

SKIN AND HAIR CONDITIONS IN WOMEN WITH SCHIZOPHRENIA OR RELATED DISORDERS

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ABSTRACT

Attractive appearance is vital to self-image, with the result that skin and hair disease can elicit substantial distress, reportedly more so in women than in men. Women who already experience a stigmatized illness such as schizophrenia or a related disorder find the added burden of an externally visible disease particularly upsetting. The aim of this review is to describe the skin and hair diseases most frequently associated with psychosis, especially as they affect women, and to discuss their treatment. Recent publications on this topic are reviewed and the pertinent diseases of skin and hair are grouped into a) delusional disorders b) medication reactions c) self-inflicted conditions and d) autoimmune disorders. Early recognition of disease allows for effective treatment. This is particularly important for dermatologic conditions because they contribute to the shame and self-stigma experienced by many women with schizophrenia and similar disorders.

Keywords: Psychosis; Skin; Hair; Medication Reactions; Autoimmune Disease

Introduction

Patients diagnosed with schizophrenia-related conditions frequently also suffer from skin and hair conditions, a reminder that skin, hair, and brain tissue share a common developmental origin. These tissues are derived from ectoderm, the external embryonic germ layer. When the ectoderm differentiates in early life, it forms the nervous system (spine, peripheral nerves and brain), the enamel of teeth, and the epidermis or outer layer of skin. It also forms the lining of mouth, anus, nostrils, sweat glands, hair and nails.

In view of the common origin of brain and skin, it is not surprising that a recent study of individuals presenting at a dermatology clinic found that fully one-third suffered mental health problems and 2.99% of the total sample had been diagnosed with schizophrenia [1].

One schizophrenia-related condition that presents initially in dermatology settings is delusional parasitosis (DP) [2] a monosymptomatic delusion or false conviction that parasites are crawling over and under the skin. There are other connections between skin and psychosis that are iatrogenic, which means they are caused not by a disease but by its treatment. An example is an allergic skin reaction to medication prescribed for a psychotic condition. Because individuals

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with schizophrenia-related disease almost always require at least one medication, the development of skin sensitivity is not rare. By the same token, psychotic symptoms (delusions and hallucinations) can be induced by medications prescribed for skin diseases; isotretinoin, used to treat severe acne, is an example of a drug that is known to induce psychosis [3].

Psychological stress is a contributing cause of both dermatologic and psychiatric disease. For instance, patients who are distressed can present with self-inflicted skin diseases secondary to skin picking or hair pulling. Stress also contributes to severe skin diseases such as psoriasis, which is reportedly more commonly found in men and women with psychotic illness than in the general population. One explanation is that psoriasis and psychosis share a common set of genetic code variations. Still other skin conditions are caused by poor hygiene or excessive exposure to sun or to cold or insect bites. Individuals who are frequently homeless, as is the case for significant numbers of persons with schizophrenia, are especially vulnerable to these types of conditions.

Women with psychosis, the population targeted in this article, are particularly susceptible to skin and hair problems. This may be because women's long hair is easily pulled and their long nails can easily lead to skin excoriations. Women are also more vulnerable than men to allergic drug reactions [4] and to autoimmune diseases that have skin manifestations [5]. Skin disease is a source of concern for many women because good skin and good hair are almost universally considered essential to attractiveness and, thus, very important to a woman's self-image [6]. Skin conditions are more than skin-deep. Across the globe, they are the fourth leading cause of nonfatal disease burden [7], which is why I decided to review their prevalence in women with psychotic disorders, and to address their treatment.

Method

This is a narrative review of recent publications on skin diseases associated with psychotic disorders. The papers cited were found by introducing the following search terms into Google Scholar: "schizophrenia or schizoaffective disorder or delusional disorder or psychosis" + "women" + "skin" + "hair" and following up the references listed in the pertinent articles. Wherever possible, publications of the last 5 years were selected in preference to earlier papers.

Delusional Parasitosis

Inexplicable skin sensations and subsequent delusions about skin infestations are not rare in psychotic disorders. After reviewing 508 publications on the subject of delusional parasitosis (DP), Freudenmann and Lepping [2] characterized the condition as a fixed belief, persisting despite all medical evidence to the contrary, that one's skin is infested with pathogens. This same condition is referred to as Morgellon's Disease by those who believe that the medical profession is incorrect by referring to it a delusion and that pathogens are in fact present even though they may not be easily perceived [8] The estimated sex ratio of DP is 2.5 women for every man, but this is true only for persons over 45 years of age. In younger age groups, the symptoms sometimes overlap with those of delirium secondary to intoxication and the sex ratio consequently favors men. The first presentation of DP, however, is usually in the middle years.

