Abnormal Results from Prenatal Blood Test Could Point to Cancer in the Mother

Noninvasive prenatal testing (NIPT) may find “truly hidden” cancers in pregnant women, finds results of a study.

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By Linda Wang

Women who are pregnant routinely undergo prenatal blood testing to screen their fetuses for chromosomal disorders such as Down syndrome. However, in rare cases, this noninvasive prenatal testing (NIPT) will result in an abnormal or inconclusive finding that isn’t related to the fetus but rather, to the mother’s DNA.

The results of a study of more than 100 women with unusual NIPT findings but a normally developing fetus now show that such findings can have serious implications for the mother. Nearly half of the women in the study turned out to have cancer, the researchers reported December 5 in the New England Journal of Medicine.

Most of these cancers were only detected through whole-body magnetic resonance imaging (MRI), which is not yet routinely used by doctors to follow up on abnormal NIPT results. In contrast, standard diagnostic tests, such as physical exams and blood work, missed many of the cancers.

“These cancers tend to be truly hidden,” said co-lead investigator Amy Turriff, MS, of the National Human Genome Research Institute. “Our study found that whole-body imaging is critical to sufficiently evaluate women who receive these [abnormal] results for cancer.”

“I hope [these findings] will increase awareness of these types of results and what should be done to triage these patients to the appropriate levels of care,” said Neeta Vora, MD, of the University of North Carolina School of Medicine, who studies prenatal genetic testing and maternal cancers but was not involved in the study.

Growing confusion over abnormal NIPT results

Around 2 million women in the United States undergo NIPT every year. This screening test, which

became commercially available in 2011 and has been recommended for use by all pregnant women since 2020, analyzes fragments of DNA from the placenta (which is used as a proxy for the fetus) that have been shed into the mother's bloodstream.

But because the mother's blood also contains fragments of DNA shed from her own cells, the test may also pick up abnormal changes in maternal DNA. Not long after NIPT became commercially available, rare reports began to emerge of unusual findings that were caused by DNA fragments from an undiagnosed cancer in the mother.

"Labs in the United States vary in how they report NIPT results, contributing to a lack of clarity in how doctors interpret and follow up on results that may indicate an issue with the mother rather than the fetus," said Padma Sheila Rajagopal, MD, MPH, of NCI's Center for Cancer Research, one of the study's investigators.

"Some [lab reports] will say 'possible cancer.' Some will say 'abnormal result.' Some will say 'non-reportable result,'" she added. "What ends up happening is that providers experience confusion over the reporting."

The researchers launched the IDENTIFY study in 2019 to learn more about the relationship between NIPT results and incidental cancer diagnoses in pregnant women and to determine the best approach for evaluating women who receive NIPT results that might suggest cancer.

Cancers diagnosed at a treatable stage

The study included 107 women who were pregnant or had recently given birth and who had received abnormal or inconclusive NIPT results, with fetal testing failing to provide an explanation for these results. Participants underwent uniform cancer screening that included whole-body imaging, a physical exam, and a variety of blood tests.

Nearly half (52) of the women were found to have cancer, with the most common types being lymphoma (31 participants), colorectal cancer (9 participants), and breast cancer (4 participants). Other cancer types included lung, pancreatic, and kidney cancers.

Of the 52 women diagnosed with cancer, 29 were asymptomatic, 13 had symptoms they thought were related to their pregnancy or to another cause, and 10 had not recognized their symptoms or had tests that reassured them they did not have cancer. Most of the women diagnosed with lymphoma had early-stage disease. Those with solid cancers generally had more advanced disease, but most were still eligible for potentially curative treatment.

Whole-body MRI was used for follow-up testing of 101 of the participants. It detected possible cancer in 48 women, all of whom were confirmed to have cancer. Six women received a false-positive result from the MRI and were later found to have benign lesions.

Only 9 of the 52 women diagnosed with cancer had abnormal results from their physical

examination. Routine blood tests did not suggest cancer in any of the participants. Tests for tumor markers were abnormal for 34 of the 52 women diagnosed with cancer, but these tests also flagged 14 women who did not have cancer.

The researchers identified a type of DNA pattern—a combination of gains and losses in 3 or more chromosomes—that was present in the blood of most of the women diagnosed with cancer. Among 49 participants who had this DNA pattern, 47 had cancer. The 2 participants with this DNA pattern who were not found to have cancer may have an undetected cancer or one that will develop later, the researchers hypothesized.

Among the 55 participants who were not diagnosed with cancer, 15 turned out, on additional testing, not to have abnormal DNA in their blood and 30 had noncancer conditions that explained the presence of the abnormal DNA.

The remaining 10 women whose abnormal results from sequencing were unexplained will be followed by the researchers for an additional 5 years.

“My hope is that we can more clearly identify [pregnant women] who are at the highest risk of cancer so that they can get prompt cancer screening that includes whole-body imaging,” Ms. Turriff said.

Identifying DNA patterns associated with cancer

Dr. Rajagopal said that it is reassuring to see that many of the cancers were detected while they were still treatable.

“That’s critical,” she said. But she noted that time is of the essence: “These patients need to be referred to an oncologist even during pregnancy.”

Studies have shown that many cancer treatments are safe for pregnant women and their fetuses.

In an accompanying editorial, Dr. Vora noted that, at present, whole-body MRIs are not typically ordered by obstetricians or covered by insurance, especially in people who don’t have symptoms of cancer.

In the meantime, she encourages doctors to work in multidisciplinary teams, including oncologists, radiologists, maternal fetal specialists, and reproductive geneticists, to develop workflows for evaluating pregnant women who receive NIPT results that might indicate cancer.

The IDENTIFY study remains open and continues to enroll participants. The researchers are also working to identify and validate patterns of DNA changes that could help determine the type of cancer in individuals with abnormal NIPT results.

Dr. Vora cautioned that while NIPT may incidentally detect cancers, it should not be used to screen

for possible cancer in nonpregnant women because of the risk for unintended harms, such as overdiagnosis and overtreatment.

“There would be a lot of downstream consequences to the health care system if we start screening asymptomatic, healthy people with a low probability for cancer,” Dr. Vora said.

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