Part I — Something’s Not Right

Dr. James Stephens is a pediatrician serving the Tarpon Springs, Florida, area who is seeing one of his new patients in the clinic today. As Dr. Stephens enters the examination room, he says “kali mera” to Stephania and Nikoleta Stamos, a greeting he uses with a number of his patients who are Greek Americans. Mr. and Mrs. Stamos have brought in their only child, beautiful little Nikoleta. It seems odd to Dr. Stephens that they are here because Nikoleta’s one-year checkup is only six weeks away. Nikoleta’s parents are very concerned and tell the doctor that the baby has been acting strangely. The father, Nikolaus, is a personal trainer and he suspects that Nikoleta has been anemic for some reason. Originally, Nikoleta had been on a low iron formula because she was experiencing gastrointestinal distress. The parents changed her formula to a high iron formula to see if it would help alleviate her symptoms, but Nikolaus tells Dr. Stephens that it did not. His daughter continues to suffer from general malaise and lethargy, and her skin looks a little pale recently. Nikoleta’s parents also tell the doctor that their daughter looks bloated all the time, and seems tired and cranky.

Dr. Stephens notices that Nikoleta’s belly appears to be swollen. Stephania mentions that she too noticed that about a month ago, but thought it was either gas or that the baby was gaining weight.

Nikoleta’s chart reveals that Nikoleta was in the 50th percentile for both weight and length at the time of her birth (7lb 8oz; 20 inches). She is current with all of her vaccinations. Both parents appear attentive and involved in her care. Mr. Stamos is average height and build while Mrs. Stamos appears to be of small stature but within normal range. Dr. Stephen’s assistant, Rebecca, has Nikoleta’s vital signs as follows: length 28 inches, weight 19lb 2oz, temperature 98.6. That puts Nikoleta in the 10th percentile for both length and weight. Dr. Stephens also makes a note of the fact that her head circumference seems relatively large.

Dr. Stephens advises the parents to switch Nikoleta back to her original formula and orders a CBC (Complete Blood Count) panel. Then, almost as an afterthought, he decides to order a radiograph of the skull. “Something just doesn’t look right about her head,” he says to himself.

Questions

1. What does it mean that Nikoleta is in the 10th percentile for both length and weight? Is that a desirable statistic if she was in the 50th percentile at birth?
2. What are the symptoms of anemia?
3. Why did the parents change Nikoleta’s formula to a high iron baby formula?
4. What are some possible reasons why Nikoleta’s abdomen is distended?
Part II – The Test Results

Dr. Stephens receives the lab reports and decides to refer Nikoleta to a hematologist. The results are as follows:

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| Hb (hemoglobin)      | 5g/dL          | Male: 13.5–16.5 g/dL
                      |                | Female: 12.0–15.0 g/dL              |
| RBC (red blood cell  | 4.6 ×10⁶ cells/ml| Male: 4.5–5.5 × 10⁶ cells/ml        |
                      |                | Female: 4.0–4.9 × 10⁶ cells/ml      |
| MCV (mean corpuscular| 65             | 80–100                               |
| volume)              |                |                                     |
| WBC (white blood cell| 15,000 cells/ml| 4500–10,000 cells/ml                |
| count)               |                |                                     |
| Platelet count       | 250,000        | 100,000–450,000                      |

Mr. and Mrs. Stamos bring little Nikoleta into the hematologist’s office and Nikoleta has her blood drawn. After a few minutes, the hematologist returns to speak with the parents. Even with just a few moments looking at the sample, he knows that there is something wrong. The hematologist reports that he observed severe hypochromia and microcytosis (lightly colored and small cells), fragmented and nucleated RBCs.

The blood sample taken in the office appears as follows:

![Figure 1A. Nikoleta’s red blood cells](image1)

![Figure 1B. Normal red blood cells](image2)

The hematologist meets with the Stamos family in the exam room. “Mr. and Mrs. Stamos, there are some things that do not look normal in Nikoleta’s blood. I am not sure of the cause, but I do know that Nikoleta’s red blood cells aren’t shaped correctly and they are not the right color. The red blood cells should be very red under the microscope and her red blood cells are light pink.”

