

Chronic Pruritus in the Absence of Specific Skin Disease: A Prospective Study from Benghazi, Libya

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Received May 23, 2019; Accepted June 06, 2019; Published December 05, 2019

ABSTRACT

Pruritus is unpleasant skin sensation that provokes the desire to scratch. It is a distressing symptom of many cutaneous and systemic diseases. We aimed to determine the variable systemic etiology in dermatology outpatient adults with complaints of pruritus. Our study was conducted over 4 years at Jumhoria Hospital and Ibn Sina Polyclinic and it included adult's outpatients with complaints of generalized pruritus without skin diseases. Complete examination of the skin was done and history was taken including systemic review. Relevant laboratory testing and radiological screen were done to almost all cases. Hundred patients were included; 66% was females and 46% was elderly. Mean duration of pruritus was 2 years. The most common cause was diabetes mellitus (19%), followed by chronic renal failure (13%), iron deficiency anemia (12%), cholestasis of pregnancy (10%), hyperparathyroidism (8%), hepatitis (8%), hypothyroidism (5%), malignancy (4%) and hyperthyroidism (3%). In conclusion, pruritus secondary to systemic diseases presents a diagnostic challenge and finding the cause usually requires a careful assessment involving a thorough history, physical examination and laboratory investigations of various body systems. Correct diagnosis and identification of the underlying cause is essential for proper effective treatment.

Keywords: Chronic pruritus, Skin, Systemic diseases, Dermatology

INTRODUCTION AND AIM

Pruritus is defined as a sensation which provokes scratching. It is a subjective symptom of many cutaneous diseases and it may be associated with a broad variety of systemic disorders. It may have an impact on the patients' overall wellbeing [1]. Chronic itching with no or minimal skin changes can be secondary to important diseases, such as chronic renal failure, cholestasis, metabolic and endocrine diseases, hematologic and malignant disorders, systemic infections, neurologic disorders and medications. Pruritus secondary to systemic diseases presents a diagnostic challenge and the search for the cause usually requires a careful step-by-step assessment involving history as well as clinical examination and laboratory investigations [2-4]. We aimed to determine the variable systemic etiology in dermatology outpatient adults with complaints of pruritus.

MATERIALS AND METHODS

Our study included adult's outpatients with complaints of generalized pruritus, in dermatology clinic at Jumhoria Hospital and Ibn Sina Polyclinic. The study was conducted over 4 years. Complete examination of the skin was done and history including systemic review, drug intake and exacerbating factors was taken; to determine if the pruritus is caused by a dermatologic condition or is secondary to an

underlying systemic disease. Patients with skin diseases were excluded. Laboratory testing including complete blood picture, serum iron and ferritin, peripheral blood film, fasting blood sugar, glycosylated HB, LFT, RFT, TFT, vitamin D assay and PTH, serology, CXR, USS abdomen and pelvis as well as stool examinations for ova, cysts, parasites and for helicobacter antigen were done to almost all of the patients. Skin biopsy was done for selected patients.

RESULTS

A total no. of 100 patients with complaints of generalized pruritus without skin diseases was included in this study; 66 % was females and the elderly constituted 46%. Mean duration of pruritus was 2 years; with longest duration were 15 years and the shortest 2 months. The most common cause

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Citation: Elfaituri SS. (2019) Chronic Pruritus in the Absence of Specific Skin Disease: A Prospective Study from Benghazi, Libya. *Dermatol Clin Res*, 5(2): 294-297.

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was diabetes mellitus (19%), followed by chronic renal failure (13%), iron deficiency anemia (12%) and cholestasis of pregnancy (10%). Other underlying diseases included vitamin D deficiency with secondary hyperparathyroidism (8%), hypothyroidism (5%), hyperthyroidism (3%), hepatitis C (4%), nonspecific hepatitis (1%), hepatitis B (3%). Xerosis cutis was seen in 10%, active helicobacter pylori infection (5%), and malignancy (4%), drug related and psychological pruritus each 2% whereas premenstrual pruritus and aquagenic were seen in single patient. In 2 patients no underlying cause could be identified. More than one etiology was found in 10 cases. **Figures 1-5** show secondary cutaneous changes in patients with chronic pruritus of systemic disease.



Figure 1. Excoriations with crusts in chronic renal failure patient.



Figure 2. Secondary eczematous changes with lichenification in chronic renal failure patient.



Figure 3. Scratch marks in patient with hepatitis.



Figure 4. Uncontrolled diabetes mellitus patient with pruritus.



Figure 5. Xerosis cutis.

