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Review Article

Assessment and classification of chronic pruritis and its relation to systemic diseases

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ABSTRACT

Although pruritis might not be a serious condition with significant healthcare impacts, it is usually associated with an unpleasant sensation that leads to scratching the skin. It has been demonstrated that the severity of the condition is significantly variable and ranges between disabling and mild conditions. Chronic pruritis has been defined as the presence of daily itching for >6 months. In the present literature review, we have discussed the different approaches that have been previously indicated to assess and evaluate chronic pruritis, and the classification of the condition its relation to the different systemic diseases. The classification of chronic pruritis can be done using a clinical or an etiological diagnosis. The clinical diagnosis is usually based a primary skin condition, while the etiological diagnosis is based on the presence of different diseases that may be systematic, neurological, or psychiatric disorders. Accordingly, conducting a thorough examination is essential to establish a proper diagnosis before adequately managing the affected patients. Furthermore, the treatment of the underlying etiology should also be adequately considered for adequate management and enhanced prognosis.

Keywords: Pruritis, Evaluation, Classification, Systemic diseases, Diagnosis

INTRODUCTION

Although pruritis might not be a serious condition with significant healthcare impacts, it is usually associated with an unpleasant sensation that leads to scratching the skin. It has been demonstrated that the severity of the condition is significantly variable and ranges between disabling and mild conditions.[1] Many etiologies have been proposed to developing pruritis, and systemic diseases are the most common typical causes among the different studies in the literature.[2,3]

Chronic pruritis has been defined as the presence of daily itching for >6 months.[4] Primary and secondary skin diseases are usually associated with pruritis, and primary lesions might include atopic dermatitis, xerosis, urticaria, drug reactions, arthropod assault, psoriasis, pemphigoid, dermatitis herpitiformis, and mastocytosis.[5] On the other

hand, secondary skin lesions usually develop secondary to the frequent itching to overcome the unpleasant sensation that is frequently experienced by the affected patients. When clinicians cannot adequately detect the presence of any underlying primary skin lesion, it should be suggested that efforts should be directed to look for the potential presence of a neuropathic or systemic disease.[6] A thorough examination and evaluation of the different systems of the patients should be approached in these situations for the potential presence of a systemic disorder that has mainly caused the pruritis. In the present literature review, we aim to discuss the assessment and classification of chronic pruritis and its relation to systemic diseases based on evidence from the current studies in the literature.

METHODS

This literature review is based on an extensive literature search in Medline, Cochrane, and EMBASE databases which was performed on 16th September 2021 using the medical subject headings (MeSH) or a combination of all possible related terms, accprding to the database. To avoid missing poetential studies, a further manual search for papers was done through Google Scholar while the reference lists of the initially included papers. Papers discussing chronic pruritis and its relation to systemic diseases were screened for useful information. No limitations were posed on date, language, age of participants, or publication type.

DISCUSSION

Assessment

Different measures should be taken to quantify and assess the severity of chronic pruritis by the attending physician. At first, a thorough medical history should be taken from the patient that includes the quality of itching, duration, time course (that might be an indicator of the presence of scabies), the onset of the condition (which might refer to winter itch or certain drug administration), relieving factors (as some atmokinesis changes might be observed when the patient changes his clothes), preceding skin change, localization (that might refer to notalgia paresthetica), drug history, atopic diathesis, exacerbating factors (exposure to knitting needles, combs, and brushes), in addition to having a previous history of weight loss, allergies, fatigue, fever, emotional distress, and other clinical manifestations that are related to the underlying etiology and associated systemic morbidities which should be adequately assessed and evaluated to establish a proper diagnosis and draw an adequate management plan to expect a better prognosis.[7,8] Having a family history of infection among any of the family members should also be adequately considered, including scabies and other parasite-related infections among the different members. Taking a history of pruritis during physical activity of the affected patient should also be considered by the attending physician. For instance, in cases with psychogenic pruritis, it has been demonstrated that sleep disturbances are rare, and awakeness is a characteristic in most of the other cases owing to other etiologies, and in cases with lymphoma-induced pruritis, weight loss is usually present. It has been furtherly demonstrated that in cases of nocturnal pruritis, patients usually suffer from fatigue, chills, and sweating, while in cholinergic pruritis, it has been demonstrated that the case is similar to atopic Aquagenic pruritus that is usually influenced by bathing or cooling of the skin. Evidence also indicates that seasonal variations are usually associated with xerotic, asteatotic, solar urticarial, atopic, and textile dermatitis. After taking the relevant history from the presenting patients, a thorough clinical examination should also be processed for these patients. This might include searching for primary skin lesions by thoroughly inspecting the skin of the affected patients, including the nails, hair, scalp, and anogenital region.[9] Moreover, physicians should also observed areas that are not usually reached by the patient's hands, including the interscapular region for instance. Additionally, after observing these lesions, a detailed record of the observed 1ry and 2ry lesions should be established, in addition to other observed skin manifestations that are related to the presence of an underlying systemic condition. When conducting the physical examination of the patient, it should be noted that general evaluatory procedures should be conducted, including the spleen, kidneys, liver, and lymph nodes.8 A psychiatric etiology should not be established until the patient has been evaluated by a psychiatrist in cases when there are no other underlying etiologies of pruritis. The physician can also consider conducting some relevant investigations to assess and quantify these cases, including the postprandial and fasting blood glucose levels, erythrocyte sedimentation rate, complete blood count serum IgE, absolute eosinophil count, and other diagnostic tests and imaging approaches that might indicate the presence of a certain etiology based on the history of the patient and the general and physical examination. After evaluating the condition of these patients, assessing the severity, and adequately determining the underlying etiology, a proper management plan should be decided based on each patient's case to relieve the symptoms and manage the underlying etiology among the affected patients.[7,8]

