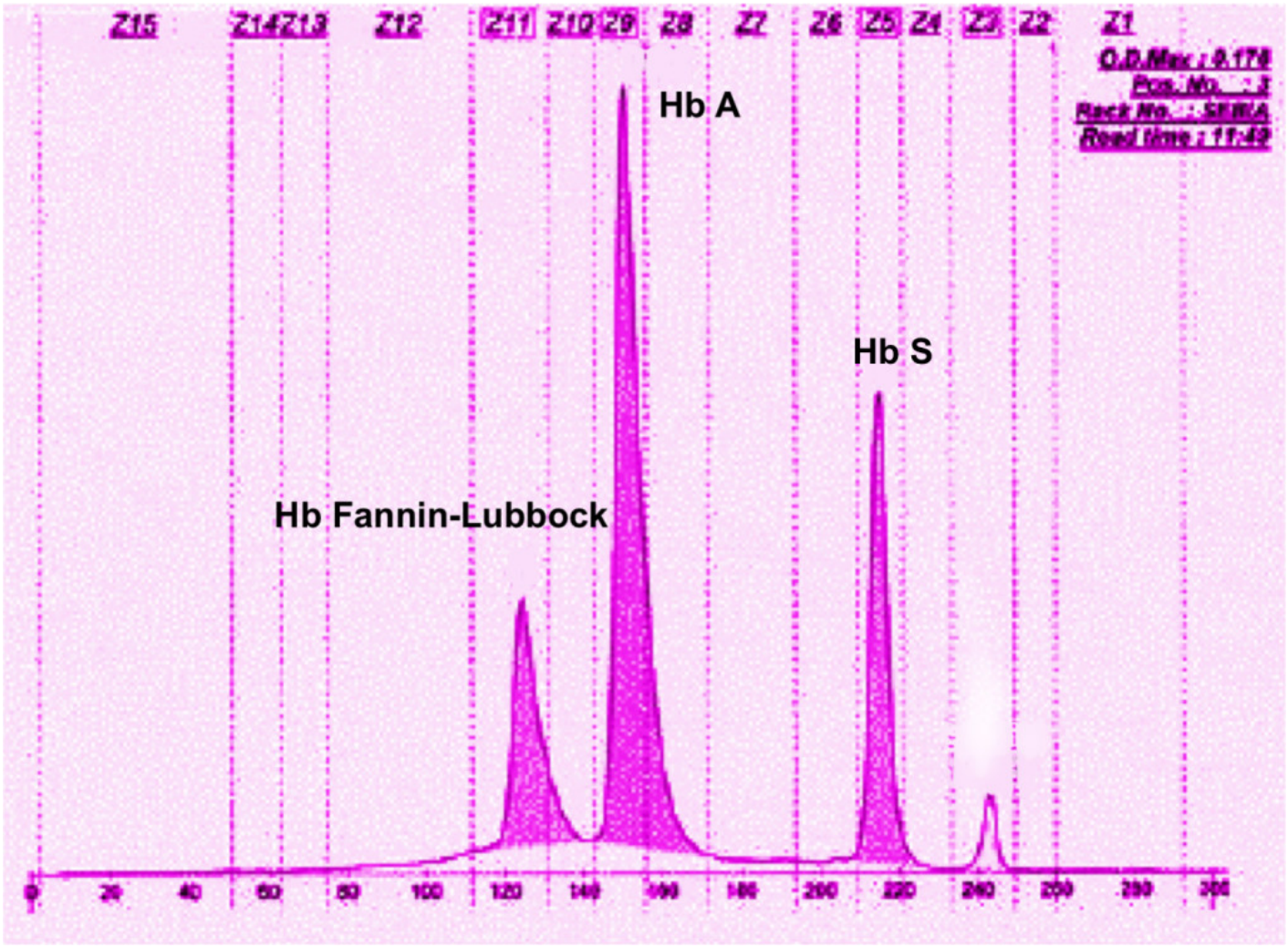
Hemoglobin diseases and their identification

Red blood cells use hemoglobin to carry oxygen from the lungs to the body and to carry carbon dioxide from the body back to the lungs in order to keep all cells alive. Hemoglobin is a big protein molecule made up of four connected glob-shaped molecules called globulin chains; two are alpha chains and two are beta chains. More than one thousand different variants of hemoglobin have been discovered, with a majority of these differences having no effect on the hemoglobin's function. People with these differences in their blood cells live normally. However, some of these hemoglobin differences cause disorders, including sickle cell disease where the blood cells change from saucer shape to sickle shape. Hemolytic anemia will occur as a result of the burst of the sickle shape red blood cells when passing through blood vessels due to the rigid sickle cell structure.



Most hemoglobin abnormalities are from one or a few amino acid changes in their protein contents, resulting from one or a few DNA base pair changes (also called mutation) in the genes. The mutation can be on either alpha and/ or beta chains. In general, diseases can only occur when both

parent hemoglobin-producing genes carry mutation(s). People who carry mutation from one parent, called trait or heterozygous mutation, can pass the mutation to their offspring without diseases. People who carry two different mutations from each parent may still not have hemoglobin diseases depending on the mutation combination. Hemoglobin S (Hb S), the hemoglobin leading to sickling, is due to mutation on the gene producing beta globin chain. People who inherit Hb S from both parents have sickle cell disease; whereas people who inherit only one copy of Hb S gene have sickle trait without disease. Hemoglobin Fannin-Lubbock reported here is also a beta-chain mutation. Hb Fannin-Lubbock has been described in several Hispanic families. Its trait, with one mutation gene, causes mild hemoglobin instability and is considered clinically insignificant. The combination of having one Hb S gene from one parent and one Hb Fannin-Lubbock gene from the other parent has been noted not to lead to disease in infants, representing one example of a person who carries two different mutations who does not have a disorder. In this article, we report the first case identified in adulthood that carries such two mutations and we further confirm that this variant is harmless as it is in children.

There are several techniques currently being used in medical laboratory to identify clinically significant hemoglobin variants. Capillary electrophoresis has recently been applied for hemoglobin detection. It utilizes the principle that hemoglobin variants have different electric charges from normal hemoglobin A (Hb A), and therefore, they can be physically separated in electrical field and shown as peaks at the different positions on a graph illustrated in the Figure. The biggest advantage of capillary electrophoresis is automation, and it provides accurate identification of numerous hemoglobin variants with easy-to-read patterns. Many of the clinical laboratories national wide currently utilize this technology. However, using this technology alone sometimes may misinterpret the data in complex cases like the case reported in the article. Adding appropriate controls in the test tube and combining with other laboratory assays will minimize error and help doctors make correct diagnoses.

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