

Impact of Familial Mediterranean Fever, MKD/HIDS, and TRAPS on Patients and Families, Data From Patient Interviews

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Introduction

Patients with rare autoinflammatory diseases of familial Mediterranean fever (FMF), mevalonate kinase deficiency (MKD)/hyperimmunoglobulin D syndrome (HIDS), and tumor necrosis factor receptor-associated periodic syndrome (TRAPS) often have long diagnostic journeys. Patient and their family experiences along this path to diagnosis are poorly understood

Objectives

- To understand the experiences of patients and their families with autoinflammatory diseases through diagnosis and treatment

Methods

- We employed 90-minute semi-structured qualitative interviews and 5-day written/video diaries of patients and families with autoinflammatory diseases

Results

- Twelve US families participated in the fall of 2015 including 4 TRAPS patients, 5 MKD/HIDS patients and 5 FMF patients. The patients' ages ranged from 1–28 years. Time to diagnosis of patients ranged from 2.5 to 24 years

Something's wrong | Intermittent illness

"He'd have these strange illnesses and we didn't think anything of it." Periodic fever syndrome (PFS) parent quote

Something's wrong | Simple explanations

"The pediatrician told me it was a virus, and I thought, 'okay, kids get viruses.'" PFS parent quote

Worsening patterns of illness raise anxiety for parents. As symptoms interfere with everyday life, parents become more and more fearful and confused

- Over time, parents said that they had stopped accepting physicians' explanations and start searching for their own answers
- Most of first-time parents indicated that they had a hard time recognising when paediatric illness is 'normal' and when it's not
- They are most likely to ride the wave of early misdiagnoses without proactively seeking answers

I had... other kids... and I knew something was wrong. It wasn't no regular virus fever, like they were telling me. I would spend every weekend and every waking moment and stay up all night long looking on line for what it would be. It was crazy, it really was. I have to pat myself on the back, I was working so hard to figure it out and eventually I found it. I knew it was Hyper IgD... Then I took it to the doctor and he thought I was crazy. But, I knew it. – HIDS Mom

"She was in the hospital with a 106° F (41.1°C) fever and her kidneys shut down. I knew that this wasn't normal." PFS parent

- Most parents in the study (86%) realised that something was seriously wrong only after medical crises and hospitalisations. The diagnostic path began in earnest then, including many specialist visits (often with long waits for appointments), extensive testing, and many misdiagnoses including Lyme disease, meningitis, H1N1 influenza, systemic lupus erythematosus, systemic juvenile idiopathic arthritis, atypical Kawasaki's disease, leukaemia, lymphoma, bone cancer, and Crohn's disease
- Most parents recall a single harrowing episode that led them to realise that there is something seriously wrong with their child
- Patients and caregivers report holding onto a memory of what normal life was like prior to the onset of symptoms, and mourning their subsequent loss of normalcy

Searching for answers | Frustration

"The medical system was like a merry-go-round, endless doctors and tests and drugs but absolutely no resolution." PFS parent quote

Most parents (92%) lost faith in the medical system's ability to find an answer to their children's symptoms, while they also struggled with unsupportive school officials and dismissive friends and relatives. Parents and patients frequently felt a loss of self-confidence and increasing alienation in the face of criticism and disbelief

After severe episodes, parents encounter the medical 'merry-go-round'

- Paediatric specialists are few and far between, and it's often difficult to find them
- Office visits with paediatric specialists are difficult to arrange, and wait times are often very long
- Payors and health plans limit specialty visits, often due to the fever flares not causing notable long-term damage, and the absence of an obvious diagnosis
- Parents lose faith in the healthcare system's ability to provide the answers they need, and may stop trying to get a diagnosis if they feel that doctors cannot help them, are not addressing their symptoms, or disregard the impact that the disease has on their lives

Searching for answers | Self-doubt

"My husband started to tell me I was imagining things. Others told me not to project my crazy on him" PFS parent quote

- Many parents had statements that showed that they had a deterioration in their sense of self and perceptions, and compounds frustration wrought by a long, inconclusive diagnostic process
- Mothers and children agonise with uncertainty
 - The long search for answers raises self-doubt
 - Many parents (generally moms) stated that they began to doubt themselves, and wondered if the symptoms and flares were indeed real, or if they were imagining things