Association with systemic diseases

Generalized pruritis without a rash can be attributed to any hepatic disease associated with cholestasis.[10,11] Patients with uremia or renal failure also experience continuous or exacerbated events of itching.[12] Diabetes mellitus is also another common etiology to develop generalized pruritis. However, data in the current literature is not sufficient to decide the frequency and prevalence of the condition among these patients. As a result of the increased incidence of infections, evidence indicates that some diabetic patients might suffer from localized episodes of itching around the infected areas, especially the genitals and anus.[13] In this context, it has been demonstrated that being infected with HIV and other generalized infections might be associated with eosinophilic folliculitis or pruritic

papular eruption. Another type of itching that has been documented in these patients is the neuropathic itching of the scalp.[14] Accordingly, it has been demonstrated that diabetes control is a major contributor to relieving these symptoms.[15] Hyper-and hypothyroidism-induced generalized pruritis was also previously indicated in many patients. Abnormal parathyroid levels were also reported to be a relevant etiology to developing pruritis. Uremic itch might also develop in these cases as a result of renal failure-induced hyperparathyroidism. On the other hand, evidence also indicates that in patients suffering from 1ry hypoparathyroidism, pruritis also manifests and develops as a result of candidiasis and dry skin.[15,16] Cholestasis-induced generalized itching might also develop secondary to the excessive administration of oral contraceptive pills. The administration of intradermal estrogen might also lead to developing generalized itching episodes. Therefore, reports show that to adequately manage perimenopausal women that suffer from episodes of generalized pruritis, hormonal replacement therapy is recommended as an optimal management modality.[17,18]

Regarding malignancy, evidence indicates the development of generalized pruritis secondary to cancer stomach, lung, colon, pancreas, prostate, and breast. Fortunately, a good prognosis has been estimated for the affected patients following surgical removal of the tumors and/or the administration of serotonin antagonists or serotonin reuptake inhibitors. On the other hand, it was also reported that the administration of antihistaminics does not abolish the condition. Moreover, flushing together with pruritis might be a characteristic in patients suffering from carcinoid syndrome. Pruritis was also reported to be prevalent among patients with brain tumors, and estimates show that nasal pruritis is prevalent in up to 50% of the cases.[15] Patients with polycythemia vera might also suffer from pruritis on exposure to hot water. It has been demonstrated that adequately receiving photochemotherapy, salicylates, and interferon-α can significantly enhance the prognosis of the condition. Hemochromatosis, iron-deficiency anemia, and post-bone marrow transplantation are also known causes for generalized pruritis.

Hodgkin's lymphoma was also reported to be a known etiology for developing generalized pruritis, and therefore, adequately managing these patients can significantly enhance the outcomes of the affected patients.[15] Some neurological conditions might also attribute to the development of pruritis, including systemic and local neuropathic pruritis, syringomyelia, transverse myelitis, neurofibromatosis, cerebral lesions, and notalgia paresthetica.[14,19-23] Pruritis might also be induced secondary to administering some drugs, including angiotensin-converting enzyme inhibitors antidiabetics, antibiotics, and antidepressants.[24-26] A previous investigation also demonstrated that local or general pruritis might also develop secondary to receiving hydroxyethyl starch.[26]

Classification

Among studies and evidence in the literature, it has been demonstrated that chronic pruritis can be classified based on a clinical and an etiological diagnosis. The clinical diagnosis is mainly based on the skin changes that are usually observed within the clinical settings. In these events, primary and secondary skin lesions should be adequately observed and recorded by the attending physician. Based on a previous report by the International Forum for the Study of Itch (IFSI), the clinical classification of chronic pruritis includes three main groups that will be discussed in the following section (Figure 1).[27]

