Update on pathophysiology of senile pruritus and its impact on quality of life

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ABSTRACT

Itch is a common dermatologic complaint in people over the age of 65 years. Chronic pruritus is considered to be a common health problem in the elderly population, and negatively impacts the quality of life in the affected individuals. Senile pruritus can be a result of multiple conditions, including aging process (xerosis, immunologic changes), cutaneous conditions (seborrheic dermatitis, contact dermatitis, psoriasis, scabies), systemic conditions (chronic kidney disease, thyroid dysfunction or malignancy), neuropathic and psychogenic causes. Senile pruritus is more like a diagnosis of exclusion, difficult to treat because polimедication has to be avoided in elderly patients. Senile pruritus and its impact on quality of life could foster comorbidities and patients must be provided with follow-up, support and education to enable better compliance and monitoring.

KEYWORDS:

Senile pruritus, aging, quality of life.

Itch is a common dermatologic complaint in people over the age of 65 years. It can be acute or chronic, the chronic one is defined as pruritus lasting 6 or more weeks (1).

Chronic pruritus is considered to be a common health problem in the elderly population, and negatively impacts the quality of life in the affected individuals (2, 3).

Chronic pruritus can be divided into 3 groups: group I, pruritus on diseased skin; group II, pruritus on non-diseased skin; group III, pruritus presenting with severe chronic secondary scratch lesions. There are also 6 categories of underlying pruritogenic diseases: dermatological, systemic, neurological, psychogenic/psychosomatic, mixed, and other. The category “other” is also called “pruritus of undetermined origin” (4). There is no specific recommendation for the treatment of senile pruritus, but there are a variety of treatments, including topical and systemic medications, as well as psychological therapies.

PATHOPHYSIOLOGY

Senile pruritus can be a result of multiple conditions, including aging process, cutaneous conditions, systemic conditions and neuropathic and psychogenic causes (5, 6, 7).

1. **Aging process** that predispose to itch has some mechanism like:

Xerosis, which is a result of multiple factors, like: decreasing of surface lipids contained in the aged skin, changes in pH, aged skin is more alkaline and dry skin activate proteases to induce chronic itch (8). Other factors that lead to xerosis are: defective desquamation, because in elderly patients the corneodesmosomes not undergo the same breakdown like in normal skin (9). The skin alterations can be divided are epidermal and dermal. Epidermal changes

consist of thinning of the epidermis, lowered hydration, and alterations in the composition of lipids. Dermal changes include decreased glycosaminoglycans and loss of collagen (10, 11, 12).

Immunologic changes are involved, because in elderly people, the immune system undergoes a process of senescence (13). A recent report of several elderly patients suffering from chronic idiopathic pruritus showed evidence of immune dysregulation, such as “T and B cell lymphopenia, eosinophilia, and hypogammaglobulinemia” (14).

Neuropathic changes: Chronic itch can represent a result of the damage to nerves responsible for detecting, transmitting, or processing itch. There are several forms of neuropathic itch described in the elderly population: brachioradial pruritus, Notalgia paraesthetica, a unilateral pruritus between their shoulder blades, Multilevel Symmetric Neuropathic Pruritus (MSNP) describes a generalized, symmetric, neuropathic pruritus (15, 16). Shingles and post herpetic neuralgia is another type of neuropathic itch, where neurons involved in itch sensation become damaged (17). Also, pruritus in diabetic patients is caused by small fiber polyneuropathy (18).

2. **Cutaneous conditions** can be the primary cause of itch, or can influence the perception of itch in the elderly.

Seborrheic dermatitis can be found in the elderly patients and seems to more commonly afflict patients with underlying neurological conditions (19).

Contact dermatitis can lead to chronic itch in the geriatric population and xerosis can promote the exposure to irritants and allergens (20).

Nummular eczema affects elderly patients, where itch can appear due to involvement of nerve damage or other inflammatory markers (21).

Lichen simplex chronicus is a common cause of chronic itch in the elderly related to neuropathic processes or dry skin and is associated with depression (22, 23).

Psoriasis is common in the elderly population and pruritus is the most common symptom (24-26).

Scabies typically presents in form of pruritic papular or vesicular dermatitis involving the intertriginous areas especially. The itch is decreased when it is associated with dementia (27).

