Warts Running Wild

This encounter illustrates a very rare condition that had been left untreated for nearly 20 years. A confirming diagnosis was needed to design a treatment to improve the patient's quality of life. Improved technology often plays an important role in identifying what infectious disease agent(s) might be present in biopsy tissue. In this case, tests used to determine the immune status of the patient also helped explain why his condition was so severe.

American dermatology expert Dr. Gaspari was tired but eager to arrive in Jakarta, Indonesia. He was on his way to investigate the case of a 35-year-old Indonesian man with a very rare skin condition, about whom he had learned by watching a Discovery Channel documentary. The people in the remote village where the man, Dede, lived referred to him as the "Tree Man of Java." From the program, Dr. Gaspari observed that Dede had cauliflower-like tumors all over his body. His hands and feet looked like branches of trees growing from the surface of his skin. Dr. Gaspari was anxious to biopsy these growths, hoping that this would help him determine the cause of growths, as well as a treatment that would cure them, or at least improve Dede's quality of life.

He contacted the Discovery Channel and was provided with contact information for the Indonesian journalist who first covered Dede's story. After months of communication and planning, Dr. Gaspari was finally on his way to meet the "Tree Man" (**Figure 1**).

The journalist who had written the first story about Dede and his condition picked Dr. Gaspari up at the Jakarta airport. They traveled by car, by boat, and on foot to Dede's home, located in a remote jungle village.



Figure 1. Dede, the "Tree man." (Drawn by Brian Ledwell.)

When the two finally met, Dr. Gaspari smiled and said, "Hello Dede, it is great to finally meet you. I would like to help you as much as I can. I believe there must be a medical treatment to help you."

Dede seemed nervous but excited to meet Dr. Gaspari. He explained that his biggest fear was that his two children would come down with his disease.

Dr. Gaspari needed to do a full body examination of Dede, but first he needed to learn more about Dede's history. This was an unusual case. He had never seen anything like it, nor had it ever been described in any medical textbook.

Dede began to speak shyly. "When I was 15 years old, I cut my knee. After that, the first **warts** started to grow. I used to work in construction, and I was a fisherman. I was married and had two children. But as time went by, the warts got worse and worse and I had to stop working when I was in my 20s. Then my wife abandoned me. I worry that the warts will cover my whole body. I worry that this disease will affect my children."

Dr. Gaspari observed the growths around his eyes, nose, and mouth.

Dede sighed, "I cannot care for my children financially. I cannot even touch my children. My sister is looking after them."

Dede looked serious and frightened. Dr. Gaspari sensed he was depressed and felt isolated by his condition. He may also have been malnourished. What he had was a unique, seemingly unstoppable infection. He listened carefully to what Dede had to say, and then gently asked, "How do your hands and feet feel?"

"Heavy," Dede replied. "I cannot use my hands for anything. I have not been able to write for over 10 years. I cannot feed myself. I have to drink through a straw. I cannot bathe myself. And it is very painful to walk." His eyes saddened as he spoke. "My brother-in-law helps care for me each day. He bathes and washes me. I need a special tailor to make clothes that will fit over my horned hands and feet."

Many thoughts ran through Dr. Gaspari's mind. What could be the cause of Dede's malady? Was his immune system compromised in any way? How is this man able to survive in this community? From Dede came an unsolicited soft-spoken reply, "I work in a circus troop, but this income is not enough to support my children."

Dr. Gaspari asked, "Have you had any treatment for this condition?"

"Doctors tried to remove some of the warts several years ago, but they grew back even faster."

The journalist chimed in, "The warts grow about 5 mm a month."

Dr. Gaspari knew this was a very challenging case. Dede had a life-threatening condition that required medical attention, but until a diagnosis could be made, proper treatment could not be possible. The wart infection had been allowed to flourish for 20 years without treatment. Dr. Gaspari also needed to figure out how well Dede's immune system was working in order to make a diagnosis. If his immune system

was compromised, could it be boosted with drug therapy? Would that help bring the warts under control?

He began a full body examination, closely observing the warts. He was concerned that Dede might have skin cancer or be at risk for developing it soon. There were also infectious agents, like fungi and viruses, which could cause the formation of warts. He needed to take **biopsies** of the warts as a first step to figuring out what was causing them to form. "Dede, I need to remove some warts so that I can study them in my research laboratory in the United States." said Dr. Gaspari.

Dede said, "I want you to treat me."

Dede's home was small and cramped, and the conditions were hot and humid. There were many flying insects in and outside of Dede's residence. Flies were landing on Dede's warts and he could not swat them away.

Before the biopsy procedure began, Dede lay in the middle of the floor on a blanket. His relatives surrounded him. They quietly and intently watched the interactions between Dede and Dr. Gaspari. None of them could speak English. The journalist acted as an interpreter for them all.

Dr. Gaspari opened his medical kit and donned a pair of latex gloves. He opened a package containing a sterile needle and a vial of anesthetic. "You will feel a sting," Dr. Gaspari said. He injected an anesthetic under the skin, numbing the area around a large wart. Using a scalpel, he surgically removed a wart and put it into a specimen vial. The area around the removed wart began to bleed more than normal. It took more than 30 minutes to stop the bleeding. This was a cause for concern. Dr. Gaspari decided to remove smaller warts in the hopes that they would result in less bleeding. By the time he was finished, he had surgically removed a total of four warts.