Patients attribute their itchiness and skin sores to specific pathogens to which they believe they have been exposed. They describe feeling vermin "crawling," "biting," "leaving marks," and "building nests," sensations that can be attributed to tactile (or haptic) hallucinations. Sometimes, patients claim to see the pathogens; in some instances, this would qualify as a visual hallucination. The disorder has an insidious onset and a chronic course, usually lasting for many years and causing great distress to patients, family members and to physicians. At times, patients believe that family members, friends, personal belongings and pets are also infested. Some patients bring with them photos or movies or specimens of the alleged culprits or "Morgellons" to prove their veracity [9] A dangerous sequela is that many patients

engage in intensive, repetitive, often dangerous self-cleansing acts in an attempt to get rid of the Morgellons. Severe self-mutilation can occur as a result, with a variety of secondary skin lesions - excoriations, ulcers, depigmentations, and inflammation. It is usually difficult to engage DP patients in therapy because they insist on the reality of the infestation. When they do agree to treatment, the symptoms respond well to antipsychotic medication [10, 11] suggesting that they are delusional in origin.

Medication-Induced Skin and Hair Problems

Most patients with psychotic disorders are treated with antipsychotic medication, which have been known to provoke a number of adverse skin reactions such as rash, photosensitivity, pigmentation and edema, sometimes accompanied by dangerous systemic symptoms (Steven Johnson syndrome) [12, 13]. There are many case reports of antipsychotic-induced skin reactions in the literature [14-18] Antipsychotics can also lead to hair loss and hyperhidrosis (excessive sweating). Both these conditions are considered to be skin-related [19-23].

A very distressing side effect of antipsychotic medication for women is hirsutism, brought about by antipsychotic-induced hyperprolactinaemia and occurring in up to 70% of women with schizophrenia treated with antipsychotic medication [24]. Hyperprolactinemia stimulates the production of dehydroepiandrosterone sulfate within the adrenal gland; subsequently this hormone is metabolized to testosterone in peripheral tissues. This results in secondary hirsutism for women, excess male-pattern hair growth (on face, chest and back), a side effect that negatively affects one's appearance and also perceptions of one's gender identity [25, 26].

Antipsychotics have also been reported to cause or exacerbate psoriasis [27-29] (More discussion about psoriasis follows later in this article).

Women with schizoaffective disorder, as distinct from schizophrenia, are usually treated with antidepressants and/or mood stabilizers in addition to antipsychotics. These drugs can also trigger skin and hair reactions [30-32].

Self-Inflicted Skin and Hair Conditions

Because of stress and perhaps also because of delusional thinking, men and women with schizophrenia sometimes harm themselves, at times intentionally, at times as a result of stress-induced compulsions. Self-inflicted harm to the skin results from scratching, skin picking, nail biting, or hair pulling and can cause local sores and ulcers that become infected. Alopecia (bald patches) can result from hair pulling, medically referred to as trichotillomania.

Dermatitis artefacta (DA) is the name given to conditions that occur as a result of a self-inflicted injury to the skin, whether voluntary or involuntary. DA is usually a diagnosis of exclusion, offered after all other possibilities have been excluded. An important clue to the presence of DA is that the skin lesions are located only on body areas within reach of the person's dominant hand. The lesions can take many shapes and can look like blisters, cuts, excoriations, ulcerations or hematomas [33] They can occur not only in the context of psychosis [34], but in other psychiatric illness as well, such as anxiety or obsessive-compulsive disorders.

Mohandas et al. [35] and Pichardo et al. [36] report a 3/1 female to male ratio for DA. They point out a danger of misdiagnosing the lesions as representing acne and treating them with isotretinoin, a drug contraindicated in schizophrenia and related conditions because it can exacerbate psychosis. These same authors [35, 36] also underscore the fact that treatment is difficult because psychiatric help is often rejected.

Trichotillomania refers to chronic hair pulling that can eventually lead to hair loss and serious functional impairment [37]. This condition is classified as an obsessive-compulsive disorder and has a reported community

prevalence of 0.5% to 2.0%, with a 4:1 female preponderance in adults. It is usually scalp hair that is pulled, but eyebrows and pubic hair are not always spared. Trichotillomania has been reported to sometimes occur in the context of schizophrenia [38, 39].

