# Secondary delusional parasitosis treated with paliperidone

**R. W. Freudenmann,* P. Kühnlein,*† P. Lepping‡ and C. Schönfeldt-Lecuona***

**Department of Psychiatry and Psychotherapy and †Department of Neurology, University of Ulm, Ulm, Germany; and ‡North Wales Section of Psychological Medicine, Wrexham Academic Unit, Wrexham, UK*

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## Summary

Second-generation antipsychotics (SGA) are increasingly used in primary and secondary delusional parasitosis (DP) because of their better overall tolerability compared with first-generation antipsychotics (FGA) such as pimozide. Controlled clinical trials with antipsychotics in DP are lacking, owing to difficulties in obtaining informed consent and in securing adherence to a study protocol by patients with DP. We present the case of an 88-year-old man with a 12-year history of DP secondary to leucoencephalopathy. After 9 days of an age-adapted dose of paliperidone, the patient no longer experienced the presence of vermin on his skin and stopped showering at night to get rid off of them. Paliperidone was well tolerated. At follow-up after 2 weeks, the DP was still remitted. Paliperidone appears to expand the therapeutic arsenal in treating DP with modern SGAs; however, this finding needs to be replicated.

Delusional parasitosis (DP) is a psychiatric syndrome characterized by the fixed, false belief that the patient is infested with vermin or small creatures in or under the skin, which cause itching.[1,2] DP occurs as a monosymptomatic delusional disorder (primary DP) or secondary to other psychiatric disorders (schizophrenia, depression), somatic illnesses or substance use (cocaine, amphetamines). Because of their somatic concept of illness, patients usually refuse psychiatric referral. Instead, they consult general practitioners and dermatologists, and perform extensive skin cleansing, which often results in real skin damage, reinforcing the delusional belief. Managing patients with DP is thus problematic and requires a close collaboration between dermatologists and psychiatrists.[3]

The traditional antipsychotic pimozide was long considered to be the substance of choice, although evidence is limited to small studies or case reports,[4,5] and the drug is no longer a first-line antipsychotic for reasons of safety (extrapyramidal side-effects, prolonged QTc interval). For atypical or second-generation antipsychotics (SGA), open or controlled trials are missing, restricting evidence to systematic reviews and case reports.[2,6] Risperidone orally or as a intramuscular depot is the most frequently used SGA in both primary and secondary DP.[7,8] Recently, paliperidone (9-hydroxyrisperidone) the main active metabolite of risperidone, has been marketed as the first SGA using a new extended release mechanism (osmotic-controlled release oral-delivery system). Efficacy and tolerability in schizophrenia have been shown in large clinical trials.[9] We report the first case of an effective treatment with paliperidone in DP secondary to leucencephalopathy.

An 88-year-old white man with a 12-year history of DP presented, with his wife, to the outpatient department of the Psychiatric University Clinic. He was convinced he was infested with vermin and bacteria after contact with his Russian son-in-law, in whom he had 'diagnosed' scabies. The patient reported that he felt the creatures move on his skin and bite his neck and back, mainly at night, possibly coming from his stomach. In order to eliminate the parasites, he took showers at least six times each night, and he and his wife cleaned the whole apartment and washed their bed

*Correspondence*: Dr Roland Freudenmann, Department of Psychiatry and Psychotherapy III, University of Ulm, Leimgrubenweg 12–14, 89075 Ulm, Germany.
E-mail: roland.freudenmann@uni-ulm.de

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linen each day. One night, the patient had slept in the garage to avoid the insects. He complained that more than 20 physicians had failed to help him, and he claimed to have seen an insect once. They were 'too small' to be caught, so he did not present any specimen ('matchbox sign'). There was no psychiatric history before the onset of DP. He had worked all his life until his retirement and still led an active life. There was no history of substance-related disorders. Scabies and other dermatological illnesses had been excluded several times. Severe leucencephalopathy had been shown on cranial magnetic resonance imaging scans taken both 4 years and 1 year previously, and the latter had shown no progression. Since a brainstem transitory ischaemic attack 6 years previously, he took acetyl salicylic acid 100 mg daily as secondary prophylaxis. Cardiovascular risk factors included arterial hypertension, hypercholesterolaemia, and type II diabetes treated with metoprolol, atorvastatin and insulin. He took no pruritogenic medication, and *Helicobacter*-positive gastritis had been eradicated several months before presentation. Five years before presentation, he had been prescribed risperidone, with very good but transient effects (possibly due to noncompliance), and 2 years before presentation, quetiapine 200 mg at night had improved his nocturnal sleep substantially.