DISCUSSION

Pruritus is defined as the desire to scratch; it is one of the most troublesome symptoms seen in dermatologic practice. Severe pruritus may have serious psychological implications [5]. Pruritus may be localized or generalized and can occur as an acute or chronic condition. Itching lasting more than 6 weeks is termed chronic pruritus [6]. Pruritus is usually caused by a primary skin disorder as atopic eczema, dermatitis herpetiformis and nodular prurigo. Invisible dermatoses with no skin findings include mild urticaria, prebullous bullous pemphigoid and mycosis fungoides which are diagnosed on biopsy. Scabies in its early stages can cause intense itching, especially during night without any evident skin lesions [7,8]. Pruritus can also be the presenting symptom of internal diseases with no or minimal skin changes [4]. Pruritus of systemic disease is usually generalized; it may be the only manifesting symptom and may precede the appearance of disease by several years [9]. In this study all cases have generalized chronic itching, with female predominance reflecting female disease as cholestasis of pregnancy and female predominance disease as iron deficiency and thyroid disease. Elderly constituted nearly half of the patients which could be a result of increase prevalence of chronic diseases, malignancy, xerosis, drug intake in elderly as well as senile pruritus [3]. Variable systemic causes of pruritus was seen; the most common cause was diabetes mellitus (19%), the pruritus in diabetes mellitus is associated with long duration and poor control with elevated glycosylated hemoglobin blood levels and it is linked to neuropathy, dry skin and drug administration [9,10]. Uremic pruritus constitute 13% of our cases, it is common in chronic renal failure and it is often intense, intolerable and distressing and can produce secondary changes as excoriations, crusts, lichenification and burnished nails [10,11]. Uremic pruritus is of multifactorial origin; common causes are secondary hyperparathyroidism, hypercalcemia, hyperphosphatemia, hypomagnesemia, xerosis, iron deficiency anemia, uremic neuropathy, hypervitaminosis A, abnormal fatty acid metabolism and combinations thereof [5,10-12]. Dry skin is generally considered to be a potential cause of itching and patients with xerosis may experience an intense pruritus, usually involving the lower legs. Skin drying and scratching may result in asteatotic eczema [3]. Xerosis cutis was the cause of pruritus in 10%. Pruritus is a frequent symptoms of hepatobiliary diseases including primary biliary cirrhosis, primary sclerosing cholangitis and hepatitis; viral or autoimmune. Surgical causes include obstruction in the extra hepatic biliary tree by carcinoma of bile ducts, gall stones, carcinoma of head of pancreas. Liver disease constituted 8% of systemic causes in our study. The itching in liver diseases may start as itchy palms and soles and then it spreads to other parts of the body. Bile salts and elevated levels of opioid peptides in the blood and skin are thought to be involved in its pathogenesis [5]. Intrahepatic cholestasis of

pregnancy constituted 10% of the cases. It is a hormonally triggered cholestasis in genetically predisposed women in late pregnancy who have a defect in the excretion of bile acids resulting in elevated bile acid levels in the serum [13]. Common endocrine disorders associated with pruritus are hypothyroidism (5%) and hyperthyroidism (3%). Dry skin in hypothyroidism and the increase skin blood flow and temperature in hyperthyroidism decreases the threshold for itching [5,10]. Hyperparathyroidism may also cause pruritus. Hyperparathyroidism secondary to vitamin D deficiency was seen in 8%. Many hematological disorders may be associated with pruritus, itching in polycythemia vera appears following hot bath [5]. Iron deficiency can cause intractable itching on the skin, even in the absence of anemia. Its pathogenesis is unknown [10]. It was the cause of itching in 12% and iron loading had abolished the symptom. Pruritus can be the initial manifestation to Hodgkin's disease and cut T-cell lymphoma. Carcinoma of the lung, stomach, colon, prostate, breast have been rarely associated with generalized pruritus. Pruritus may be directly or indirectly related to malignancy treatment [9,10]. In our study pruritus was seen in association with malignancy in 4%; lymphoma, renal cell carcinoma, multiple myeloma and leukemia. Pruritus can be a side effect of drugs; directly or indirectly through intrahepatic cholestasis as oral contraceptive. Subclinical sensitivity to any drug may cause pruritus. Morphine, opioids, angiotensin converting enzyme inhibitors, analgesics, estrogen, chloroquine and sulfonamides are among the drugs that may induce pruritus [14]. Drug induced pruritus was seen in 2 patients. Diagnostic criteria of psychogenic pruritus include chronicity, absence of somatic cause, association with psychological disorder and improvement by psychotropic drugs [15]. Two elderly patients with delusion of parasitosis were seen; they had pruritus and believed that they are infested with parasites. Brain diseases like stroke, sclerosis multiplex and brain tumors may sometimes induce severe generalized or localized pruritus. No cases of neurogenic pruritus were observed in this study. Infectious disease as helminthosis, parasitosis may cause pruritus, in addition itching is a common primary symptom of HIV infection. Recent studies suggest that *Helicobacter pylori* infections play a role in the pathogenesis of a variety of skin diseases including chronic pruritus [16]. Active helicobacter pylori infection was present in 5% whose pruritus resolved after eradication of *H. pylori*. Premenstrual pruritus was reported in 1%, due to recurrent cholestasis [17]. One patient with aquagenic pruritus was seen, where the levels of histamine are sufficient for a sensory but not a vascular response. The two patients with chronic idiopathic pruritus advised for follow up and periodic re-evaluation as underlying disorder can manifest later.

CONCLUSION

Systemic causes of generalized itching are to be considered only after ruling out the common skin diseases in their latent or early stages, they presents a diagnostic challenge and the search for the cause usually requires a careful evaluation involving a thorough extensive history, clinical examination and laboratory investigations of various body systems. Correct diagnosis and identification of the underlying cause is quite important for proper effective treatment.

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