Group	Clinical presentation and underlying disease	Diagnostics
I. Pruritus on primarily diseased, inflamed skin	Clinical picture: skin disease aetiology: mainly category I (see Table V)	Skin biopsy, laboratory investigation if necessary (e.g. IgE, indirect immunofluorescence)
II. Pruritus on primarily normal, non-inflamed skin	Clinical picture: normal skin aetiology: mainly category II, III, IV	Laboratory and radiological investigation, adapted to the patient's history and pre-existing diseases
III. Pruritus with chronic secondary scratch lesions	Clinical picture: chronic secondary scratch lesions like prurigo nodularis aetiology: category I-IV	Skin biopsy, laboratory and radiological investigations, procedure adapted to the patients history and pre-existing diseases

Figure 1: The IFSI clinical classification of chronic pruritis which is based on skin disorders.[27]

Group I includes patients that suffer from different skin diseases that are associated with itching that might impact the skin of the affected patients and can also lead to secondary skin changes based on the frequent itching. Group II includes patients that suffer from chronic pruritis that is attributable to different systemic, psychiatric, or neurological disorders. No skin diseases are involved in this group. Nevertheless, secondary skin lesions might also be noticed among the affected patients as a result of frequent itching. It should be noted that this group was previously called "pruritus sine materia". However, the condition has been alternatively named pruritis owing to non-inflamed and non-diseased skin. The old name of the condition has been attributed to different reasons, including chronic pruritis that develops secondary to systemic diseases with no primary skin changes, pruritis with no skin lesions, pruritis with no apparent origin, pruritis in the elderly population, and pruritis with no apparent manifestations that indicate itching dermatosis.[27,28] It has been furtherly demonstrated that when the rash is not observed among the affected patients with pruritis, it should be noted that other etiologies rather than systemic diseases should still be considered. On the other hand, it was also elaborated that if skin changes are observed among the affected patients, clinicians should not exclude the presence of systemic disease. Consequently, patients should be examined by a dermatologist before establishing an adequate diagnosis. In group III, patients usually develop mechanical harmful habits that can significantly lead to the development of skin lesions. Crusts, excoriations, nodules, papules, and lichenification. It has also been demonstrated that these changes usually heal by leaving hyper-and hypopigmented skin within the affected regions. Lichen Vidal, lichen simplex chronicus,

macular amyloidosus, prurigo nodularis, and lichen amyloidosus are all names that refer to the different skin lesions that are usually observed among patients with chronic pruritis. Furthermore, it has been observed that these lesions are of variable sizes and are scattered within different regions of the skin. Secondary skin changes are usually associated because of prolonged itching among these patients. The previous report by the IFSI also proposed another classification for chronic pruritis that is based on the etiological diagnosis of the condition. Therefore, patients should be adequately assessed and evaluated to establish a proper diagnosis based on the physical, laboratory, and imaging investigations for these patients to detect the underlying etiology, which has been estimated to account for a huge number of cases with chronic pruritis. In Figure 2, we have presented the different categories of this classification based on the IFSI report.

Category	Diseases
I. Dermatological	Arising from "diseases of the skin", such as psoriasis, atopic dermatitis, dry skin, scabies and urticaria
II. Systemic	Arising from "diseases of organs" other than the skin, such as liver (e.g. primary biliary cirrhosis), kidney (e.g. chronic renal failure), blood (e.g. Hodgkin's disease), and certain multifactorial (e.g. metabolic) states or drugs
III. Neurological	Arising from "diseases or disorders of the central or peripheral nervous system", e.g. nerve damage, nerve compression, nerve irritation
IV. Psychogenic/ Psychosomatic	Somatoform pruritus with co-morbidity of "psychiatric and psychosomatic diseases"
V. Mixed	Overlapping and coexistence of several diseases
VI. Other	Undetermined origin

Figure 2: The IFSI etiological classification of chronic pruritis which is based on the underlying systemic disorder.[27]

CONCLUSION

The classification of chronic pruritis can be done using a clinical or an etiological diagnosis. The clinical diagnosis is usually based on the presence of a primary skin condition, while the etiological diagnosis is based on the presence of different diseases that may be systematic, neurological, or psychiatric disorders. Accordingly, conducting a thorough examination is essential to establish a proper diagnosis before adequately managing the affected patients. Furthermore, the treatment of the underlying etiology should also be adequately considered for adequate management and enhanced prognosis.

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