"...Many times you begin to even doubt yourself and wonder if this is all in your head. Sometimes you wonder if you had something that would never be diagnosed, or would only be diagnosed during an autopsy. Heck, sometimes you wondered if you would ever know a day without pain..." PFS parent quote

I had to fight for the diagnosis. I know that sounds insane, and when I think about it, well yeah. It was insane. ... And they were telling me I was crazy. It went on like that for years, and I kept going to different hospitals. I couldn't get anyone ... to believe me... – HIDS Mom

Searching for answers | Empowerment

"Without an advocate, I would never have gotten him the diagnosis." PFS parent quote

- Most of the parents felt that a physician advocate helped them to finally get their child diagnosed (often a Rheumatologist); some mothers had to become their own advocate
- Receiving the diagnosis of an autoinflammatory disease provided vindication and relief, as well as a focus for further education and treatment

"After we got the diagnosis, I could look at people and say, 'see, I'm not crazy!'"

- Relief comes with the ability to match up genetic findings and a cluster of symptoms to a previously-described disease entity
- Although, many parents indicated that it took them a long time to trust the healthcare system again, diagnosis brings a clearer direction for treatment and care

The relief of diagnosis | Unanswered questions

"I thought that the diagnosis would bring us some closure, but in a way diagnosis is where the real story started." PFS parent quote

Diagnosis leaves many questions unanswered

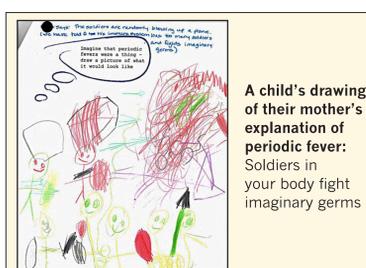
- None of the families that we met had a perfect match between all of their child's symptoms, diagnosis (TRAPS, MKD/HIDS or FMF) and their ancestry
- Families are left without a clear understanding of the causes, triggers of flares, the natural history of the disease, and what their child can expect

"...I was somewhat relieved to have an answer, a direction... But here we are with nearly as many questions as before..." PFS parent quote

The relief of diagnosis | Communication

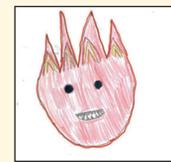
"How are you supposed to explain this to your child when you don't understand it yourself." PFS parent quote

Parents have to find a way to communicate the disease to their children, in an age-appropriate and clear way



What children said about their PFS

We asked children with PFS to draw what their disease feels like. They drew monsters



Girl, age 8



Boy, age 5

Getting worse | Daily symptoms

"I don't know anyone (in our patient group) online who is symptom free. I just don't think that happens" PFS parent quote

- Many patients (64%) reported disease symptoms between flares that were rarely recognised as related to PFS by their health care professionals
- Patients reported daily symptoms that are often only partially treatable
- Symptoms reported by families in our study included muscle pain, swollen lymph nodes, mouth sores, fatigue, and gastrointestinal issues
- These daily symptoms persist irrespective of flares and independent of fevers
- Parents hold little hope for treating these daily symptoms
- Parents are frustrated with physicians' (even specialists') lack of recognition of these daily symptoms
- Experience of daily symptoms is especially prevalent in the patients that we interviewed with MKD/HIDS, but is also present for some people with TRAPS and FMF in our study

"We'd like for more research to be done on all the symptoms of [periodic fever]. Research focuses only on the flares but doesn't look at what happens between flares. We don't feel it's ever 100% gone between flares." PFS parent quote

Getting worse | Routine childhood illness

"I've learned to tell HIDS flares from the flu, but that took quite a while." PFS parent quote

PFS kids continue to get common childhood illnesses, such as colds or the flu

- Parents often struggle to differentiate routine bouts of cold and flu from periodic fever flares
- Very often, distinguishing between a flare and an infection can be difficult and next to impossible for clinicians as well

How do you draw boundaries about what is and isn't FMF? I throw everything into the pot now. I feel like I am a cancer sniffing dog, I am hypervigilant now and I try not to overreact, but I am also monitoring him every minute of every day. I don't know how his FMF [symptoms] could change and that means that everything that happens to him could be FMF. – FMF Mom

Getting worse | Isolation

"The hardest part is isolation. I'm 28 years old and I just haven't had the same experiences as my peers." PFS parent quote

- Living with a rare disease leads to isolation, as others (including family members and friends) struggle to understand what's happening. Patients and families suffer from emotional and psychological consequences of periodic fevers