Psychosocial dysfunction, low self-esteem and social anxiety result from trichotillomania and also from skin picking, another self-inflicted skin disorder. In both conditions, patients are prone to blame themselves for not being able to stop the behavior, especially so when it results in visible sores or patches of baldness [40, 41].

Over 20% of patients eat their hair after pulling it out. This is called "trichophagia", and it can result in gastrointestinal obstruction with the formation of intestinal hair-balls "trichobezoars" that can require surgical removal [42].

Harm to the skin is not always a direct effect of a psychological problem. Harm can be indirectly inflicted, as when poverty and homelessness secondary to illness lead to poor hygiene and exposure to weather extremes, infections, and infestations.

An unusual hair disorder that is thought to result from inadequate self-care is called plica polonia or plica neuropathica. Plica neuropathica (PN) is a condition of the hair shafts in which strands of hair, because of lack of hair care, are matted together into a form of unkempt dreadlocks. This is thought to be secondary to a psychological disturbance occurring predominantly in women [43], sometimes in conjunction with a diagnosis of schizophrenia [44, 45]. This interesting condition can have a spiritual dimension – matting one's hair is seen by some as a way of seeking divine intervention during a time of trouble [46].

Autoimmune Disease

As stated earlier, autoimmune disease (conditions in which the body produces antibodies to its own tissues) is more prevalent in women than in men [5]. This group of diseases is present in about 3.6% of individuals with schizophrenia. Furthermore, approximately 3.1% of those with autoimmune diseases have a family history of schizophrenia [47, 48]. The presence of schizophrenia or related disorder in one's family predicts an increased risk of immune disorders [49]. There are many autoimmune diseases and a well-researched article by Benros et al. [47] includes a Table of the odds by which each autoimmune disease is more prevalent in individuals with a family history of schizophrenia than it is in the general population.

Psoriasis

Psoriasis is a chronic inflammatory autoimmune disease of the skin that affects up to 3% of the adult population and exerts a substantial negative effect on quality of life [50]. Eighty-four percent of patients with psoriasis have been reported to suffer from psychiatric co-morbidities [51]. A study using the Danish nationwide registry suggests that the incidence of psoriasis is nearly twice as high in patients with schizophrenia as it is in the general population [52]. This has also been demonstrated in studies from Taiwan and China [53, 54]. An even stronger link has been reported between psoriasis and mood disorders, including schizoaffective disorder [55]. Notably, in psoriatic patients, the presence of schizophrenia and related disorders is more prevalent in women than in men, especially in those over 40 years of age [53].

Some of the increased prevalence of schizophrenia in psoriasis patients could be due to the potential of antipsychotic drugs triggering a psoriatic response [27-29]. There are, however, common susceptibility gene variants that are shared between schizophrenia and psoriasis, at least in the Han Chinese population. Yin et al. [56] identified 5 single nucleotide polymorphisms (SNPs) in the human leukocyte antigen (HLA) region on chromosome 6 that contribute to risk

for both diseases. One causal mechanism may be that exposure to infection can trigger both psychosis and autoimmune disorders in susceptible individuals [47]. The risk for psoriasis in individuals with a family history of schizophrenia is 1.10 according to the Benros Table [47], not much higher than that observed in the general population.

Sjögren's Syndrome

For Sjögren's Syndrome (SS), that risk is estimated at 1.48 [47]. SS is an autoimmune disorder characterized by dry eyes and mouth and also dry skin with rashes [57]. One explanation for the raised risk in co-morbid schizophrenia is that SS, like many autoimmune disorders, is treated with corticosteroids and these agents are known to be potent inducers of psychotic reactions [58].

Idiopathic Thrombocytopenic Purpura

Idiopathic thrombocytopenic purpura (ITP) is an autoimmune disorder that is characterized by easy or excessive and painful bruising and bleeding caused by too low a level of platelets. The risk for individuals with a schizophrenia family history has been calculated by Benros et al. to be 1.13 relative to the general population [47], perhaps partly because antipsychotic medications can induce purpura symptoms [59]. Psychogenic purpuras (Diamond-Gardner Syndrome) have also been described [60].

Vitiligo

Vitiligo is an autoimmune disease characterized by patchy loss of skin color. It affects at least 1% of the population and is more common in individuals with a family history of schizophrenia by a Benros et al. odds ratio of 1.29 [47]. A predominance of women with this disease may reflect the fact that women, who place comparatively greater value on appearance than do men, are more likely than men to present for treatment [61]. There are two case reports of vitiligo in conjunction with schizophrenia [62, 63]. Subjectively, the impairment in quality of life of women affected with vitiligo is reported as equaling the impairment caused by psoriasis [64].

