

A skin disease, a blood disease or something in between? An exploratory focus group study of patients' experiences with porphyria cutanea tarda

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Summary

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Accepted for publication

14 June 2014

Funding sources

This study was funded by research grants from the Western Norwegian Regional Health Authorities.

Conflicts of interest

None declared.

DOI 10.1111/bjd.13198

Background Porphyria cutanea tarda (PCT) is characterized by fragile skin with blistering on sun-exposed areas. Symptoms typically develop in late adulthood and can be triggered by iron overload, alcohol intake, oestrogens and various liver diseases. Treatment consists of phlebotomy to reduce iron, or increasing urinary porphyrin excretion by administering chlorochin. To optimize patient care, health personnel need to understand the subjective experiences of PCT.

Objectives To explore the experiences of persons with PCT with regard to symptoms, treatment, follow-up and prevention of the disease.

Methods Interpretive description was used as a qualitative approach. Twenty-one participants attended three focus groups. All participants had experienced PCT symptoms during the last 5 years.

Results Participants' experiences varied from trivializing symptoms and fragile skin to what was described as a desperate situation, with huge blisters, skin falling off and feeling as if one was in a 'horror movie'. For some, itching was very troublesome, preventing sleep and delaying skin healing. In managing PCT a shift in focus from skin to blood was described. PCT was perceived as a chronic and systemic disease causing a range of health problems. Strategies for preventing symptoms ranged from doing nothing to frequent controls and check-ups.

Conclusions Participants had a systemic perception of PCT, and a tendency to attribute a range of health problems to the condition. This study adds insight into the experiences patients have with PCT.

What's already known about this topic?

- Photodermatoses can have a profound impact on quality of life, but little is known of the subjective experiences of porphyria cutanea tarda (PCT).

What does this study add?

- Participants' symptoms varied from fragile skin to what was described as a desperate situation.
- Participants had a systemic perception of PCT and a tendency to attribute a range of health problems to the condition.
- Itching was reported to be a severe problem for some participants.

Porphyria cutanea tarda (PCT) is a rare disease characterized by fragile skin and blistering on sun-exposed areas. Increased urinary porphyrin excretion causes red- or dark-coloured urine.

Symptoms typically develop in late adulthood and can be triggered by hepatic iron overload, alcohol intake, oestrogens, hepatitis C and various liver stressors, in combination

with exposure to light. The prevalence of symptomatic disease is estimated to be 1 in 10 000.^{1,2} The condition exists in both a familial and sporadic subtype. Compared with 25% of cases worldwide, about 50% of cases of PCT in Norway are hereditary because of two founder mutations.^{3,4} Penetrance is very low, and only an estimated 10% of mutation carriers develop symptoms throughout life. Treatment consists of avoidance of precipitating factors, phlebotomy to reduce iron or increasing urinary porphyrin excretion by administering chloroquine.⁴

It might take 6–15 months before complete clinical and biochemical remission is reached,^{5,6} but the prognosis is good, and many patients experience lifelong remission. To detect relapse, urinary porphyrin concentration, iron and liver functions should be assessed annually.^{4,7}

The principal aim of the Norwegian Porphyria Centre is to optimize the diagnosis, treatment and follow-up of patients with porphyria. Although the clinical benefits of mutation screening are controversial,⁴ distinguishing between sporadic and familial cases appears to be important to many patients and their relatives,³ and NAPOS therefore offers, in hereditary cases, predictive genetic testing and counselling to at-risk adult family members.

Photodermatoses can have a high psychological impact.⁸ Jong *et al.*⁹ investigated quality of life (QoL) in patients with a range of photodermatoses, including PCT. They concluded that, overall, photodermatoses had a major impact on QoL, but that PCT had a lower impact on QoL than did other cutaneous porphyrias. Very little knowledge of the psychosocial impact of PCT is available and more information on the subjective experiences is therefore needed to secure optimal treatment, follow-up and counselling of this group. The aim of the present study was therefore to explore the experiences persons with PCT have regarding symptoms, treatment, follow-up and prevention of the disease.

Methods

This study was based on interpretive description, which is a well-documented qualitative approach with emphasis on clinical practice and exploration of health-related issues.^{10–12} Focus groups with interactive discussions were deemed appropriate.¹³ The study complied with the principles of the Declaration of Helsinki and was approved by the Norwegian regional ethics committee (2012/1078).

