Chapter 3: Living with Chronic Myeloid Leukemia – What we feel

＊ **Excerpts from 14 experiences.**

Thoughts about our children

1. Thinking back on my daughter's treatment

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Diagnosis

My daughter was diagnosed with chronic myeloid leukemia (CML) in September 2010. She was 12 years old and in the sixth grade of elementary school. That summer was scorching hot, so I thought my daughter's exhaustion during the school break was from summer heat. But when looking back now, she had symptoms from the swelling of the spleen and in addition, she had severe night sweats. After the school break was over, she still did not feel well. Her blood was tested at a nearby clinic. We received a phone call from the doctor early the next morning, telling us, "Your daughter's white blood cell count is abnormally high. You should immediately go to a larger hospital with the referral I'll give you." I asked the doctor, "Does that mean my daughter may have leukemia?" The doctor replied, "Don't jump to conclusions."

After my daughter was examined at the recommended university hospital, the doctor there said, "We will examine her more closely. I am afraid to tell you, but your daughter may have leukemia." While I was having lunch with my daughter and waiting for the test results to come, the doctor approached and told us, "Good news for you. This is not an acute type of leukemia. Your daughter will not have to stay at the hospital for long. Just taking medicine will be OK, but she'll have to take it for the rest of her life." I was relieved by what the doctor told us, but at the same time was apprehensive about her taking a prescription for the rest of her life.

Treatment with Gleevec

My daughter's treatment began with Gleevec (400mg). She suffered from side effects, nausea, pain and cramping in her legs, fatigue, bone marrow suppression, but the treatment overall was good. After 18 months of treatment, and nearly reaching Major Molecular Response (MMR), there were signs that her white blood count was increasing.

I talked to Dr. Shimada, an advisor to the Pediatric CML Liaison, about her symptoms. He suggested, "There is an ongoing clinical study on a drug called Tasigna, which seems to result in

better outcomes than Gleevec. The physical examination performed before the study may give us more details about your daughter's condition. Would you consider including your daughter in the Tasigna clinical study?" After consideration, we decided to transfer my daughter to the Keio University Hospital to take part in the clinical study.

Treatment with Gleevec and interferon

The physical examination before the clinical study identified a genetic mutation called T315I. The result was that my daughter was not able to take part in the clinical study. This was because the existing TKIs are resistant in the presence T315I. We learned that the only treatment option was a transplant. We then started to prepare for the transplant. This was in spring of 2014.

As preparation for the transplant, we first had to find a donor with a matching human leukocyte antigen (HLA), but no matching donor was found in either our family or the bone marrow bank. Because my daughter could not take TKI and because we could not find a donor, she had to be treated with a combination of interferon and Gleevec. Interferon is an auto-injection product, so my daughter stayed at the hospital for a week to practice injecting herself. She had to take a fever reducer to prevent fever, a side effect of the interferon.

Iclusig treatment

Despite the ineffectiveness of TKI, her condition was maintained for a year, perhaps because of the interferon. But her white blood count suddenly increased. This was the turning point to start treatment with Iclusig (30mg). We requested this treatment. Iclusig was also considered effective for T315I mutation. At that time, Iclusig was not commercially available in Japan. For a while, we had to privately import it for her treatment.

Iclusig was excellent, and her major cytogenetic response (MCyR) reached MMR in a month. A laxative became indispensable for reducing the side effects. My daughter had very dry hair, but did not suffer from nausea, pain or cramping in her legs or fatigue. The Iclusig treatment went quite well at the beginning, but by the time the long-awaited Iclusig became commercially available in Japan, it was no longer effective. This was the same result as her Gleevec treatment. We had tried all available treatment options, but all fell short of expected effects. The only option was a bone marrow transplant. By this time, three years had passed since the first discussion about a transplant.