Alopecia Areata

Alopecia areata (AA), also known as spot baldness, is a chronic autoimmune condition in which hair is lost from some or all areas of the body. AA is usually associated with psychiatric disorders other than psychosis [65-67]. Benros et al. state that the odds risk of AA in a person with schizophrenia in the family is essentially that of the general population: 1.08 [47].

Scleroderma

Scleroderma refers to a group of rare autoimmune diseases that are characterized by hardening and tightening of the skin and connective tissues. The Benros et al. odds for scleroderma are 1.10 [47]. Several case reports have documented scleroderma and schizophrenia occurring in the same person [68, 69].

Pemphigus and Pemphigoid

Pemphigus is a group of relatively rare skin disorders that cause blisters and sores on the skin or mucous membranes. The two main types are pemphigus vulgaris and pemphigus foliaceus and the Benros et al. odds ratio is 1.6 [47]. Kumar et al. [70] reported that 40% of individuals in their sample with this diagnosis had psychiatric co-morbidity.

Of this 40%, 3.3% were diagnosed with paranoid schizophrenia while another 3.3% had psychotic symptoms but were given other diagnoses.

More recently, Kridin et al. [71] found that, in a sample of 1985 pemphigus patients and 9874 controls, the prevalence of schizophrenia was 2% versus 1.3% in the controls. They found an odds ratio for pemphigus and schizophrenia of 1.5, very similar to the estimate by Benros et al. [47]. In the Kridin et al. sample, the association between the two diseases was most prominent in women, in Jews, and in patients over the age of 60.

Bullous Pemphigoid is a group of rare autoimmune diseases similar to pemphigus, but here the blisters are filled with fluid. The Benros et al. odds for this condition are 1.41 [47] but a 2016 paper puts them substantially higher, at 2.65 [72].

Systemic Lupus Erythematosus

The Benros et al. odds ratio for Systemic Lupus Erythematosus (SLE) is 1.47 [47]. SLE is a chronic inflammatory autoimmune disease that has protean manifestations and is best known for conferring a pronounced facial butterfly-shaped flush. SLE follows a relapsing and remitting course and more than 90% of cases occur in women, the disease frequently starting during the childbearing years. SLE is a systemic illness that involves multiple body organs including the brain. Central nervous system involvement can produce psychotic symptoms, which makes it sometimes difficult to differentiate SLE from schizophrenia. In a recent study of 5018 patients with SLE and 25,090 controls, Tiosano et al. [73] found SLE to be independently and positively associated with schizophrenia.

In a case reported by Mack et al. [74], a woman with schizophrenia symptoms treated with antipsychotics developed a severe generalized rash that was thought to be an allergic reaction to her medications. The rash remitted with treatment that included cortisone and azathioprine (an immunosuppressant). The patient was well for 16 years on low dose antipsychotics and azathioprine. She then became pregnant so the azathioprine was stopped. Subsequently, she experienced a relapse of psychosis accompanied by very severe skin lesions. At the end of two years of severe symptoms, a diagnosis of SLE was made. Belimumab, the first targeted biological treatment for SLE [75] was prescribed along with antipsychotic medication, and the patient recovered [74]. This case study shows how difficult it can be to disentangle skin problems secondary to drugs from the primary symptoms of a systemic autoimmune disease. SLE attacks the skin among many other organs, including the brain. For this reason, it is a diagnostic challenge to distinguish the central nervous system symptoms of SLE from psychotic symptoms secondary to cortisone and also from primary psychotic symptoms.

Discussion of Treatment

Jafferany [76] offers guidance on the treatment of skin diseases that accompany psychiatric disease. The approach may differ somewhat depending on whether the treating physician is a psychiatrist, a dermatologist, or a general practitioner, but should start with a thorough history and physical and mental status examination. The next step is the elimination of drugs or other potential allergens as a primary cause or as a trigger to either the skin condition or the psychiatric condition. Psychiatric drugs, as we have seen, can induce a number of skin reactions and drugs used for skin conditions can trigger psychiatric reactions. Because high levels of stress can lead to both psychiatric and dermatologic conditions, meditation exercises and relaxation techniques are very helpful, as are referral to psychology for cognitive behavioral therapies that address specific stressors. Behavioral techniques that effectively interrupt the itch-scratch cycle can be critical for the patient. Skin conditions are visible to others and therefore engender shame and problems of self-esteem and self-image. For this reason, education as well as individual, group, or family-based supportive psychotherapies

