Diagnosis and management of delusional parasitosis

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Delusional parasitosis is a monosymptomatic hypochondriacal state that causes great suffering for the patient and great suffering for those around them. Dermatologists are experts in the diagnosis of cutaneous disease and frequently encounter such patients. This review provides an overview of the diagnosis and management of delusional parasitosis and the differential diagnosis. (J Am Acad Dermatol 2019;80:1428-34.)

Key words: chronic tactile hallucinosis; delusional parasitosis; delusions of parasitosis; delusory parasitosis; Ekbom syndrome; psychogenic parasitosis.

Delusional parasitosis (DP), also commonly referred to as delusions of parasitosis, delusional infestation, or Ekbom syndrome, is a monosymptomatic hypochondriacal psychosis in which affected individuals have a fixed, false belief that they are infested with living organisms. The German term *Dermatozoenwahn* (parasitosis) was originally cited in 1938 by Karl Axel Ekbom to describe this disorder. The name Ekbom syndrome was later used to describe this disorder; however, this eponym is ambiguous because it can also be used to refer to restless leg syndrome.[1] Morgellons disease is a condition in which a patient perceives fibers or threads emerging from or attached to the skin. Many of these patients demonstrate fixed ideation of infestation that affects their work and relationships—manifestations that are typical of delusional parasitosis.[2,3]

DP is a type of delusional disorder, somatic type (*Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* code 297.1 F22).[4] Previous editions of the *Diagnostic and Statistical Manual of Mental Disorders* required individuals with this diagnosis to have nonbizarre delusions, which is no longer a requirement. Criteria include the presence of a delusion for ≥1 month where the criteria for schizophrenia have not been met, the patient is functioning in general outside of the delusion of parasitosis, mood episodes have been brief relative to the duration of the delusional period(s), and where the disturbance is not attributable to medical conditions, substances, or another disorder.[4]

We summarize the current literature regarding epidemiology, diagnosis, and management in this review. Evidence-based recommendations for pharmacologic management and side effect profiles of the available agents are discussed in the context of the authors' experience.

METHODS

The PubMed database was queried for relevant articles using the following search terms: delusional parasitosis OR delusions of parasitosis OR delusional infestation OR delusory parasitosis OR psychogenic parasitosis OR chronic tactile hallucinosis OR Ekbom syndrome (NOT restless leg). The search produced a total of 597 articles, 122 case reports, 22 case series, 58 reviews, 2 systematic reviews, 1 randomized controlled trial, and 1 metaanalysis. Articles were selected for review based on their relevance to the presentation, differential diagnosis, evaluation, and management of DP. Side effect profiles were extracted from the results of pharmaceutical trials included in the product labeling. Recommendations are based on the published literature and the authors' experience in managing the disorder.

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Funding sources: None.
Conflicts of interest: None disclosed.

Accepted for publication December 3, 2018.

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Published online December 11, 2018.
0190-9622/$36.00

https://doi.org/10.1016/j.jaad.2018.12.012

DISCUSSION

Presentation

The mean age of patients with DP is 57 years, there is a roughly 3:1 female:male ratio, and females may have a longer duration of symptoms compared with males.[5] Past or comorbid psychiatric conditions are reported in roughly 80% of patients with DP.[6,7] The most common comorbid psychiatric illness was depression (74%), followed by substance abuse (24%) and anxiety (20%).[6] Patients are often highly distressed and the condition dominates their lives, disrupting personal and professional relationships. Some remain tremendously successful at work while their private lives are consumed by the delusions. Many of the patients have read extensively about the parasites they believe infest them. They typically bring "specimens" as proof of their infestation and may relate accounts of failed drastic measures to eradicate the infestation. The "matchbox sign" is the classic presentation of various materials that have been collected by the patient as evidence of infestation, including anything from dust/dirt, plant or animal fibers, scabs and skin debris to photographs of old/previous lesions or parasites. One can often find real insects/arthropods in the matchbox, but they are typically innocent peridomestic organisms. Patients may describe an exposure to a dirty environment or a sexual encounter that they believe to be the origin of the infestation. In some cases, they believe family members are also affected and may expose them to significant risk in their attempts to cure them. *Folie à deux*, a condition in which a psychiatric condition (delusion or hallucination) is transferred from one individual to another, is not uncommon in this setting.[8] Patients experience formication, hallucinatory crawling sensations on the skin attributed to the presence of the alleged parasites.