Getting worse | Hypervigilance

"I am always aware, always conscious, always looking for that next flare waiting around the corner." PFS parent quote

Parents remain hypervigilant regarding their children's health

- Parents live in constant anticipation of the next flare or episode, no matter how seemingly successful the current therapy may be
- The next flare is "always around the corner"

"...I try to 'fly under the radar' as I monitor his health I don't want him to feel sick. A hug is not always just a hug... it's also a thermometer!" PFS parent quote

Getting better, getting worse | Moms take the lead

"I would say that I'm in charge of her care. I'm her mom, so that falls to me." PFS parent quote

- Few centers offer collaborative care, so the mothers often coordinate collaboration and care between their child's general paediatricians, specialists, school nurses and all other parties

What does it mean to be a parent of a child with periodic fevers? It means you and your child will know more about your disease than your family doctor. Your family will most likely be the first one to leave events due to your child's illness. The school nurse will know you by first name. The school teacher will never question your child if they ask to go home due to illness. Your family will have your insurance company phone number on speed dial... You will learn medical terminology and how to read lab results. But most of all you will learn how to be your child's biggest advocate..." quote from caregiver



One mother's resolve

The advice is easy...don't ever give up. It takes years to even get a diagnosis, and then you have to contend with treatment (or lack thereof). Don't ever stop pursuing either. Listen to your gut. My gut has served me more as a mother than any book or article or doctor ever has. I continue to search for answers, for treatments to improve my son's life, and I will never stop. I've had so many doctors tell me that I was overreacting. One suggested I'd be torturing my son to subject him to weekly shots of Neupogen, the medication that ended up saving his life a year later. What if I had listened? Educate yourself. When the internet failed me (as it often does for rare diseases), I purchased a hematology textbook used by medical students. I borrowed medical textbooks from his doctors. I started scouring used book stores for affordable text books on hematology and rheumatology. I took free on-line biology classes offered by MIT. I did all of this to understand the nuts and bolts of what we were dealing with. To understand neutropenia and TRAPS, I had to first understand the body and where everything was going wrong. I was shocked at what was involved with the makings of a fever. How neutrophils and TLR receptors are involved with each other. How maybe these two diseases, which many doctors say are not related, just might have something to do with each other.

What I have learned from this experience is that despite how good your doctors are, they don't know you or your child like you do. Find doctors that you trust. Help them and be a team player, an informed one. Learn the basics so that you can have an intelligent discussion. Do not let these diseases just "happen" to you or your child. Do not take it lying down. Stand up and fight. This will show your child that nothing will stop them from leading a normal life.

Uncertainty | Uncertainty is the cornerstone of life with PFS

"I don't know and I can't predict anything. Not today, not next week, and not in 20 years." PFS parent quote

- The natural history of periodic fevers is still being studied and is not fully determined for many autoinflammatory diseases. Uncertainty about the future is emotionally challenging for parents and their children

"The hardest part about this disease is the difficulty in predicting what my day is going to look like. I can set all the plans in the world, but this disease can steal it all away. I'd love to spend every day like my best days, but for all I know I'm going to start crashing at 10AM with joint pain, fevers, etc. I may need to travel, or maybe I want to go out that night with friends. I will always push myself to do what I can, but I've cancelled a lot of night plans. This impacts me socially...and then there's the physical impacts. Maybe I need to be at 100% because my job depends on it. Maybe I need to go to 3 days of 12 hour meetings. I don't have time for my temperature to start spiking..." TRAPS patient, age 28

The uncertainty. Not knowing what each day is going to bring. We have good weeks, months. Sometimes its just days. There is a thought that is always buzzing in the background of my brain, that this could all get worse. Or stay the same, or maybe get better.

3. What is the hardest part about caring for a child with periodic fevers?

Conclusions

- Patients with autoinflammatory diseases often encounter long diagnostic delays, causing significant stress and confusion for the patient and their families. Distrust of the medical establishment may persist even after diagnosis. Loss of normalcy is a core tragedy for many families. Confusion and uncertainty continue to mark these families' lives, even after diagnosis
- Initiatives that improve the speed and accuracy of diagnosis, standards of care and treatment, more consistent, comprehensive patient education, and support patients and their families with these lifelong, chronic diseases have the potential to greatly improve the lives of patients with autoinflammatory diseases

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