

Am I a Girl, or a Boy? An Unusual Case of Ambiguous Gender

by

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Part I – An Ambiguous Beginning

Being a third year medical student at the University of Florida, you have just begun your rotation in the obstetrics wing of Shand’s Hospital in Gainesville, Florida. You’re excited to have this as your first rotation because it has long been a dream of yours to become a pediatrician.

There’s a full moon the evening of your first night shift in labor and delivery (L&D). A petite Latina woman comes in with her husband. From the chart, you see that Mrs. Santiago is 40 weeks pregnant and her chart has the pregnancy code “Gravida 4, Para 2” (shortened to G4 P2). Everything appears to be in order and you begin to talk to the couple about the baby. You ask them if they know whether they are having a boy or a girl. They tell you no, they want it to be a surprised, like with their other children. The attending MD, Dr. Jackson, reviews Mrs. Santiago’s chart and asks a few questions.

“Mrs. Santiago, I see here in your chart that you are 31 years old and that you were born in Santo Domingo. I love the Dominican Republic. It is such a beautiful country. My wife and I went there last winter and had a wonderful time.” Dr. Jackson looks through the chart some more and turns to you and asks: “How far apart are the contractions?”

“About three minutes,” you respond.

Dr. Jackson continues, “Ok, Mrs. Santiago, we are getting close. We are going to move into the delivery room now.”

After the delivery room is set up and the epidural is in place, Mrs. Santiago has noticeably calmed down but is feeling the urge to push. Dr. Jackson asks you to check her cervix, and then he checks it. “What do you think?” he asks.

You reply, “100% effaced and dilated 9 centimeters.”

He says, “I’d say it is more like 10 centimeters. She is completely effaced and dilated. Mrs. Santiago, when you feel the next contraction, go ahead and start pushing.”

Questions

1. What does “G4 P2” mean in Mrs. Santiago’s chart?
2. How many other naturally born children has Mrs. Santiago had?
3. What is *effacement*?
4. What is *dilatation*?

Part II – It’s Time to Push

After about an hour of pushing, the baby has crowned and is moving fairly quickly through the birth canal. You think, “This isn’t so bad after all; maybe I should consider becoming an obstetrician.”

Finally, with one last push, the baby is delivered. Dr. Jackson says, “Congratulations! It’s a...” Then Dr. Jackson becomes very quiet.

You look at the baby and think to yourself, “It’s a girl... wait. If you look this way, it’s a boy. Hang on. Is this baby a boy or a girl?”

After some deliberation, the otherwise totally healthy baby is identified as a girl. Dr. Jackson explains that sometimes the presence of excessive hormones associated with the pregnancy can cause swelling of the baby’s genitalia. Since the delivery was uncomplicated, Mrs. Santiago and baby Maria Esperanza Santiago go home from the hospital.

As you continued through medical school and your residency, you sometimes reflected on the case and wondered what had happened to that little girl.

Six years later...

You were very lucky to have the opportunity to begin a new practice of pediatrics based in Mercy Hospital in Miami. As you walk to the door of the exam room, you are reviewing your next patient’s paperwork. You think, “Maria Esperanza Santiago... where have I heard that name before?”

The new patient is a healthy six-year-old girl accompanied by her attentive parents. The very precocious little girl immediately tells you that she is on a tee ball team and is ready to play in her fourth game after she leaves the office. She’s very proud to tell you that she is the star player even though she is a girl.

You tell Mrs. Santiago, “Maria needs a couple of vaccinations, but everything looks great. The nurse will be in soon.” Turning to your new patient, you say, “Maria, good luck at that game. Don’t let the boys pick on you! Girls are great ball players, too.”