CAPSULE SUMMARY

- Delusional parasitosis can be effectively managed with second-generation antipsychotic agents.
- Extrapyramidal and metabolic side effects are major limiting factors in the choice of therapy.
- Based on the published data on efficacy, the incidence of side effects, and attributable risk, risperidone (0.5-4 mg/day) is a reasonable first-line choice for pharmacotherapy.

Differential diagnosis

A thorough evaluation is required, including a complete history and physical examination. Table I lists some of the more common diseases on the differential diagnosis. It is important to rule out genuine parasitosis. Older patients with scabies often have atypical presentations, and burrows may not be evident. Some patients actually isolate individual scabies, zoonotic, or environmental mites, and it pays to examine the specimens that the patient provides. Bites and infestations may produce clinically nonspecific lesions, and obtaining a biopsy specimen can help rule out genuine arthropod reactions. Wedge-shaped perivascular polymorphous infiltrates often with eosinophils and endothelial swelling are characteristic of the latter.

Mites, both scabetic and nonscabetic, are the most common causes of cryptic arthropod-induced pruritus. They range in size from 0.1 to 2 mm and may be difficult to see without magnification. Many lack host specificity, and avian mite-induced dermatitis may result from contact with either birds or rodents, including pet gerbils and hamsters. Mites are widely distributed in nature, and conditions such as "grocer's itch" may be related to a wide variety of agricultural products. Pet-induced dermatitis and natural fillings for pillows and mattresses have also been associated with cryptic mite-induced dermatoses. Caterpillars and moths often appear in great numbers, and their dislodged hairs can cause urticaria and pruritus.

Formication and pruritus caused by medications, such as amphetamines (both illegal and prescription), dopamine agonists,[9] opioids, topiramate,[10] cocaine,[11] or alpha-adrenergic agents must also be considered. Pruritus related to systemic diseases, including hyperthyroidism and renal and liver disease, may present with generalized itch or a crawling sensation in the skin. Exposure to fiberglass may produce itching of unknown etiology, and fiberglass-contaminated clothing placed in the laundry can result in itching in an entire family.

Other psychiatric disorders should also be considered, including schizophrenia spectrum disorders, dementia, affective psychoses, substance-induced psychoses, and psychoses caused by a general medical condition (eg, iron deficiency anemia). Anxiety disorders, obsessive compulsive disorder, and somatoform disorders should be carefully distinguished from delusional states and may be comorbid with delusional disorder.

Evaluation

A complete blood cell count, metabolic panel, thyroid-stimulating hormone, obtaining a biopsy specimen of lesional skin, and perilesional skin for direct immunofluorescence may help to rule out organic disease and help to establish an effective physician–patient relationship. Dermatologists can use adhesive tape, cyanoacrylate stripping of skin, and dermoscopy to detect evidence of mites. Patients and exterminators can examine the house and office for evidence of nesting birds or vermin. We have sometimes found it helpful to evaluate the vacuum cleaner bag contents (most forms of inanimate debris will sink, but mites will float on alcohol or hypertonic sugar solution). In the rare cases where mites are identified, an acarologist can comment on their relevance. A qualified veterinarian should examine pets. Specimens should be cleared with lactic acid or lactophenol, washed with water, and mounted in Hoyer medium, which remains clear regardless of whether mites are prepared with water or alcohol. Hoyer medium is typically prepared by the laboratory handling the specimen. Local and state health departments, university entomology departments, and military entomologists can be extremely helpful. In our experience, they have always been generous with their time and expertise. Many dermatologists are familiar with arthropods that are commonly associated with human disease, images of which are readily found in the dermatology literature. When necessary, an expert can be consulted. It is important to properly isolate and preserve arthropod specimens before submitting them. If substance-induced psychosis is suspected, a urine drug screen is highly valuable as well as a search of controlled substances that are being prescribed via a database network search.