Each time a wart was removed, a strong odor emanated. Dr. Gaspari considered that there was likely some bacterial colonization around the warts because it is very hard to keep them clean and free of microbes. As Dr. Gaspari left for the evening, he found himself concerned about the excessive bleeding caused by removing the warts. He worried that this would be a source for additional bacterial infection and didn't know if Dede's body could fight off such an infection. He was very concerned that he may have a weak immune system. The next day, Dr. Gaspari returned. It was raining, hot and humid. The flying bugs were irritating.

"How are you doing, Dede?" said Dr. Gaspari with a smile. Dede smiled shyly. Dr. Gaspari analyzed the biopsy areas on Dede. "Your biopsy sites look good. You are healing. Dede, I need to figure out if your immune system is working right. In order to do that, I am going to inject some yeast cells under your skin. If the area turns red and swollen, it means your immune system is responding to foreign cells—that your immune system is normal."

Twelve hours after Dr. Gaspari injected the yeast, Dede's reaction was very weak. This was not a surprise to Dr. Gaspari. It affirmed his suspicions that Dede's immune system was impaired.

"Typical warts do not become this consuming. Warts come and go in individuals with healthy immune systems," explained Dr. Gaspari. "Because your body cannot fight off what is causing the warts, medical treatment is necessary to reduce them. I will need a blood sample from you and your family to help figure out what is causing these warts so that we can treat them with a drug. Blood samples will determine if your relatives are hidden genetic carriers of a disease or have a tendency towards a disease, which may have been passed to you, which is causing these growths. It will also help me learn more about your immune system."

"Do what you need to do," replied Dede.

Subsequently, Dr. Gaspari drew blood samples from Dede, his parents, sister, and children. As he took the samples, he continued to explain. "Surgically removing all of the warts will not solve the problem. A combination of surgery and chemotherapy may provide the best treatment so that Dede can live a more normal life."

"I want to be able to return to fishing and take care of my children," said Dede.

Taking the samples he had collected, Dr. Gaspari returned to his university laboratory in Baltimore, Maryland. He spent 2 months studying the biopsy samples, looking for agents like fungi, poxvirus, herpesvirus, or papillomavirus that could be the source of infection. Thorough tests were done on the blood samples. He was surprised to discover Dede had a nearly nonexistent immune system and a very low white blood cell count. He wondered if Dede could have **AIDS**.

He was also able to detect a papillomavirus in the warts. While papillomaviruses are very common throughout the world, the severity and extent of Dede's infection was unique. His first assessment was that Dede needed to be treated with a retinoid such as acetretin, which is a laboratory-derived form of vitamin A to reduce the warts. Retinoids work by regulating the growth of epithelial skin cells, which had raged out of control in Dede's condition. Another possibility was using interferon to help boost Dede's immune system to fight the viral infection.

Dede received worldwide attention. Once a diagnosis was made, local doctors began surgically removing Dede's warts at a hospital in Bandung. They removed over 4 pounds of warts. Unfortunately, there were complications. The bones of his fingers and toes were weak from so many years of disuse. He was treated with anti-osteoporosis drugs and calcium to strengthen his bones. He underwent skin grafts to heal the areas most affected by the warts.

After several months, Indonesian doctors began working with Dr. Gaspari to treat Dede chemotherapeutically. Dede received vitamin A and an antiviral drug that was only available in the United States. Today, Dede is improving. He has hope.

Update

Dede was in the hospital over 9 months recovering from numerous operations. Although unconfirmed, there were rumors that Dede also suffers from tuberculosis and hepatitis B. Today he can use his hands and walk. He will likely need more surgical procedures because the growths will continue to reappear in other locations of his body or regrow.

Questions to Consider

- 1. How could a laboratory technician discern that the warts were caused by a human papillomavirus and not a human herpes 8 virus or a monkeypox infection?
- 2. The disease described was left untreated for nearly 20 years. Could early treatment have prevented this condition? Why or why not?

- 3. How many types of papillomaviruses are there?
- 4. There are three distinct categories of papillomaviruses: low-, intermediate-, and high-risk types. Explain what this means.
- 5. Why is the disease in this encounter rare in humans?
- 6. If Dede also suffers from tuberculosis and/or hepatitis, how might this complicate his treatment?
- 7. Would the **GARDASIL**[®] or **CERVARIX**[®] vaccines have prevented this infection in Dede? Why or why not?
- 8. Research acetretin. For what types of maladies is acetretin used as a treatment option? Are there side effects to this drug?
- 9. Research interferon. When is interferon used as a treatment option? Does it have side effects?
- 10. Why was it difficult to remove Dede's warts surgically? Why was a combination of treatments used in Dede's case?

References

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Wang, C. W. W., et al. 2007. Multiple Cutaneous Horns Overlying Varruca Vulgaris Induced by Human Papillomavirus Type 2: A Case Report. *Br J Dermatol* 156:760–762.

Wang, C., et al. 2007. Detection of HPV-2 and Identification of Novel Mutations by Whole Genome Sequencing from Biopsies of Two Patients with Multiple Cutaneous Horns. *J Clin Virol* 29:334–342.

Internet Resources

Indonesian Treeman, Department of Dermatology, University of Maryland, Dr. Anthony A. Gaspari, http:// www.umm.edu/dermatology/treeman.htm

My Shocking Story—Half Man Half Tree: Discovery Channel, http://www.discoverychannel.co.uk/video/myshocking-story-half-man-half-tree/