In the following years, you get to know Maria and her parents, but everything changes just before Maria’s 12th birthday. The Santiagos show up at your office a few months before Maria’s regularly scheduled yearly exam. In the exam room, Mrs. Santiago is crying and Mr. Santiago is holding his cap in his hands. Maria is just staring at the floor in front of her feet. You ask the Santiagos the reason for the visit, “Is Maria not feeling well?” Mr. and Mrs. Santiago look at each other back and forth and then look at Maria. Finally, Mrs. Santiago blurts out, “*Que ha crecido un pene.*”

Bewildered, you ask, “Excuse me? My Spanish is not perfect so maybe I misunderstood what you just said. Did you just say that Maria has grown a penis?”

“Yes! What is happening? Is she a *guevedoce*?” Mrs. Santiago exclaims.

It is at this moment that you make the connection between your first experience in L&D at Shand’s years ago and now. You think, “Could this possibly be the same child with ambiguous genitalia? She is the right age.”

“Mrs. Santiago, if she is, finding out will require only one test.” You turn to speak with Maria. “Maria, do you know what chromosomes are?”

Maria replies, “Yes, I learned a little about chromosomes from my health teacher. I know humans have 46 chromosomes and two of them decide whether you are a boy or a girl.”

You explain, “Right. I’m going to order a special test called a karyotype. A karyotype reveals the number and types of chromosomes of an individual. As humans, we have 46 chromosomes. Of those 46 chromosomes, two of them are different and determine whether a person is male or female. They are called the sex chromosomes and we represent

them as X or Y. Normally, a female will have two X chromosomes and a male will have one X and one Y chromosome. We will take a sample of your blood and determine which chromosomes you have.”

Maria looks confused and asks, “But until just a little while ago, I looked like a girl. I don’t understand.”

“Well, Maria, there is a difference sometimes between what you see and what your chromosomes are. What you see is called your phenotype. When you were younger, you looked like a girl. We would say that you were a phenotypic girl. A karyotype will indicate whether you have two X chromosomes or an X and a Y chromosome. Although I am sure you have many questions right now, I’m going to have a karyotype done on your cells and we will talk more after the results are back.”

The Karyotype

Karyotyping reveals that Maria is 46,XY. Chromosomally, Maria is male. Yet she was identified to be female at birth and has lived as a female until now. Maria’s parents may be right. She may indeed be a *guevedoce*.

Figure 1. Maria’s Karyotype.



Source: Karyotype of a human male courtesy of National Human Genome Research Institute, <http://www.genome.gov/glossary/resources/karyotype.pdf>

Questions

1. Maria’s karyotype is 46,XY. What would a normal female karyotype be?
2. Describe the difference between phenotypic and chromosomal sex.
3. Is Maria a true hermaphrodite?
4. What is a *guevedoce*?

Part III – Changing Lives

You bring the Santiagos back into your office once the test results come back so that you can discuss the results with the entire family.

You tell Maria, “Remember what we said about chromosomes? If an individual has two X chromosomes, they are normally girls—and those with an X and a Y are boys. Your results came back and you have an X and a Y.”

“Then I am a boy? Why did the doctors say that I am a girl when I was born? What happened to me?” she asks.

You reply, “Early in development of a fetus, boys and girls look the same. After a while, they begin to look different. This is one reason why you can’t tell if a fetus is a boy or girl by ultrasound until 16 weeks into the pregnancy. Before that point, it cannot be determined just by looking. However, if some cells were taken from the fetus and karyotyping was performed, as it was done on you last week, it would show whether the baby was XX or XY. If your karyotype had been done when you were born, it would have shown that you are a boy. You have very low levels of a key enzyme called 5- α -reductase. It made your private parts look kind of in-between a girl and a boy when you were born. But when you got old enough to go through puberty, you began to make enough testosterone to jump start your development into a male.”

Maria blurts out, “Am I going to turn back into a girl?”

You answer, “You don’t have to worry; you won’t turn back into a girl. You always were a boy, but your body just didn’t show it until now.”

“Well, I guess that explains why I was always better at tee ball when I was little.”