Management

Reassurance regarding the lack of evidence of organic disease rarely provides relief to the patient, and patients often see multiple physicians in search of someone who will believe them. It is important to establish a positive physician–patient relationship and to emphasize the importance of global evaluation and management to address all aspects of the problem, including pharmacotherapy to alleviate symptoms. Direct confrontation with the patient regarding their delusions is rarely successful—by definition, they are fixed and unchangeable. Some confrontation occurs in cognitive behavioral therapy approaches to delusional disorder, but this requires significant expertise and patients who are open to psychotherapy.

Table I. Differential diagnosis of delusional parasitosis

Scabies
Avian mite-induced dermatitis
Grocer's itch
Pet-induced dermatitis
Caterpillar and moth dermatitis
Fiber glass dermatitis
Substance-induced (amphetamines, opioids, cocaine, etc)
Pruritus related to systemic diseases
Schizophrenia spectrum disorders
Dementia
Other psychiatric disorders

Patients will often ask questions, such as "Do you think I'm crazy?" Experienced physicians have differing strategies for how to reply to questions like these, and none are universally effective. Some patients respond to "I believe you are really suffering, and I would like to try to help you." Others have responded with "I think we're all a bit crazy at times. It's okay. Let's focus on your symptoms and getting you better." Another approach is to answer with a question that is directed at the patient's anxiety. For instance, "Has someone told you that you were crazy?" or "What would it mean if you were?"

Topical antipruritic agents containing camphor and menthol or pramoxine may provide temporary relief of dysesthesias. A small, randomized controlled trial found that *N*-acetylcysteine has been shown to decrease skin-picking behavior in picking disorders.[12] This drug is thought to modulate glutamate levels and may help with compulsive behavior, such as skin picking and trichotillomania; however, dermatology-specific outcomes (ie, the number of excoriations) has not been studied. This has not been studied in the setting of DP. If the patient demonstrates compulsive picking of suspected sites of the infestation, this may be a helpful pharmacotherapy with a low side effect profile.

Antipsychotic agents are the most effective agents to treat DP, but many dermatologists are uncomfortable with the pharmacologic management of DP. One study found that only 3% of dermatologists were comfortable prescribing the required agents.[13] Our objective in this section is to familiarize dermatologists with the efficacy and side effect profile of antipsychotics in treating DP. With this knowledge, it is our hope that dermatologists will feel more comfortable administering these medications to patients with DP. When appropriate drugs are

Table II. Comparison of side effects of pharmacotherapy for delusional parasitosis

Therapy	Suggested dose	Adult short-term side effects	Total event rate, %	Attributable risk, %
Pimozide	1-10 mg/day	Sedation	70	45
		Akinesia	40	40
		Akathisia	40	40
		Rigidity	10	10
		Visual disturbance	20	20
		Adverse behavioral event	25	25
Risperidone	0.5-4 mg/day	Total cholesterol (<200-≥204)	4.3	1.6
		Triglycerides (<500-≥500)	2.7	1.6
		Weight gain (≥7% increase from baseline)	8.7	5.8
		Parkinsonism	14	6
		Akathisia	10	7
		Sedation	10	8
Aripiprazole	2-10 mg/day	Total cholesterol (<200-≥240)	2.5	−0.3
		Fasting triglycerides (<150-≥200)	7.4	0.4
		Weight gain (≥7% increase from baseline)*	5.2	3.6
		Extrapyramidal disorder	5	2
		Akathisia	10	6
		Sedation	7	3
Olanzapine	5-10 mg/day	Total cholesterol (<200-≥240)	2.8†	0.4
		Fasting triglycerides (<150-≥200)	9.2‡	4.8
		Weight gain (≥7% increase from baseline)*	40.6	30.8
		Asthenia	10	1
		Akathisia	3	1
		Somnolence	29	16

*Data based on an adolescent patient population. All data were from the product insert of each drug.[40-43]
†After 48 weeks, 14.8% event rate.
‡After 48 weeks, 32.4% event rate (no placebo group).