Treatment by transplant

Transplants are not 100% safe, so we wanted to avoid this option if possible. If necessary, a transplant must be performed in the chronic period. The treatment is more likely to succeed with

fewer residual CML cells. We spent these three years carefully investigating options. During those three years, we found a source of transplant with two HLA loci mismatches by umbilical blood, but we decided to go with a bone marrow transplant from her brother. This was a three-loci-mismatched donor (haploidentical transplant). The three reasons for selecting her brother as the donor were (1) a haploidentical transplant may cause strong graft versus host disease (GVHD) and strong graft-versus-leukemia (GVL), (2) we could expect an extremely strong effect by infusing her brother's lymphocytes in case of disease relapse, and (3) it involves mild pretreatment so we can expect to enhance tolerability.

When she was 18 years old, my daughter was hospitalized for a transplant. That was in May 2017. GVHD was not a problem. She successfully recovered, and was discharged from the hospital two months after the transplant.

Today

My daughter is now 20 years old. She returned to her university last April. She has a healthy life free from all medications.

When I look back, my daughter's treatment was not easy. She simply accepted her treatment, and we were able to support her. We might have not made it through this extremely difficult time if it had not been for Dr. Shimada. He explained CML so we could understand it. He educated us about each treatment. He was generous with his time whenever we had questions. During the transplant, we felt very reassured because we knew we could rely on him. We are deeply grateful to him. Our gratitude extends to Tamura-san, chair of Izumi-no-Kai, for all his efforts in establishing the Pediatric CML Liaison and giving us the opportunity to meet Dr. Shimada. Thank you so very much.

2. That day

N.H., Tokyo

Time has flown by - it has been 12 and half years from that day. For the rest of my life, I do not think I would ever forget the day my oldest daughter was diagnosed with CML. I never imagined that we would fall victim to the disease, a one in a million chance. I used to think, “How could such an unlucky thing happen to us, my poor daughter.”

Now I think, ”My daughter was lucky.” Three months after she started kindergarten, my daughter was hospitalized. I was in tears looking at her still new school uniform on a hanger, thinking, “She may never be able to wear this or go to kindergarten again.”

I tried to be optimistic even when every test showed a high WBC count. I was disheartened watching my daughter cry herself to sleep during a 24-hour intravenous infusion. I would try to keep her spirits up when she could not eat the hospital meals. I borrowed a small 24-inch wide bunk bed and slept in a corner of her hospital room. That was my everyday life, being there for her. I was depressed to think that this life could go on indefinitely. After more than two weeks of hospitalization, including out of hospital stays, my daughter’s condition became stabilized, and she was discharged. This was unexpected. We were so happy to be able to go home. Sometimes, she had to stay at the hospital for a half day for follow up examinations, but thanks to the innovative oral medication, we could live daily life mostly on an out-patient basis until she needed to change her medication.

When my daughter began imatinib treatment, we as parents were constantly worried because there was almost no research about children taking imatinib. My daughter continued to suffer from symptoms thought to be side effects for a long time, but the symptoms were not serious. During the first grade in elementary school, besides a bereavement leave, she was absent from school for only six days. Some people would sometimes worry seeing her face so pale, but other than that, she was no different from her classmates. From looking at her, no one would think she had cancer. We were very lucky that imatinib was developed and indicated for my daughter. I am deeply grateful for that.

We also had luck with the medication, the environment, and the chance to meet supportive people. We lived not far from a hospital specializing in pediatric treatment with many excellent doctors. Our family pediatrician noticed my daughter's abnormal signs and referred us to the hospital. We also met Tamura-san from Izumi-no-Kai. If Tamura-san did not meet our daughter to talk and if we did not have the chance to speak to him, he would probably not have organized the Pediatric CML

Liaison. Without this liaison we would have had to go through days of torment being unable to share and solve the issues that we parents have.

We are parents to children who cannot fully understand what doctors tell them. We suffer because we cannot take our children's place. All we can do is stay beside our children. We too fight against the disease, as do the children. Brief outpatient examinations do not solve all issues when we have questions about how to medicate our children and about life at school and home.