are almost always needed. Always useful is practical advice, such as avoidance of sun or cold, the use of protective gear, and recommendations about appropriate hygienic measures, shampoos or cosmetics. Importantly, patients need to understand the potential triggering role of infection and inflammation and how one can protect against them and counteract them. Individuals who are homeless need social assistance; individuals with suicidal tendencies may require involuntary hospitalization. Suicide has been reported in relation to skin disease [77] and is particularly critical to try to prevent in people with psychosis, already at high risk for suicide.

Specific diseases will have specific treatment protocols to follow and appropriate referral to specialists to be made. The most difficult conditions are those, such as delusional parasitosis or dermatitis artefacta, where the patient disowns psychological contributions. This requires the gradual development of a trusted doctor-patient relationship and, in some cases, the active involvement of family members in treatment [78-81]. Continued monitoring and observation are essential.

An intriguing possibility has been raised about the role of diet [82, 83]. Arck et al. [82] propose a new, unifying model of interaction among body systems, the gut-brain-skin axis. This concept suggests that modulation of the human microbiome by the use of probiotics can reduce stress-induced skin inflammation and can even affect hair follicle cycling. These investigators suggest that ingesting the right kind of bacteria can exert beneficial effects on skin homeostasis, skin inflammation, hair growth and the response of peripheral tissue to perceived stress. This is a promising new field, still in its infancy.

An important consideration for women is the effect of cycling hormones on their dermatologic and psychiatric symptoms. Autoimmune disease, for instance, can either improve or worsen during pregnancy. Perimenstrual exacerbations of dermatoses such as psoriasis are commonly reported [84]. The underlying mechanisms are thought to be reductions in immune and barrier functions resulting from cyclical fluctuations in estrogen and/or progesterone. It has been postulated that factors linked with reproductive hormones are responsible for the female preponderance seen in autoimmune disease [85].

For example, women with SLE are at increased risk for serious medical and pregnancy complications [86, 87]. In a study of 13,555 women with SLE who gave birth, maternal mortality was 20-fold higher than in the general population of women. The risks for thrombosis, infection, thrombocytopenia, and transfusion were each 3–7-fold higher for these women. New mothers with SLE also had significantly more cesarean sections, preterm births, and preeclampsia than other women. Women with SLE were also more likely than other women to experience medical conditions, including diabetes, hypertension, and thrombophilia, all potentially leading to adverse pregnancy outcomes. Gonadal hormones aggravate SLE; they can also trigger SLE. This is seen at menopause when the risk for SLE has been reported to correlate with the duration of use of postmenopausal hormone supplementation [88].

The current thinking is that endocrine changes during pregnancy influence the onset and progression of autoimmune and inflammatory diseases by affecting T cell cytokine-mediated responses during the gestation period as well as the post-partum and beyond. It is important to note that pregnancy worsens some autoimmune diseases but diminishes the symptom severity of others [89, 90].

Hormonal relationships with symptom levels can be seen in skin conditions other than autoimmune disorders. For instance, the urge intensity and frequency of hair pulling is exacerbated during the premenstrual period and lessened during menstruation and for a short period afterwards. Both exacerbation and alleviation of this condition have been reported during pregnancy [91].

Fluctuations in severity have also been observed in psychotic symptoms over the menstrual period, during pregnancy and the postpartum, and after menopause [92]. Women need to be informed about potential risks of a pregnancy to themselves and to their infants. These women may require contraceptive advice. Psychiatrists treating women with schizophrenia and related disorders who also have a skin condition need to pay careful attention to variations in symptom severity and to consult with endocrinologists, dermatologists, rheumatologists and obstetricians on how best to overcome the many challenges posed by this combination of problems.

Conclusion

In summary, women with psychotic disorders experience a variety of skin and hair conditions that can aggravate already compromised self-esteem. Importantly, serious underlying conditions such as systemic lupus may be present. Physicians are encouraged to enquire about dermatology problems and to refer to appropriate specialists whenever necessary. This manuscript has reviewed recent publications on this extensive topic and grouped skin and hair conditions associated with psychosis under a) delusional disorders b) medication reactions c) self-inflicted conditions and d) autoimmune disorders, with recommendations for their rapid recognition and effective treatment.

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