Recruitment

A convenience sample was recruited in connection with a biennial patient seminar arranged by NAPOS in 2012.¹² Information regarding the focus groups was included with invitations to the seminar. Experience with symptoms during the last 5 years was set as the inclusion criterion. Forty-six people with PCT participated at the seminar and 23 provided written consent to participate in the focus

groups. Two were excluded because of clinical remission exceeding 5 years.

Data production and participants

The patient seminar consisted of joint sessions and lectures on symptoms and treatment, in addition to conversation groups for patients to share their experiences. Three focus groups with seven participants were held over two consecutive days at the seminar.¹⁴ In light of the rich information provided, the sample size was deemed satisfactory.¹² The interviews lasted approximately 90 min. The participants included 11 women and 10 men, aged 31–77 years. Three participants reported having haemochromatosis (Table 1). The interviews were moderated by the first author (J.A.), who is experienced in counselling patients with porphyria. One co-moderator participated in the first two groups while a second participated in the third group. The interviews were semistructured and focused on three main themes with sub-questions. The main themes of the interview guide were: (i) experience with symptoms; (ii) treatment; and (iii) future expectations. Emerging themes that were not addressed by the interview guide were followed up in consecutive interviews.

Analysis

Analysis was performed in accordance with interpretive descriptive guidelines and was also influenced by systematic text condensation.^{11,12,15} Analysis was primarily performed by the first author (J.A.), with discussions and guidance from the other authors (E.G., S.S. and M.R.). Audio recordings of the interviews were transcribed verbatim and initially read as a whole. In the first step, focus was on reflections and main impressions and four preliminary themes were identified: (i) large variations in symptom experience; (ii) taking control; (iii) treatment; and (iv) prevention of symptoms. In step two, coding and text condensation were performed based on these themes, while special attention was given to avoidance of premature closure of coding.¹² Coding was first conducted cross-case, followed by longitudinal coding at an individual level.¹⁵ In step three, coding was elaborated with subgroups and further text condensation. Step four was an iterative process where focus shifted from the decontextualized codes and the transcripts as a whole; based on this, a synthesis of the coded material was presented as three main themes with sub-themes. For validation, the full transcripts were re-read several times and systematically searched for data that challenged the results.

Results

The results are presented as three main themes with subsections. Quotes are used to elucidate and elaborate the experiences of the participants. Participants are anonymized.

Table 1 Participant characteristics

Sex	Age (years)	Year of elevated urinary porphyrin levels	Type of PCT	HFE status
Group 1				
Nick	61	2001, 2009	Sporadic	Normal
Frank	59	2009	Sporadic	Heterozygous H63D
John	56	2005, 2008	Familial	Normal
Linda	60	2008	Sporadic	Normal
Michelle	62	1998, 2009	Sporadic	Normal
Nora	34	2012	Sporadic	Homozygous C282Y
Alice	52	2010	Familial	Normal
Group 2				
Peter	67	2006	Familial	Normal
Jack	56	2004, 2008	Familial	Normal ^a
Simon	57	2010	Familial	Normal
David	68	2005	Sporadic	Normal
Andrea	62	2006	Sporadic	Heterozygous C282Y ^a
Lucy	66	2010	Sporadic	Normal
Julie	58	2008	Sporadic	Heterozygous H63D
Group 3				
Tony	77	2001, 2009	Unknown	Unknown
Martin	51	2009	Familial	Heterozygous C282Y ^a
Sandra	64	2011	Familial	Normal
Lilly	58	2009	Familial	Normal
Monika	55	2009	Familial	Heterozygous C282Y
Rachel	56	2010	Familial	Heterozygous C282Y
Veronica	31	2009	Familial	Normal

PCT, porphyria cutanea tarda; HFE, haemochromatosis gene. ^aParticipants reported having haemochromatosis.

Theme 1: large variations in participants' experiences of skin symptoms – from trivializing to nightmare descriptions

Trivializing symptoms

Participants' skin symptoms typically presented as small blisters or very fragile skin, and simple things like putting hands into a pocket could cause skin trauma. Slow-healing sores were suspected by participants to have been caused by burning or cutting themselves without noticing, or from allergic reactions to chemicals or similar incidents. Discoloured urine was explained by drinking too little. This tendency to trivialize PCT symptoms as being caused by 'normal things' resulted in participants waiting to seek medical expertise, which contributed to a delayed diagnosis. Several persons explained that other people's comments about their skin made them realize they needed to see a doctor. When they finally did, diagnosis was often missed, especially if they were not referred to a dermatologist. Veronica explained:

I haven't had those really large, fluid-filled blisters. But I had very small blisters and really fragile skin. I've had to be very careful not to bump into things when it was at its worst, because it didn't take much, just barely scraping with a fingernail. And it never healed; it just itched. And also the part with the coloured urine,

because that started long before the symptoms on my hands did.

