“But, doctor, what should I do?”

Michelle was sitting in her OB-GYN’s office, having just confronted him with the dilemma she was facing.

“My mother died of breast cancer when I was little and now I find out that her mother, my grandmother, has bone cancer and my grandmother’s brother and my grandfather both have lung cancer. My mother was 40 when she died and I’m almost that now myself. Should I have my breasts removed to prevent me from getting breast cancer?”

The doctor tried to calm her down and clarify the family tree. As far as Michelle knew, her mother was the oldest of four girls and two boys in the family and the only one to have cancer. In fact, her grandfather also had a brother and two sisters, and none of them showed any signs of cancer.

“It’s not strong enough evidence to suggest you should remove your breasts,” the doctor said. “Actually, breast cancer susceptibility is not linked to lung cancer. Lung cancer, especially, is usually linked to environmental factors, like smoking or exposure to asbestos. Does your father smoke?” the doctor asked.

“Yes,” Michelle replied. “But I don’t want to get cancer and have my two little boys watch me die the way I did with my mother.”

The doctor suggested Michelle gather more information about her family tree and then come back and he would contact a genetic counselor about the possibility of genetic testing.

A month later, Michelle went to see her doctor again after having talked with her grandmother extensively about the family. She had uncovered two very interesting family facts. First, the man she thought was her mother’s father was not her biological grandfather, but his brother. Her real grandfather had no history of cancer. Second, Michelle found out her mother had an estranged older sister, Anne, who had recently been diagnosed with ovarian cancer. The doctor now felt the family connection was strong enough to advise Michelle that there was a possibility of a cancer gene linkage in the family.
The doctor contacted Laura, a genetic counselor in the area, and found out that the most likely candidates were the breast cancer genes BRCA1 and BRCA2. Mutations in one of these two genes are found in 90% of tumors from breast and ovarian cancer. Women with hereditary mutations in one of these genes are 30 times more likely to develop breast cancer by age 50, while men have a three times higher risk of developing prostate or colon cancer if they inherit this mutation. The genetic counselor clarified that a variety of studies have suggested that mutations in BRCA1 are more often linked with breast and ovarian cancer, while mutations in BRCA2 are most often linked only with breast cancer. The fact that Michelle’s grandmother, the mother of both affected women, had bone cancer and not breast or ovarian cancer might be the result of a metastasis from the original site of the tumor in the breast. Thus, Laura felt this family was a candidate for a BRCA1 mutation.

With Michelle’s consent, the doctor arranged to have the breast biopsy sample from her mother sent to a DNA testing facility, Myriad Genetics in Salt Lake City, Utah. A month later they found out that the sample was a poor one, making it difficult to get any information. The testing facility thought that the sample might not have been prepared or stored properly and thus the DNA in it was degraded beyond usefulness. So, there was no data to indicate that Michelle’s mother’s cancer was due to a mutation in BRCA1. No other samples existed of Michelle’s mother’s tumor or other tissue from which they could do another analysis.

Michelle’s doctor contacted Laura, the genetic counselor, to discuss the case. Laura felt that in order to make any assessment, a DNA sample from an individual with cancer was needed. This sample could then be used as a comparison for the sample, namely Michelle’s, with unknown cancer risk. If the DNA from an individual with cancer showed a mutation in the BRCA1 gene, Laura explained, then they would look for the same mutation in Michelle’s DNA. Ideally, the mother’s DNA would have provided them with this information, but without it, a DNA sample from another close relative with cancer was essential. Otherwise, they wouldn’t be able to be certain that a DNA change in Michelle’s BRCA1 gene was necessarily linked to cancer. DNA from the estranged, cancer-carrying aunt would be very useful and could be obtained from a sample of her blood.

Laura had a lengthy conversation with Michelle in which they went over Michelle’s complicated family situation. Laura then wrote a letter to Anne, the aunt who lived in a remote town two hours away, in which she explained the process and asked for her informed consent to give a blood sample to get DNA. After two weeks had gone by with no reply, Laura tried contacting Michelle’s aunt a second time. Again, she received no reply. After the third time, Laura finally got the aunt on the phone. Anne reluctantly agreed to meet with Laura for coffee—not in her home, but in a restaurant in her small town—and as long as Laura paid for it.

Laura met Anne at the restaurant at the appointed hour. Anne was accompanied by a younger woman who turned out to be her daughter. The daughter read the menu for her mother and Laura suspected that the older woman was illiterate.

After introducing herself, Laura said: “I’m here representing your niece, who would like to arrange to get some information from you to help her decide if she has a cancer gene.”

Anne looked confused. “What’s a gene?” she asked.

Laura explained: “Our bodies are made up of small parts called cells that contain a substance called DNA. DNA is the blueprint for our cells and controls everything about us. DNA is the same in all your cells. It is passed from one generation to the next, provided from both mother and father at fertilization. So, the DNA found in Michelle should be similar to your DNA, since the two of you are related.”
Changes in your family’s DNA may have made several of its members more susceptible to cancer and would explain why several of you have gotten the disease. This would include your sister, Michelle’s mother, who died from breast cancer. Michelle would like to know if there is such a change in your DNA and also in her own DNA. If there is such a mutation, Michelle might then decide to remove either her breasts or her ovaries to prevent her from getting cancer. Michelle would like you to give a blood sample at your doctor’s so that DNA can be isolated and the gene sequence determined.”

Anne was silent for a moment and then asked Laura, “Who would pay for this? I haven’t got any money.”

“I don’t know that yet. Who covers your medical bills?” asked Laura.

“My medical bills are covered by Medicaid,” Anne said.

Laura knew that the BRCA1 test costs in the neighborhood of $2500 for the complete information about this gene and that Medicaid would not pay for it.

Anne’s daughter interjected belligerently, “Why are you doing this, Mom, when they ignored you for so many years and haven’t given us any money since you left?”

Questions

1. Create a family tree using standard symbols for the people mentioned in the case and include some designation to indicate those affected with cancer.

2. What part of the blood sample would be used for the DNA analysis and why?

3. What techniques can be used to determine whether Anne’s DNA has a mutation in the BRCA1 gene?

4. Why might the degradation of the DNA from Michelle’s mother make the information obtained unusable? Are there other approaches one could use to get around that problem?

5. What do each of the people in this scenario want to get out of this situation?

6. What problems do you foresee with the different agendas—the different needs—of the people involved in this case?

7. What are ways that one could solve these problems?