Stain more deeply eosinophilic than normal skin. In the papillary dermis, where the collagen normally consists of loosely arranged fibers, the collagen may appear homogeneous (Reed et al., 1956). The eccrine glands appear markedly atrophic, and the fatty tissue normally surrounding them is greatly

reduced in amount or absent. Instead, they are Surrounded and appear tightly "bound down" by newly formed collagen.

The collagen that has replaced the fat cells in the subcutaneous tissue consists of thick, pale, sclerotic, homogeneous or hyalinized bundles with only Few Fibroblasts. Few blood vessels are seen withen the sclerotic collagen; they often have a fibrotic wall and a narrowed lumen (Fleischmajer and Ned Wich, 1972).

The fascia and striated muscles underlying the lesions may be affected in the linear, Segmental, subcutaneous and generalized types of morphoea. the Fascia shows fibrosis and sclerosis like that seen in the subcutaneous tissue. The muscle fibers appear vaculated and Separated from one another by oedema and Focal collections of inflammatory cells (Hickman and Sheils, 1964).

Bullae, Seen only on rare occasions in generalized and in subcutaneous morphoea, arise Subepidermaly, probably as a result of lymphatic obstruction causing Subepidermal oedema (Synkowski et al., 1981).

Nishioka et al., 91987), classify the pathologic changes in Scleroderma into three grades:

Grade I: In Which there is Oedema of both papillary and reticular dermis with partial homogenization of collagen bundles in the reticular dermis.

Grade II: In which there is homogenization of the collagen bundles in the reticular dermis but not in the papillary dermis.

Grade III: In which there is homogenization of the collagen bundles in both papillary and reticular dermis.

Skin of grade I and II corresponded clinically to Oedematous or Scleroedermatous skin and that of grade III to sclerotic skin.

II. Histopathology of Systemic Scleroderma

The histologic appearance of the skin lesions in Systemic scleroderma is similar to that of morphoea, so that the histologic differentiation of the two types is not possible. However, in early lesions of systemic scleroderma, the inflammatory reaction is less pronounced

than morphoea. so that only mild cellular infiltrate is present around the dermal vessels, eccrine coils and in the Subcutaneous tissue. The vascular changes in early Lesions are slight, as in morphoea. In contrast, Systemic Scleroderma in late stage shows more pronounced vascular changes than morphoea, particularly in the Subcutis (Lever and Schaumburg- Lever 1990).

These changes Consist of a paucity of blood vessels, thickening and hyalinization of the wall and narrowing of the lumen (Fleischmajer et al., 1972).

Also in the late stage of Systemic Scleroderma, the epidermis including the rete ridges appears normal (Morley et al., 1985). But occasionally the epidermis shows disappearance of the rete ridges (O'Leary et al., 1957). Autopsy examination of the digital arteries in sclerodermic patients with Raynaud's phenomenon has revealed Severe intimal Fibrosis resulting in considerable narrowing of the lumen, Often there is also adventitial Fibrosis (Rodnan et al., 1980).

AETIOPATHOGENESIS OF SCLERODERMA:-

The aetiology of Scleroderma remains unknown. There is some evidence that an autoimmune process may be