Itching – an underestimated problem?

It became evident that itching was a problem, with some considering itching to be the worst aspect of PCT. Itching was attributed to skin healing and seen as a sign of rising porphyrin levels. Participants would itch both when experiencing symptoms and when in remission. The itching was predominant at night, and would typically start after going to bed. It was debatable whether this was because of the warmth of the bed, or because it was more noticeable at this time. The itching disrupted or prevented sleep, and already fragile skin was easily ruptured, resulting in bleeding, further delaying skin healing and increasing the probability of infection. Some slept with gloves on to prevent inadvertently hurting themselves. Nick said:

It itches so much [several nods in agreement], so that's what I feel is the biggest problem. And then you lie awake at night and you scratch and it bleeds. Because of this, it never heals because it is scratched too often. . . . It is there all the time, but it is at night that I scratch because I cannot help myself. So yes, that is when I notice it the most. It itches all the time, but that is when you might hurt yourself.

Skin symptoms at their worst: 'living in a horror movie'

At its worst, PCT was painful, causing large fluid-filled blisters that would rupture, run and cause fragile skin to fall off. Fluids from blisters would squirt when shaking hands with others, and one explained that she drained her blisters with hypodermic needles. Bandaging was time-consuming and, when removed, skin would be ripped off. Participants would wear hats and cotton gloves to protect their skin and hide their symptoms from others, which would result in comments that they were 'snobs'. One participant had to empty blister fluids from his gloves while working. Everyday situations such as putting on shoes could cause the skin to peel off and sometimes these areas would become infected. When the PCT symptoms were at their worst, the situation was experienced as dramatic and described as 'being in a horror movie'. Lilly said:

I was just desperate! And my grandchildren? At that point, I didn't know if I could touch them or give them a hug or what, you know? It just kept running! It was burning! . . . So, it was a desperate situation, also because you don't know what it is. I was thinking, "Oh my god! Am I going to lose the skin on my entire body?" You know? Can no one help me?

Theme 2: a skin disease, a blood disease or something in between?

A shift in focus from skin to blood

After their diagnosis was established, participants described a shift in focus. One participant explained that she was surprised when she understood that PCT was not a simple skin disease. At first, PCT presented as skin symptoms, and diagnosis was based on patients seeking medical care for this. However, after diagnosis was established, the focus shifted from the skin to the blood. The use of phlebotomy as a treatment for PCT emphasized this. Blood samples, blood values and phlebotomy introduced a technical aspect, and many participants displayed a keen interest. They brought copies of their blood work to the focus groups and compared and discussed who had the highest ferritin levels and at what level they preferred to undergo prophylactic phlebotomy. Nora said:

Yes, and it's like I can feel something crawling in my skin. And after I learned about this, I just feel the porphyrins flying around.

Suspecting porphyria cutanea tarda caused more health problems than skin symptoms

Many participants suspected PCT caused health problems that were not limited to the skin. They felt that porphyrins were in their blood, and that genes and enzymes were involved,

which made them comment that things in the body were connected. A variety of symptoms caused by PCT were proposed and the participants showed a growing need to find legitimate reasons for other health complaints. Maria explained:

Perhaps it is a bit more complicated than what is believed? That there are actually more symptoms? That more things are connected to it? Because this is something that happens inside the body; that's what I think, that there might be.

Their suspicion was explained by the fact that the symptom in question arose at the same time as their skin symptoms appeared, and that other explanations had not been detected. Participants learned that they had similar health problems after speaking with other patients, which confirmed their suspicions. Fatigue was explicitly discussed as being related to PCT, but known acute porphyria symptoms, such as stomach pains and muscle aches, were also attributed to PCT, both by participants and sometimes by local health personnel. Participants questioned why these symptoms were not recognized by medical experts as being related to PCT and pointed to the need for further research. However, the focus on what could be attributed to PCT was so evident in the groups that some participants commented that surely not everything could be caused by the disease.

Theme 3: managing porphyria cutanea tarda – strategies for prevention, treatment and controls

Preventive strategies: frequent controls, taking calculated risks or doing nothing?