Bullous pemphigoid is an autoimmune condition that has been found to be in association with pruritus in the elderly population. According to several reports, such an atypical presentation without any skin lesions, but only consisting of pruritus can be found in the elderly (28).

3. Systemic condition

Chronic kidney disease pruritus is found in a large number of patients afflicted by advanced kidney disease, including those receiving the dialysis treatment. Itch can be present in up to 70% of those on dialysis. Often the itch aggravates during the night (29). Anemia, hyperparathyroidism, increased levels of histamine, and alterations in calcium phosphate balance can be incriminated in pathophysiology of this type of pruritus.

Cholestatic pruritus appears in patients with hepatobiliary diseases which has a negative impact on their life quality. Prevalence of pruritus in this disease is in the range from 15

to 69%, and depends on the type of underlying condition (30, 31).

Hyperthyroidism, is thought to be associated with chronic pruritus.

Malignancy- Paraneoplastic itch is defined as “the sensation of itch as a systemic (not local) reaction to the presence of a tumor or a hematologic malignancy neither induced by the local presence of cancer cells nor by tumor therapy” (32, 33).

Medications: Polypharmacy is a frequent occurrence in this patient population, especially in elderly, because they have many chronic diseases. There are numerous medications that have been found in association with itch. Some of these agents include MU opioids, anti-hypertensives such as ACE inhibitors, antidiabetics, hypolipemics, chemotherapeutics, antibiotics, anti-epileptics, psychotropic drugs, and cytostatics (33, 34). The newer targeted anti-cancer biologics have pruritus as a side effect (35). Because many of these medications are commonly used in the elderly, medication-induced itch should be on the list of differential diagnoses when encountering an elderly patient with chronic itch.

4. **Psychologic abnormalities** have been associated with psychogenic itch. Typically, patients experience an increased urge to scratch or pick at normal skin. Those patients affected by severe dementia can pick at their skin which leads to worsening of itch scratch cycle. Additionally, such factors as stress or anxiety, might cause the exacerbation of pruritus in several cutaneous conditions, including psoriasis, lichen simplex chronicus, and nummular dermatitis. A psychiatric consultation might be considered when

evaluating an elderly patient with normal skin after systemic conditions have been excluded.

It was identified an unusual link between age-related loss of a sensory cell type and aberrant sensory processing: during aging, the loss of specialized skin cells called Merkel cells results in alloknesis, the pathological sensation of itch in response to innocuous mechanical stimuli. Enticing therapeutic routes for treating alloknesis involve either finding a way to prevent Merkel cell loss in the first place or noninvasively increasing activity in remaining Merkel cells, thus avoiding the damage that results from the painful itch-scratch cycle (36).

A study in elderly patients with dry skin showed decreased amounts of skin surface lipids, primarily sebum-derived triglycerides, and amino acids, impairing the water-holding capacity of the stratum corneum. This was thickened and keratohyaline granules were decreased. Aging leads to diminished clearance of transepidermally absorbed materials from the dermis, decreased sweat and sebum production, and decreased vascular responsiveness to histamine. Another study found increased histamine release and skin hypersensitivity to histamine in 60 patients with senile pruritus (37). The stratum corneum of elderly patients has been demonstrated to have slower barrier repair. And this could lead to exacerbation of subclinical eczema and pruritus, which should respond to emollients and low-potency topical corticosteroids (38).

Itch sensation mainly emanates from the upper levels of the skin due to inflammation and interactions between immune cells, keratinocytes, and nerve fibers (39). The itch sensation is mostly transmitted by unmyelinated C-fibers. These are pruritus specific nerves and are mainly histamine-

independent (40). Patients affected by chronic itch may experience a component of peripheral or central neural hypersensitization, including alloknesis and hyperknesis, which play a role in itch perception (41). Due to a variety of interactions that contribute to development of itch sensation on the cell, tissue, and organ levels, the pathophysiology of itch is complex.

EVALUATION OF PATIENT

When a old patient is evaluated, there are 2 main information to obtain: if the itch is localized or generalized, and if there is a rash or not. There are also some key for the history like: onset of the itch, severity of the itch, timing of the itch, if there are factors that relieve or exacerbate, previous treatments, travels or exposure, past medical, medication history or pets.