A mental status examination found the patient to harbour an unshakeable conviction that he was infested with animals and that he had tactile sensations caused by them. He was the inducer of a shared psychotic disorder (*folie à deux*) in his wife, who held the same delusion but with less intensity. Unlike other patients with DP, the patient accepted antipsychotic medication for treatment of the abnormal perceptions, the preoccupation with the pests and the itch. Cognition was normal and intellectual ability was excellent. There were no symptoms of schizophrenia or depression. He was not suicidal. Full written informed consent was obtained.

The patient's biological age appeared to be much below 88 years. Physical examination was unremarkable except for rashes at the neck and back due to excessive showering. Skin microbiological testing and laboratory tests were unremarkable (including C-reactive protein, thyroid-stimulating hormone, HbA1c, vitamin B12, folic acid and vasculitis screening). Secondary delusional parasitosis in leucencephalopathy was diagnosed. The criteria for organic delusional disorder [Internation Classification of Diseases (ICD) code-10 F06.2] or psychotic disorder due to a general medical condition (*Diagnostic and Statistical Manual of Mental Disorders* code TR 293.xx) were met.

The patient was admitted to hospital, while his wife returned home. He was given an age-adapted dose of 3 mg paliperidone once daily. After 7 days, he took only one shower at night. After 9 days, he noted the absence of animals for the first time in 12 years and stopped showering at night. He was discharged on day 11 with almost full remission (he still thought that he had been infested before the treatment). There were no side-effects. Electrocardiography controls and laboratory tests after starting paliperidone, including blood glucose levels, were unremarkable. Paliperidone serum level was 14 ng/mL (as intended, slightly below the normal range in young adults of 20–60 ng/mL). At follow-up by phone after 2 weeks, the DP was still remitted. Unfortunately, the patient recently died from a myocardial infarction, but until his death had remained in full remission from his DP.

This is the first report of successful treatment with the SGA paliperidone in a patient with typical DP secondary to leucencephalopathy who was the inducer of a *folie à deux*. A real pharmacological effect was likely in view of (i) the previous response to risperidone (i.e. the parent drug), (ii) the clinical response occurring after about 1 week (according to the anticipated drug effect when reaching a steady state after about six drug half-lives), and (iii) the continuing remission after returning home to his wife (excluding the possibility of the main therapeutic intervention being the separation of the couple in a shared psychotic disorder). For ethical reasons, we did not perform a rechallenge, because the patient was symptom-free for the first time in 12 years.

Like its precursor risperidone, paliperidone blocks $5\text{-HT}_{2A}$ and $D_2$-receptors, hypothesized to be responsible for the antipsychotic effects in schizophrenia and other psychotic disorders. Some pharmacokinetic properties render paliperidone particularly valuable in DP, i.e. in patients who lack insight into their illness and are often elderly or treated with several drugs due to multimorbidity. Firstly, once-daily dosing is possible due to the drug's long half-life (24 h). Secondly, due to its mainly renal elimination (> 60%), paliperidone has a low risk of hepatic drug–drug interactions involving the cytochrome P450 isoenzymes 2D6 and 3A4. However, age-adapted doses and careful monitoring of adverse effects in the mainly elderly population of patients with DP is recommended, especially assessment of renal function, which may warrant a dosage decrease to 3 mg daily.

In order to further estimate the clinical value of paliperidone in the treatment of DP, case reports replicating our findings or controlled trials are needed, even though such studies will be difficult to conduct.

In patients with DP, full written informed consent is difficult to obtain and a low adherence to any study protocol is likely.[10] Therefore, standardized reporting of DP cases using our reporting criteria[2] might help to gather data that will allow subsequent pooling of cases.

In conclusion, paliperidone is a promising new treatment option in the treatment of DP.

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