PCT was perceived as a chronic condition that patients needed to manage for the remainder of their lives. For some, this meant frequent controls and a vigilant lifestyle, with a focus on eating habits, avoiding the sun and generally being careful. For others, prevention involved taking blood samples and having control intervals. Control intervals varied greatly, from having ferritin levels never checked to having them checked every 2 weeks, every month and twice a year. The merits of this were debated by participants, and the more 'experienced' patients with PCT were asked for advice as to how often they should be tested, which test should be done and who should perform them. A few participants said they did nothing to prevent PCT. As Lilly said, 'I have a disease, but I'm not ill'. Most took calculated risks and would enjoy alcohol, sun and good food, but in moderation. They said they knew they risked skin symptoms, but it was worth it. However, the suspicion that PCT caused other problems was more worrying. Lilly said:

I think about it. But I choose to do it. And I think, like, if I'm traveling to sunny places, if I happen to get a blister, well that's just. . . I have a blister, blood samples and bloodletting. But what I might think about

sometimes is, what does it do to other things in the body? Right? I'm thinking cirrhosis. Kidney failure? I mean, what if I defy this and perhaps avoid getting a blister. But perhaps I got it because I didn't take the precautions I should. And I just used bloodletting as a way to exceed my limitations. Do you understand what I'm saying? Because I don't want that, but this is something you don't know a lot about yet. Right? What it does to other organs? Because if it's just a rash that can be treated with draining blood? Well, then we can just do whatever we want, can't we?

Phlebotomy: simple and effective, but also demanding and exhausting

Phlebotomy was viewed as very effective and provided rapid relief from skin symptoms. Participants described the process of letting blood as uncomplicated and easy, but, when they were asked for further details, aspects that were more problematic emerged. There were discussions as to whether participants could lose important components of the blood that their bodies needed. Some explained they would not drive a car or ride a bicycle the same day, or they needed to take the day off because they would get very tired. Several had stories of fainting and of 'going too low in blood values', some to the point that hospitalization was considered. Andrea dreaded having phlebotomies:

Ah, I just felt that I was sweating and I was just about to faint. So now when I am to let blood, it never used to bother me, but now! Uh! Will they hit the spot or not? So I start sweating already then. Because when the needle is inside, and they start looking for the vein. No. I'm finished. I dread it! Really!

Disagreement over the genetic testing of family members

Participants agreed that genetic testing was a choice that every individual needed to make for themselves and that whatever choice was made should be respected. There was disagreement as to whether they would recommend testing of healthy family members. For some, knowledge of genetic status was very useful; for others, it was a cause of unnecessary worry. Several pointed out that knowledge of PCT could be acquired without genetic testing. Moreover, participants who did not worry much about their own PCT were anxious about whether their children and grandchildren had inherited the predisposing gene. Exactly how genes were involved and how this would affect their health seemed to be unclear and contributed to making PCT more serious, as the following quote from Julia illustrates:

I've told both my sisters, they know I have this. But they weren't interested in testing themselves and one of my sisters, she has two grandchildren, she didn't even want them to know that I have this. This was in regards

to not wanting it to ruin their chances of having children. It was their choice.

Discussion

This was a qualitative study and the transferability of results must be viewed in relation to context and the sociocultural setting.¹⁶ PCT is associated with haemochromatosis,¹⁷ hepatitis and certain lifestyle factors, such as the intake of alcohol, which should be considered when interpreting the results. In the present study, all participants claimed to have normal or restricted alcohol consumption, and hepatitis and alcohol as predisposing factors therefore probably do not influence the results or their interpretations. However, the psychosocial stigma connected to hepatitis and alcohol abuse might have prevented persons from volunteering to participate in the focus group or limited their willingness to share this with the group, a common problem in research based on voluntary participation. The interviews were held in association with a patient seminar, which might have heightened the participants' awareness of PCT and thus affected their reflections. This might have contributed to richer information, which is desirable in qualitative studies. We argue that participants' awareness does not compromise the validity of the study, but rather reflects that human experiences cannot be reduced or separated from their context.

The results showed a large variation in experiences, from trivializing symptoms to very dramatic symptoms with a great psychosocial impact on those afflicted. This is interesting in view of the findings of Jong *et al.*,⁹ where PCT had a lower impact on QoL, measured by the Dermatology Life Questionnaire Index, (DLQI), than other cutaneous porphyrias. That the DLQI did not capture this variation in experiences is, perhaps, not surprising. Health-related quality of life measures are important for the assessment of disease severity, especially in nonlife-threatening diseases such as skin diseases.¹⁸ However, they are especially aimed at generalization through a focus on central tendencies, and condition-specific instruments such as the DLQI are designed to be responsive to change.¹⁹ Both these aspects can be problematic considering that there were only 12 people with PCT included in the study of Jong *et al.*,⁹ and they were likely in clinical remission.⁹ However, the qualitative design of the present study was aimed directly at exploring health issues and providing substantive and rich descriptions of the participants' experiences with PCT. We argue that focus groups based on interactive discussions might be especially suited for capturing and elaborating the diversity of experiences of participants in clinical remission.

