SKIN MANIFESTATIONS OF PANCREATIC DISEASES

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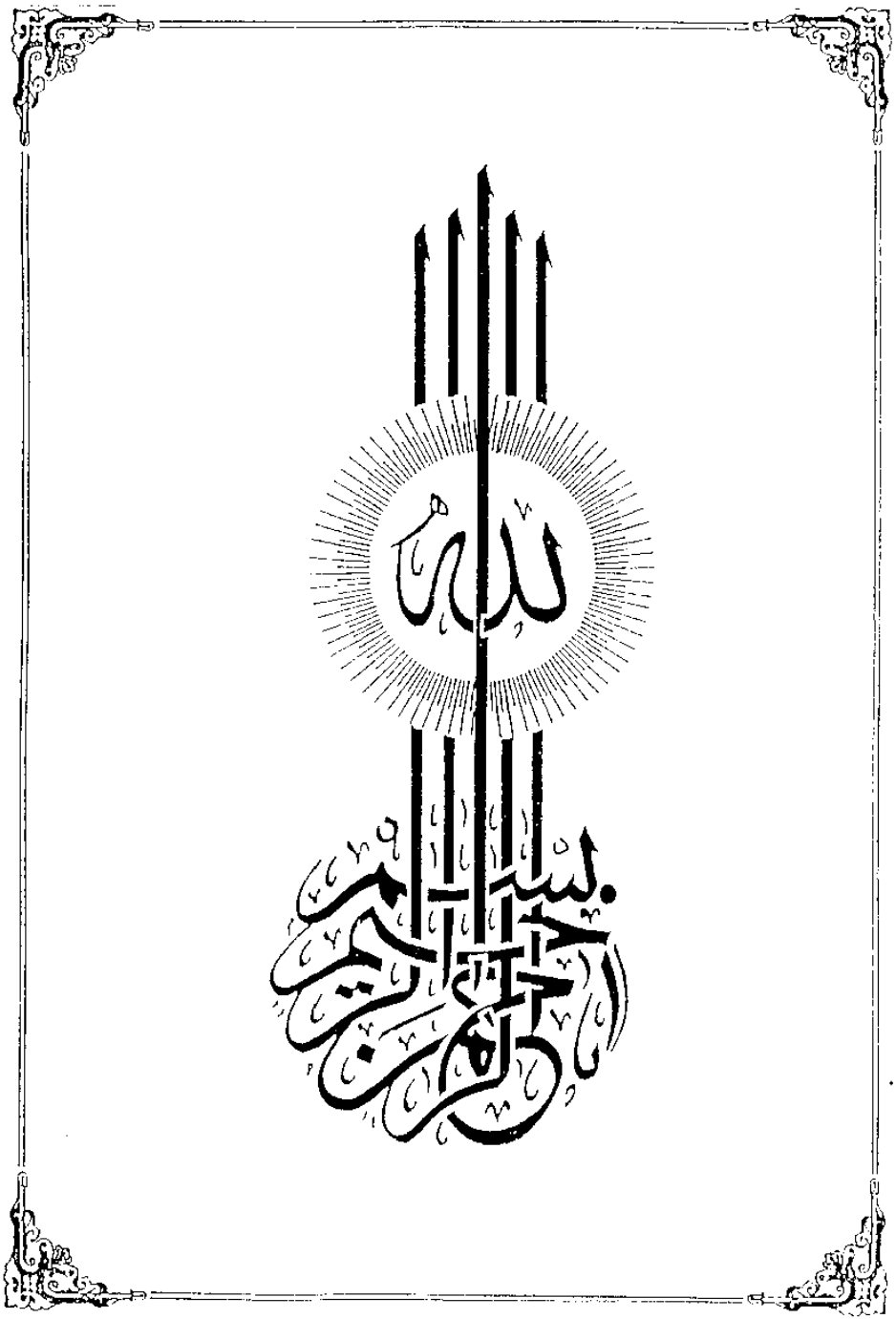

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INTRODUCTION

Skin manifestations of pancreatic diseases though had been studied since the nineteenth century, yet few authors dealt with this field. The present study may be considered of importance for it may reflect the different aspects of affections of the pancreas.

This literature review, will include the physiology of pancreatic secretion with the different actions of pancreatic enzymes, and also the different pancreatic diseases, namely acute pancreatitis, chronic pancreatitis and cyst and tumors of pancreas.

Acute pancreatitis as one of the causes of acute abdomen, must be differentiated from the other causes by its clinical manifestations, laboratory investigations and its specific skin manifestations.

Skin manifestations of acute pancreatitis are : subcutaneous nodular fat necrosis, Weber-Christian syndrome, local discoloration around the umbilicus, Livedo reticularis like eruption, urticarial rash and jaundice.