Mrs. Stamos asks, “Does it matter if her red blood cells aren’t red?”

The hematologist replies, “Yes, it does matter. Healthy red blood cells are very red and carry oxygen. Nikoleta’s red blood cells aren’t able to carry much oxygen to her tissues. I have an additional concern as well. Sometimes disorders like anemia can have a genetic basis. I would like to have both of you to give a sample of blood for a complete blood count.”

The findings from both parents are mild hypochromia and macrocytic (lightly colored and large cells) anemia. The hematologist gives a diagnosis of erythroblastic anemia for both Mr. and Mrs. Stamos.

Questions

5. Are the lab results of the CBC normal? Which values are normal and which are not?
6. Why are there different normal values for hemoglobin levels and RBC count in males and females?
7. Do red blood cells normally have nuclei?
8. Why was an analysis of Mr. and Mrs. Stamos’ blood ordered?
9. Would a picture of Mr. Stamos’ red blood cells look like Nikoleta’s red blood cells?
10. What is erythroblastic anemia?

Dr. Stephens receives a full report from the hematologist and digital images of Nikoleta’s skull.

Figure 2A. Nikoleta’s skull radiograph.  
Figure 2B. Normal skull radiograph.

**Question**

11. Does the radiograph of Nikoleta’s skull appear normal? How are the two radiographs different?
**Part III – The Family Returns**

Dr. Stephens calls Mr. and Mrs. Stamos and asks that they come in for a follow-up visit. This time the parents meet with Dr. Stephens in his office, not in the exam room. After they are seated, Dr. Stephens informs them that Nikoleta’s condition is very serious.

“I am sorry to give you bad news. Nikoleta does have anemia but, unfortunately, giving her a high iron formula was exactly the opposite of what should be done. Nikoleta’s disorder has a genetic basis.”

“But neither one of us has any of the problems Nikoleta has. We aren’t tired all the time. We work out every day,” replies Mr. Stamos.

“That’s a very good thing, and it has probably helped to keep you and your wife healthy. You both have a much milder form of anemia. Unfortunately, Nikoleta’s condition is more severe.”

**Questions**

12. What is the most likely diagnosis for Nikoleta?

13. What are the general features of this disease?
Part IV – The Doctor Continues

Dr. Stephens continues, “Nikoleta has what is known as beta-thalassemia, which is also called Cooley’s anemia. Do you remember when I spoke with you about hemoglobin and how it functions to carry oxygen? Well, there are two types of hemoglobin proteins involved in the process of carrying oxygen, alpha and beta. You need both of them in order to have properly working hemoglobin. Nikoleta’s beta proteins don't function correctly. I have spoken to Dr. Jeff Williams, a hematologist who specializes in childhood disorders of the blood. Nikoleta’s condition is very grave and it has a high mortality rate. Her life span may be significantly shortened. Dr. Williams is the best specialist in this area and I believe he will give her the best care possible. He will keep me informed of Nikoleta’s progress. Meanwhile, Nikoleta will still need to see me for her regular checkups. Also, I don’t know what you are considering for the future of your family, but because of these findings, I suggest that you see a genetic counselor before deciding to have another baby. A genetic counselor will give you all the information about how beta-thalassemia is transmitted from parent to child so that you can make an informed decision about having more children naturally.”

Questions

14. What is the structure of hemoglobin and how is oxygen bound to it?
15. What are some possible treatments that Dr. Williams will suggest?
16. If you were the genetic counselor, what would you suggest to Mr. and Mrs. Stamos concerning having more children? Why?

References

Infant formulas.

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3D models of hemoglobin showing binding of heme and iron.
http://www.umass.edu/molvis/tutorials/hemoglobin/heme.htm


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Fig. 1B—Digitally altered version of a public domain image from CDC, ID#12104, http://phil.cdc.gov/phil/details.asp.

Fig. 2A—Radiograph from the “Film Teaching Collection” assembled by David J. Sartoris, used with permission of collection custodian, Tudor Hughes, http://bonepit.com/Cases/David%20Sartoris/David%20Sartoris%20Thalassemia.htm.

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