Laboratory examination should be pursued if signs or symptoms of internal disease are elicited. A suggested screening regimen is CBC, TSH, T4, creatinine, alkaline phosphatase, bilirubin, glucose, CXR-PA and lateral or an age-appropriate cancer screening. Clinical suspicion should drive additional testing, which might include serum protein electrophoresis, skin biopsy (special stains for mastocytosis and immunofluorescence for pemphigoid), stool for ova and parasites, urine 5-HIAA, computed tomography (CT) scans of chest and abdomen, and HIV testing. Elderly patients with a negative workup for generalized pruritus fall into the category of “idiopathic” pruritus

Senile pruritus is itch in an elderly patient in whom primary skin disease, xerosis, drug reaction, and underlying systemic causes have been excluded (42).

TREATMENT

There is no specific recommendation for the treatment of senile pruritus, but there are a variety of treatments, including topical and systemic medications, as well as psychological therapies.

Local therapy includes the use of: topical moisturizers/emollients for treatment of xerosis and mild localized itch. Salicylic acid applied topically has some keratolytic and emollient effects, with antipruritic effect. Coolants (menthol, camphor, phenol) can be used in order to control itch. Topical Capsaicin has a role in modifying itch and can be used in neuropathic itch, prurigo nodularis, aquagenic pruritus or uraemic pruritus. Topical steroids due to their anti-inflammatory effects have antipruritic effect. It is well known that potent steroids can cause skin thinning, which is already an issue in the elderly patients, and for this reason, chronic steroid use is not indicated (43). Topical calcineurin inhibitors such as tacrolimus and pimecrolimus can be used in itch treatment. Topical anesthetics can control pruritus. The combination of lidocaine and prilocaine can be used in neuropathic itch (44). Topical amitriptyline and ketamine combination has been used for treatment of localized neuropathic pruritus (45).

Systemic treatment: Antihistamines are often the first treatment for pruritus, including senile pruritus (46, 47). Anticonvulsants: Gabapentin and Pregabalin are antiepileptic drugs that have been beneficial in neuropathic disorders causing itch or pain (48). Antidepressants: Mirtazapine, a selective norepinephrine reuptake inhibitor can be used in malignancy-associated pruritus or nocturnal pruritus in atopic dermatitis. Selective serotonin reuptake inhibitors (SSRIs): Paroxetine, Sertraline, Fluvoxamine can be used in pruritus associated with

depression and/or anxiety. Tricyclic antidepressants decrease itch by antagonizing H1 receptors and having anticholinergic properties: Doxepin in chronic idiopathic urticaria or Amitriptyline in neuropathic itch. μ -Opioid receptor antagonists: Naltrexone in pruritus associated with cholestasis, atopic dermatitis, chronic urticaria. It inhibits the spinal opioid receptors and increased activity of nociceptive fibers tonically inhibit the spinal "itch fibers". κ -Opioid: Butorphanol and Nalfurafine, the last one. It is only approved in Japan for severe pruritus in hemodialysis patients (49). Aprepitant is an oral selective neurokinin-1 receptor antagonist. It blocks the effects of an itch mediator (Substance P) which works by binding to the Neurokinin-1 receptor. Aprepitant was found to have some effect in decreasing itch in patients with drug-induced, paraneoplastic, and brachioradial pruritus (50, 51, 52). Thalidomide, an immunomodulator and neuromodulator has been reported to be effective in pruritic dermatoses (prurigo nodularis, uraemic pruritus, actinic prurigo) also thought to be from a central depressant effect (53).

Phototherapy can be: UVB broadband and narrowband, UVA, combined UVA and UVB, PUVA, oral and topical has indication in atopic dermatitis, psoriasis, uraemic pruritus, cholestatic pruritus.

Acupuncture has been beneficial for itch associated with chronic kidney disease. Although there is not strong evidence for this mode of therapy, it may be reasonably offered as a treatment with no adverse effects to elderly patients not responding to first-line treatments (54, 55).

It is essential to understand the pathophysiology of senile pruritus, because there are many factors which can induce it, such as cutaneous, systemic diseases, neuropathic and

psychogenic factors. Senile pruritus is more like a diagnosis of exclusion, difficult to treat because polymedication has to be avoided in elderly patients. Senile pruritus and its impact on quality of life could foster comorbidities.

Patients must be provided with follow-up, support and education to enable better compliance and monitoring.

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