As regards skin lesions of chronic pancreatitis they may be one of the following: subcutaneous nodular fat necrosis, Weber-Christian syndrome, necrolytic migratory erythema, xanthoma and jaundice.

PHYSIOLOGY OF PANCREATIC SECRETION

Guyton (1976), wrote elaborately about the physiology of pancreas. He dealt with many points about the characteristics of pancreatic juice. He stated that the total daily volume of pancreatic juice has been estimated to be between 1500 - 3000 ml, it contains enzymes for digesting all the three major types of food. It also contains large quantities of bicarbonate ions which play an important role in neutralizing the acid chyme. The proteolytic enzymes are trypsin, chemotrypsin, carboxypolypeptidase, ribonuclease, and deoxyribonuclease. The first three of them split whole and partially digested proteins, while the nucleases split the two types of nucleic acids, ribonucleic, and deoxyribonucleic acids. The digestive enzyme for carbohydrates is pancreatic amylase. The enzyme for fat digestion is the pancreatic lipase. The proteolytic enzymes as synthesized in the pancreatic cells are in the inactive forms: trypsinogen, chemotrypsinogen, and procarboxypolypeptidas and they become activated only after being secreted into the intestinal tract. Guyton (1976) reported that the same cells that secrete the proteolytic

enzymes into the acini of the pancreas secrete simultaneously another substance called trypsin inhibitor, which prevents activation of trypsin both inside the secretory cells, and in the acini, and ducts of the pancreas. The same author determined that when the pancreas becomes severly damaged or when a duct becomes blocked, large quantities of pancreatic secretion pool in the damaged areas of the pancreas leading to digestion of the entire pancreas within few hours, giving rise to acute pancreatitis.

Pancreatic diseases may manifest themselves in the form of acute and chronic pancreatitis or as tumors of pancreas.

SKIN MANIFESTATIONS ACCOMPANYING ACUTE PANCREATITIS

Patients with acute pancreatitis may be presented either by physical signs and symptoms or/and some cutaneous manifestations. The underlying mechanism in the production of pancreatic inflammation as described by Brooks (1975) is by the escape of activated enzymes into the interstitial tissue. He reported that the earliest responses to this chemical irritation are edema and vascular engorgement of the pancreas.

Brooks (1975) reported that the most characteristic feature of acute pancreatitis is; pain which is characterized by its sudden onset in the epigastrium, or right hypochondrium, it usually persists and radiates most frequently through to the back, to either shoulder, or to one of the iliac fossae before spreading to involve the whole abdomen. Nausea and vomiting are frequent and constipation is almost always present. The patient looks ill and in severe cases profound shock soon supervenes with

cyanosis, clammy skin, rapid thready pulse and a subnormal temperature.

Cutaneous manifestations of acute pancreatitis may be one of the following :

1- Subcutaneous nodular fat necrosis.
2- Weber-Christian syndrome.
3- Livedo reticularis like manifestation.
4- Local discoloration of the abdominal wall.
5- Urticarial rash.
6- Jaundice.

1- Subcutaneous nodular fat necrosis

Acute pancreatitis leads to fat necrosis, which may be intra abdominal e.g. "in the mesentery, the omentum, the peritoneum, the peripancreatic tissue and even in the pancreatic tissue itself", or extraabdominal as in the mediastinum, the bone marrow, and the skin, It is presented clinically in the form of subcutaneous nodular fat necrosis. Cohen et al., (1959).

This clinical entity has been first briefly described and recognized as far ago as 1889 by Hansemann. Blauvelt (1946) was the first to describe fat necrosis with pancreatitis in details. He

described a case of acute pancreatitis with characteristic skin lesions which appeared during the first week of illness over the extremities. The lesions were of different sizes, varying from a pin prick to rounded or oval nodules of about 3.5 Centimeters in diameter. Blauvelt (1946) suggested that there was a relationship between the blood vessels draining the pancreas and the wide distribution of fat necrosis. In quotation of his words "when the gland is acutely inflammed favourable condition exist for the transference of minute particles of pancreatic tissue to the portal blood-stream. The portal vein is formed near the head of the pancreas by the union of both the splenic and superior mesenteric veins, the pancreas - itself is drained by many small vessels which open directly into the splenic, the superior and inferior mesenteric veins and the veins along the greater curvature of the stomach, so when the head of the pancreas is inflammed and swollen, the portal vein is likely to be pressed upon close to its origin, as a result of this venous obstruction the pancreas becomes congested and the microscopical portion of tissue may be absorbed and eventually reach the systemic circulation."