The Santiagos have several questions about Maria's future development. You explain that Maria will develop like a normal male with two exceptions: lack of a full beard, and will probably not experience a receding hairline. Maria will develop more masculine characteristics just like all other boys with larger muscles and a deeper voice. No one will know that Maria is any different at all. Also, Maria has a decreased risk of having prostate cancer when he is older.

“How could this happen? How can Maria be a *guevedoce*? Manuel and I are not related to one another,” Mrs. Santiago points out.

Questions

1. Why is it important in this story that the parents are from the Dominican Republic?
2. Why did Mrs. Santiago bring up that she and her husband are not related to one another?
3. What is the normal function of 5- α -reductase reductase and what does it have to do with this disorder?
4. What would lab results reveal about the testosterone and dihydrotestosterone levels in Maria at puberty?
5. As the pediatrician, what advice would you give the Santiagos? If you were Mr. or Mrs. Santiago, what would you do to help Maria acclimate to a new life? How would you encourage Maria's decisions?

Part IV – The 13-Year-Old Checkup

For the 13-year-old checkup with the Santiagos, you are anxious to see what has happened in the last year. As you enter the examination room, you are greeted by a young man wearing a baseball cap. Maria now goes by the name Mario Manuel Santiago and is playing short stop on his school's junior varsity baseball team. He is very excited to tell you that they will be going to the state tournament next weekend. You tell him how proud you are of him. Mr. and Mrs. Santiago seem very proud of him as well.

You notice that Mario has begun to grow a mustache and his voice is deeper this year. You ask Mr. and Mrs. Santiago to leave the room so that you may talk to Mario alone for a few moments. Once the parents are out of the room, you ask Mario how the adjustment has gone.

Mario replies, "At first, I didn't know what to do. I was very confused. But my family moved to a different town to make my adjustment easier. I like it at my new school, but some of the kids found out that I sort of used to be a girl. I got bullied some, but my teachers stood up for me. Some of the kids called me a hermaphrodite. I looked that up on the internet and found out that I'm not really a hermaphrodite. I'm a boy that just looked like a girl when I was born. Now that I am on the baseball team and helped the team make it to the state tournament, most of the students like me, but some still don't. My parents said that if it is too hard on me, we can always move back to where they are from. You know, the Dominican. But I like Florida."

Later in your office you speak with Mr. and Mrs. Santiago. They tell you that they had driven back to meet you for this visit, but they have moved to Tampa to get away from Miami in order to help Mario with his adjustment. Mrs. Santiago tells you, "I called my mother in Santo Domingo to tell her what had happened and after asking some questions we found out that Manuel and I are second cousins. We were shocked, but that made Mario's condition make more sense."

You reply, "How has Mario's adjustment been?"

Mr. Santiago begins, "I had to go to the principal's office more than once about Mario getting bullied. Mario stood up for himself, though. His big brother, Josef, has helped a lot, too. This has been difficult on our family, though. We never thought this would happen in our lives. We are trying to get Mario's birth certificate changed to show that he is male now so there is no question for him to answer when he plays sports."

Question

1. Should Mario's birth certificate be changed to reveal his sex as male instead of female? Why or why not?

Epilogue: The Clinical Significance of 5- α -Reductase Deficiencies

The case of *guevedoces* was originally studied in the early 1970s when several cases of the disorder were discovered in the Dominican Republic. The endocrinologist who did the study was Dr. Julianne Imperato-McGinley, an endocrinologist at Cornell Medical College. After analyzing the data, it was determined that the disorder was due to a deficiency in 5- α -reductase, the enzyme responsible for converting testosterone to DHT. It was found that this decrease in 5- α -reductase leads to having a smaller than normal prostate gland and a significantly decreased chance of having benign prostatic hypertrophy (BPH) and prostate cancer. Men generally express their highest levels of DHT in the prostate. A class of drugs was subsequently developed to block the formation of DHT, 5- α -reductase inhibitors (ARIs). Use of these drugs stops the prostate from growing. ARIs like finasteride and dutasteride block the formation of DHT and are used in the treatment of BPH. It is also used to treat hair loss.

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