Table III. Advantages and disadvantages of pharmacotherapy for delusional parasitosis

Therapy	Advantages	Disadvantages	Recommendations
Pimozide	Has the most published literature supporting its efficacy	High side effect profile (akathisia, akinesia, rigidity, and sedation) make this unfavorable	Second-line
Risperidone	Lower rate of EPS compared with pimozide; lower rate of metabolic effects compared with olanzapine; more literature supports its efficacy compared with other atypical antipsychotics	Slightly higher risk of EPS compared with aripiprazole; higher risk of prolactinemia compared with other atypical antipsychotics	First-line*
Aripriprazole	Lower rate of EPS compared with pimozide; lower rate of metabolic effects compared with olanzapine; less risk of EPS and prolactinemia compared with risperidone	Less literature that supports its efficacy compared with risperidone	Alternate first-line
Olanzapine	Lower rate of EPS compared with pimozide	Much higher rates of metabolic effects compared with other atypicals make this unfavorable	Second-line

EPS, Extrapyramidal symptoms.
*Usual first-line recommendation.

prescribed, the clinical response rate to antipsychotics ranges from 50% to 100%.[14-17]

In the past, pimozide was used as the first-line agent, but it has a less favorable side effect profile compared with second generation (atypical) antipsychotic agents, and electrocardiograms are recommended to measure the Q-T interval before treatment[18] (Tables I-III). There is level 1B evidence

Table IV. Major drug interactions of pharmacotherapy for delisional parasitosis

Therapy	Major drug interactions[40-43]	Potential effect
Pimozide	Macrolide antibiotics	(CI) Prolonged QT intervals, may decrease metabolism (CYP3A4 inhibitor)
	Citalopram and escitalopram	(CI) Increases QTc by unknown mechanism
	Sertraline	(CI) Decrease clearance
	CYP2D6 inhibitors	(CI) Decrease clearance of pimozide
	CYP3A4 inhibitors	(CI) Decrease metabolism of pimozide
Risperidone	CYP2D6 inducers	Increase clearance of risperidone
	CYP2D6 inhibitors	Decrease clearance of risperidone
Aripiprazole	Strong CYP3A4 inhibitors	Decrease clearance of aripiprazole
	Strong CYP2D6 inhibitors	Decrease clearance of aripiprazole
	Strong CYP3A4 inducers	Increase clearance of aripiprazole
	Antihypertensive drugs	Hypotension
	Benzodiazepines	Orthostatic hypertension, sedation
Olanzapine	CYP1A2 inducers	Increase clearance of olanzapine
	CYP2D6 inhibitors	Decrease clearance of olanzapine
	CYP1A2 inhibitors	Decrease clearance of olanzapine
	Alcohol	Orthostatic hypotension
	Diazepam	Orthostatic hypotension
	Antihypertensive agents	May potentiate hypotension

This is not an all encompassing list. A more comprehensive list can be found in the package insert of each medication. Inhibitors include quinidine, parozetine, and fluoxetine. CYP2D6 inducers include cabamazepine. CYP3A4 inhibitors include azole, macrolide, protease inhibitors, nefazodone, zileuton, and fluvoxamine. CYP3A4 inducers include cabamazepine and rifampin. CYP1A2 inhbitors include fluvoxamine. CYP1A2 inducers include carbamazepine.
CI, Contraindicated; *CYP*, cytochrome P450.

for using pimozide, with 1 small randomized crossover trial, 5 case series, and several case reports.[5,19-21] While pimozide is still used successfully to treat DP, we prefer newer atypical antipsychotic agents because of their favorable side effect profiles.