Swerdlow et al., (1960) described three cases of acute pancreatitis with multiple tender, erythematous nodular lesions, which varied from few millimeters to 3 Centimeters in diameter. They were distributed over both extremities, and some of them were confluent. Szymanski and Bluefarb (1961) reported five cases of acute pancreatitis with skin eruption, formed of multiple erythematous nodules of 1-2 Centimeters in diameter which varied in number from few up to thirty nodules. The lesions appeared first over the lower extremities, and subsequently on the trunk and upper extremities. In two cases the eruption was preceeded by the appearance of the clinical features of pancreatitis. Schrier et al., (1965) reported twelve cases of acute pancreatitis with skin lesions in the form of raised, erythematous nodules, which were tender in almost all cases. The lesions varied in size but most of them were less than 2 Centimeters in diameter, they were found mostly on the lower extremities, but in some cases the lesion were seen over the abdomen, chest and buttocks. The nodules showed some softness in the center than in the periphery, and resembled small abscesses, but with no suppuration in any one of them. They persisted from few days to few weeks, and healed with no residual scarring. The authors

added that these skin lesions were simulating erythema nodosum, periarteritis nodosa or Weber-Christian disease, but the laboratory investigations and the histological pictures of the lesions excluded all these possibilities.

Dowson and Slattery (1979) were the first to describe a case of acute pancreatitis with skin lesions in a newly born infant. The first lesion started at the site of B.C.G. vaccination as erythematous patches which then followed by multiple dusky red lesions on the arms, back, hips and thighs. The surface of the lesions was of the same level as the surrounding skin, but on palpation, there was a firm underlying induration. The size of the lesions varied from 0.5 - 2 Centimeters in diameter and the largest of them was coinciding with the B.C.G. site of vaccination. These lesions healed spontaneously within two months after the amylase level had returned to normal. Accordingly, the authors suggested that there might be a certain relation-ship between acute pancreatitis and these skin lesions.

Histological features of subcutaneous nodular fat necrosis

Szymanski and Bluefarb (1961) found that all the histological changes have occurred in the subcutis. There was no involvement neither of the epidermis nor of the dermis except for some inflammatory reaction. In sections stained with hematoxylin and eosin, the foci of fat necrosis were characterized by a "ghost-like cells" having thick "shadowy" walls and no nuclei. Granular basophilic material appeared in section, and was interpreted as being dystrophic calcifications which were located within and around the necrotic fat cells. An inflammatory zone surrounded the foci of necrosis, and consisted of all types of cells, including polymorphonuclear leucocytes, eosinophils, lymphocytes, histiocytes, foam cells, and foriegn body giant cells. Hemorrhage was noted in the area of inflammation in some sections.

Mechanism of formation of subcutaneous nodular fat necrosis in acute pancreatitis

Blauvelt (1946) suggested that fat necrosis was due to the action of lipase upon the neutral fat of the tissue, and that the immediate result

of this reaction was the production of glycerin and fatty acids. These fatty acids unite with calcium to form an insoluble soap, which was the essential constituent of the opaque plaques characterizing fat necrosis. He stated that lipase may be carried from the diseased pancreas to various regions, where fat necrosis had been observed in a number of ways. Swerdlow et al., (1960) confirmed the former hypothesis. They also added that the hypocalcemia which was noted in patients with pancreatitis was probably due to combination of Calcium with fatty acids.

2- Weber Christian syndrome

Weber Christian syndrome, also known as relapsing febrile nodular non suppurative panniculitis"., was first described by Pfeifer (1892).

Graciansky in (1967), was the first to describe the syndrome with pancreatic diseases. He reported that females were more affected than males, mostly adults between 20 and 60 years. The author divided the syndrome into three groups, the most essential symptom common to them was the skin nodules which were variable in number, asymmetrical, occuring mainly at sites where there was abundant adipose

tissue. They were described to be firm or soft in consistency, and reasorption occurred within few weeks either without any trace, or with areas of subcutaneous atrophy, which was marked by a fairly large rounded, saucer-like depression. In some cases these nodules became fluctuant, and discharged an oily substance, which on analysis showed an extraordinary abundance of fatty acids formed by decomposition of neutral fat under the effect of lipase The eruption did not respond to antibiotics.

The first group according to the author's, classification was known as "Lipo granulomatosis subcutanea of Rothman - Makai", and it evolved without general signs, Leaving no residual atrophy. The second group was associated with arthritis, serous membrane and deep fatty tissue affections. Arthritis was sometimes symptomless and was only detected by chance during radiological examination. The third group represented a modification in the classical clinical picture, where the symptoms attracted attention to pancreatic lesions "either acute or chronic pancreatitis and/or cancer of the pancreas". It may be associated with diabetes pleurisy, ill defined digestive disorders like pain, nausea and vomiting.