Had it not been for Izumi-no-Kai, we would not have had opportunities to let doctors know about our frustrations. We realized that connecting patients and connecting parents contribute to improving the quality of life for our children with this rare pediatric disease. The challenges have many issues that we parents need to resolve, including the very expensive medical costs, potential organ damage from long-term cancer treatment, and emotional issues as our children become adults. Even though we may have issues not yet foreseen, we parents and children will continue to move forward together with Izumi-no-Kai for the long journey of treatment ahead.

6. Connection is priceless

N.A.

My daughter's history

My daughter was diagnosed with CML in January 2014. She was in the second grade of elementary school.

At the end of November 2013 I noticed something unusual. At a marathon tournament, she reached the finish line last. She looked extremely exhausted. She could not double jump a jump rope, which she had been easily doing before. She got tired. At that time, I thought that she had not been getting enough exercise to maintain her physical abilities.

She had a fever at the end of the year and visited our family doctor. She was diagnosed with a common cold and given a prescription. Eventually her temperature returned to normal.

After the New Year in January 2014, we were concerned about her swollen stomach, so we went to our family doctor again. The doctor said perhaps she might be constipated. She received an enema, which did not work. We then got a referral to a local hospital.

At the hospital, she had an echography. We found out that her spleen and liver were swollen. We then got another referral to a university hospital. The examination at the university hospital revealed 0.6 million WBCs, raising suspicion of CML. She was immediately hospitalized where she is currently receiving ongoing treatment.

Later, she concurrently underwent detailed examinations and treatment, which confirmed the CML diagnosis. She was hospitalized for about a month for treatment, and currently goes to the hospital once a month as an outpatient and continues her medication.

Pediatric CML Liaison

During the hospitalization, there were many pediatric leukemia patients in the hospital ward, but none had CML. There was no one I could share my concerns and thoughts with. I was feeling doubtful about my daughter's future. The chief doctor had told me about the Pediatric CML Liaison, but I did not have the courage to contact the liaison for a long time.

In June 2016, more than two years after my daughter’s CML diagnosis, I finally took part in the Pediatric CML Liaison. I met many people from different backgrounds, parents with children

younger and older than my daughter, and parents with children who had recent and not so recent diagnoses. I listened to stories about different treatments. At the liaison, I learned about the varied family backgrounds, side effects and problems, and how their children are living with and fighting CML. I was encouraged to know that my family was not alone.

We had an opportunity to listen to a very helpful lecture from Dr. Shimada at Keio University Hospital. Dr. Shimada examined the disease time-course and test data of my daughter, and gave us helpful advice.

Since then, I take part in the Pediatric CML Liaison every six months. I chat with participants and ask Dr. Shimada about my daughter's time-course after treatment.

Dr. Shimada said the following about my daughter:

• Better to measure her blood concentration
• Better, if possible, to stop taking the prescription medication for her severe nausea
• Have a bone density test
• Advice on whether to receive vaccinations
• Advice on whether to increase the medication dosage

I explained his advice to her attending doctor. The doctor responded positively to all the advice.

◉ Epilogue

• My daughter is now in her first year of junior high school. Five years have passed since she was diagnosed. Now she is part of a brass band club and enjoys club activities as well as studying at school.

• I am very grateful to Dr. Shimada for examining my daughter's data and providing advice on treatment at every Pediatric CML Liaison.

• I am grateful to her attending doctor who responded positively to the advice.

• I am truly thankful for Onosaka-san and Maruyama-san who host and manage the Pediatric CML Liaison, the participants, and Tamura-san of Izumi-no-Kai who provided valuable time and a venue for the meetings.

• I will continue taking part in the Pediatric CML Liaison to exchange information with other participants. For those who have not yet taken part in the liaison, I would say you might want to try once. Here you learn what you cannot get from either books or the internet.

Children's Work

Miniature bakery

Confectionery made of clay

Stamp made with eraser