Atypical antipsychotic medications other than pimozide do not require an electrocardiogram before beginning pharmacotherapy. As a rule, atypical antipsychotic medications require the periodic monitoring of laboratory values. We recommend that all patients who are receiving any medication in this class of drugs undergo a baseline lipid panel assessment and have their fasting glucose and Hgb A1c levels checked, then later rechecked after being on the medication for 3 months and then checked again after 1 year. It is also important to monitor the patient's weight at these intervals. While electrocardiograms are not needed as part of routine care for patients who are taking risperidone, attention to possible drug interactions is important.

Risperidone,[22-24] olanzapine,[19,25] aripiprazole,[26-28] paliperidone,[29] ziprasidone,[30] and quetiapine[31] have all been successfully used as monotherapy for DP. Serotonergic drugs have also been listed as effective in case reports.[32,33] Of these, risperidone, aripiprazole, and olanzapine appear most frequently in the literature. These drugs and pimozide's side effects, advantages and disadvantages, and drug interactions are compared in Tables II to IV.

Olanzapine has limited evidence to support its efficacy in DP.[19,25] The evidence is limited to 1 systematic review, 2 case series (in which some of the patients were treated with olanzapine), and a few case reports. One systematic review found its efficacy to be 72%.[15] Patients have responded to doses as low as 2.5 mg.[25] The problem associated with olanzapine is its metabolic effects (Table II). We do not recommend olanzapine as first-line pharmacotherapy for DP, but if patients do not respond to atypical antipsychotic medications, olanzapine can be started at 5 mg per day and worked up to 10 mg per day. Patients should be monitored for the metabolic effects, including triglycerides and cholesterol.

Although aripiprazole has the lowest side effect profile of the atypical antipsychotic medications, it also has the least amount of evidence, limited to 7 case reports. If patients are concerned about the weight gain associated with atypical antipsychotic medications, aripiprazole may be an alternative because it is not associated with increased weight gain.

The literature to support risperidone comes from a systematic review, case series, and several case

reports.[15,17,22-24] Efficacy in the systematic review was found to be 69%.[15] There are no randomized controlled trials. We recommend risperidone starting at 0.5 mg and working up to 4 mg because it has more evidence to support its efficacy than aripiprazole and fewer side effects than olanzapine. Tables II, III, and IV list the common side effects and drug interactions that should be reviewed before starting these medications.

Patients are typically more receptive to prescription medications once the physician–patient relationship has been established. In our experience, statements such as "This medication will help eliminate the crawling sensations that you are experiencing" or "I want to focus on managing your symptoms, and this medication will help" are effective. We often add that medications have many uses—for example, "Doxepin is an antidepressant, but we commonly use it as an antihistamine. Other drugs used in psychiatry are also valuable to dermatologists."

The median onset of a clinical response after starting therapy is 1.5 weeks, with a maximum effect often achieved by 6 weeks.[15] Discontinuation of therapy after clinical response commonly results in a relapse of symptoms.[19]

Side effects are a common cause of discontinuation of therapy. While serious side effects are uncommon in our experience, 1 randomized controlled trial found that 36.5% of patients with schizophrenia treated with an average of 3.8 mg of risperidone for 8 weeks experienced some extrapyramidal symptoms (EPSs), with an average dropout rate of 38.5% (average 50.8 days after starting therapy).[34] EPSs resulting from risperidone therapy are dose-dependent.[35] Antipsychotic medication–induced movement disorders occur more frequently in elderly patients.[36] If EPS occurs after treatment, short-term treatment strategies include lowering the dose or using a different agent. Benztropine may be used for parkinsonism; however, this is not optimal for long-term management because of its side effects (tachycardia, problems with memory, and other anticholinergic effects).[37] Akathisia may be treated with a short course of low-dose propranolol[38] or a benzodiazepine.

Psychotherapy alone has a reported efficacy of 10%; however, if the patient is amenable, psychotherapy in combination with pharmacologic therapy may be more helpful.[39] Advice from an experienced psychiatrist is invaluable. They are experts in the use of psychoactive medications, but because many patients reject the idea of referral to a psychiatrist, the dermatologist also needs a working knowledge of the agents used to treat this challenging disorder. We hope that this review will help dermatologists provide more effective therapy for these patients.

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