Some participants with PCT mentioned itching to be a troublesome symptom. Although pruritus is not well documented in PCT, it has been reported previously.²⁰ Itching is common in many skin conditions and is likely to delay skin healing, and is associated with reduced QoL, depression and sleep disturbances.^{21–24} Consequently, this unsuspected finding warrants further investigation. To obtain more information on

this topic, the Norwegian Porphyria Registry has introduced this as a variable in the questionnaire sent to patients.

Based on the experiences of the participants in this study, venesection was an acceptable first choice in treatment; however, some problematic aspects were introduced and, as low-dose chloroquine is widely used,⁴ this might be preferable for some patients. Our findings suggest that too vigilant a strategy in the prevention of symptoms might lead to medicalization rather than benefitting the patient. To the best of our knowledge, there seems to be a lack of data regarding biochemical and clinical relapse frequency. However, an annual assessment of urinary porphyrin concentration and iron metabolism is suggested in the detection of relapses.⁴ Although PCT has been associated with changes in glucose metabolism,²⁵ and an increased risk of liver cancer,²⁶ the mechanisms are unclear and do not warrant the frequent check-ups (every 2 weeks or every month) reported by some participants.^{27–29}

PCT is generally defined as a skin disease but, aetiologically, it is also a hepatic and metabolic disorder.^{5,30} Because the symptoms are of a cutaneous nature, one would expect that the patients experienced PCT as a skin condition. However, participants in this study described a shift in focus from skin to blood and began to perceive PCT as a chronic and systemic disease. The tendency to attribute health problems to PCT was striking. We are all 'naïve psychologists' seeking to explain why events occur and to attribute causal explanations.³¹ According to the common sense model (CSM) of illness,^{32,33} there are five components of illness representations that help people make sense of their symptoms: the identity or the label given to the condition; the perceived cause of the condition; the predictive understanding of how long the condition will last; the individual's beliefs about the consequences of the condition; and whether the condition can be cured or controlled.³⁴ In this case, the identity of the condition is 'porphyria'. Porphyrias are a group of diseases, and separating PCT from other porphyrias can be difficult for both patients and healthcare providers. Patients with PCT may perceive the disease as being chronic and systemic because porphyrins, enzymes, blood and genes are involved, and treatment consists of bloodletting. This perception can, in turn, explain why participants in this study attributed a number of their health problems to PCT. The CSM uses the perception of the condition to guide which further actions are taken.³⁴ Lilly stated that medical experts do not fully understand the possible long-term complications that this patient group might expect, and therefore phlebotomies cannot be an 'easy fix' if symptoms arise. As Lilly commented, 'if it's just a rash that can be treated with draining blood, well, then we can just do whatever we want to, can't we?' The genetic component of PCT also seemed intriguing to the participants. A worry that a PCT mutation might prevent anyone from having children, as was the case in the family of one participant, emphasizes that the perceived cause of the condition and the understanding of its consequences should not be underestimated. When addressing the issue of symptoms, consequences and controllability of PCT in clinical consultation, it is therefore important to

recognize that the patient's illness representation can influence perception of risk and how they express and act upon this information.

The results show that, at their worst, PCT symptoms can be experienced as dramatic, and that a shift in focus from skin to blood after establishing the diagnosis led to the perception of PCT as a chronic, systemic disease that may cause a range of unknown health problems. This suggests there is a need for information and reassurance in clinical consultations, and as long as patients are in biochemical remission and follow control guidelines,⁴ there is little reason for them to expect health problems related to PCT. The effects of itching in PCT should not be underestimated and was reported to be a severe problem for some participants. It is important that physicians and healthcare personnel, as well as specialist centres that give advice on PCT, are aware of the differences in how the patients experience their disease, and that many of them experience it as much more than a skin disease, so that patient care and disease management can be optimized.

Acknowledgments

We wish to thank the study participants for their time and effort in sharing their experiences. We are also grateful for the assistance received from Gro A. Strandnæs and Anette Andersen in co-moderating the focus groups, and their valuable feedback during transcription and the initial analysis of results.

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