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Clinicians report success with first test of drug in a patient with life-threatening blood clotting disorder

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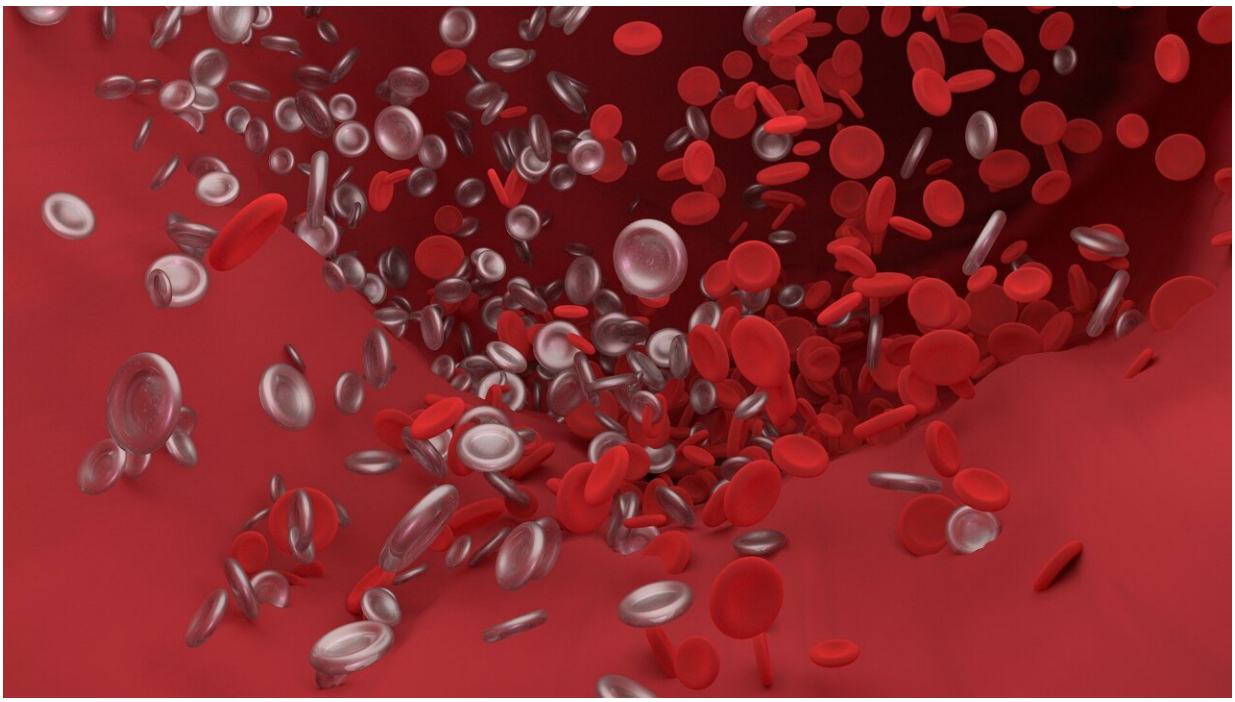

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A team led by investigators from Massachusetts General Hospital used a new drug to save the life of a patient with immune thrombotic thrombocytopenic purpura (iTTP), a rare disorder characterized by uncontrolled clotting throughout the small blood vessels.

The group describes the first clinical use of the drug for iTTP in the *New England Journal of Medicine*.

"The drug is a genetically engineered version of the missing enzyme in iTTP, and we showed that it was able to reverse the disease process in a patient with an extremely severe form of this condition," said lead author Pavan K. Bendapudi, MD, an investigator in the Division of Hematology and Blood Transfusion Service at Massachusetts General Hospital and an assistant professor of Medicine at Harvard Medical School.

iTTP results from an autoimmune attack against an enzyme called ADAMTS13 that is responsible for cleaving a large protein involved in blood clotting. The current mainstay of therapy for this life-threatening blood disorder is plasma exchange, which removes the harmful autoantibodies and provides extra ADAMTS13.

Plasma exchange induces a clinical response in most patients but can restore at best only about half of normal ADAMTS13 activity. By contrast, a recombinant form of human ADAMTS13 (rADAMTS13) offers the possibility of greatly increased ADAMTS13 delivery.

rADAMTS13 was recently approved for patients with congenital thrombotic thrombocytopenic purpura, which occurs in patients born with complete loss of the ADAMTS13 gene.

It's questionable whether rADAMTS13 could be effective in iTTP given the presence of inhibitory anti-ADAMTS13 autoantibodies, but Bendapudi and his colleagues received permission from the US Food and Drug Administration to utilize rADAMTS13 donated from the manufacturer under a compassionate use protocol in a dying patient with treatment-resistant iTTP.

"We found that rADAMTS13 rapidly reversed this patient's disease

process despite the current dogma that inhibitory autoantibodies against ADAMTS13 would render the drug useless in this condition," said Bendapudi.

"We were the first physicians to use rADAMTS13 to treat iTTP in the United States, and in this case it helped to save the life of a young mother."

Bendapudi noted that the infused rADAMTS13 overwhelmed the inhibitory autoantibodies in the patient and reversed the thrombotic effects of iTTP. This impact was observed almost immediately upon administration of rADAMTS13, after daily plasma exchange had failed to induce remission.

"I think rADAMTS13 has the potential to replace the current standard of care in acute iTTP. We will need larger, well-designed trials to evaluate this possibility," said Bendapudi.

A Phase IIb randomized clinical trial of rADAMTS13 in iTTP has been initiated.

More information: Pavan K. Bendapudi et al, Recombinant ADAMTS13 for Immune Thrombotic Thrombocytopenic Purpura, *New England Journal of Medicine* (2024). DOI: 10.1056/NEJMoa2402567

Provided by Massachusetts General Hospital