How personalized medicine helps to control the effects of acromegaly earlier

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New research has taken a significant step in terms of research and care for acromegaly, a rare disease caused by an excess of growth hormone secretion, which occurs in over 99% of cases due to a generally benign

pituitary tumor. The research team includes The Endocrine, Thyroid and Obesity research group of the Germans Trias i Pujol Research Institute (IGTP), a center associated with one of the major university hospitals in the Barcelona area, the Germans Trias i Pujol Hospital.

This group, an international reference in this field and led by Dr. Manel Puig, has managed to develop a protocol with biomarkers to help patients with acromegaly control the effects caused by the disease earlier. One of its main problems is that it is diagnosed with a delay of about 10 years. This happens when a series of striking skeletal and facial changes become evident, such as the growth of hands and feet, or other health problems such as heart disease or the development of joint lesions or various types of cancer.

The group's finding is the result of a nationwide clinical study that, for the first time in the world, has demonstrated that these biomarkers are useful for predicting the effectiveness of the drugs indicated for the control of this disease. For example, the classic treatments—such as the so-called first-generation somatostatin receptor ligands (fgSRL)—until now only have a 50% effectiveness.

In this regard, another relevant outcome of this study is that the use of these biomarkers helps to indicate personalized therapies that increase the effectiveness to 80% and more quickly than with the classic treatment.

Manel Puig and his team have been working on acromegaly research for 12 years. During this time, they have managed to position themselves internationally in various aspects of this rare disease and have created an international group with a Spanish team that has shown growing scientific activity and geometric progression in the last five years.

"Until now, no prospective study had been conducted testing protocols

with response markers that, depending on what they indicate, allow for one treatment or another. This is, in fact, the demonstration that precision medicine for treating acromegaly is possible, something that has been debated internationally for years," emphasizes Puig.

Treating a rare disease as early as possible

As a disease considered rare, acromegaly is very uncommon: it affects about 70 people per million inhabitants in the world, and each year 6 to 9 new cases are diagnosed per million inhabitants. In fact, at the Germans Trias Hospital, no more than 6 new cases are usually seen per year.

It can affect anyone and is usually diagnosed from the age of 40, but there may also be cases in childhood that, if not diagnosed in time, cause gigantism. In addition to these facial and skeletal deformities, which become very noticeable, the excess growth hormone produces severe alterations in other parts of the body: increased heart size, which can lead to heart failure, a tendency to diabetes, sleep apnea, and an increase in the development of various tumors, especially colon cancer.

The treatment aims to normalize hormone levels, eliminate the tumor, and treat associated complications, something that can be achieved first with surgery or with drugs. In this latter sense, regarding medical treatment, an approach of trial and error has been followed until now, so that for a time that can last years, only certain drugs are indicated to try to control the pathology.

"Once the disease is diagnosed, it is crucial not to waste time in treating it. Until now, patients could spend months trying drugs that, at best, are only useful for half of the patients. Now, with these markers, we will rule out treatments that will not work and focus on other therapeutic modalities that will, with superior efficacy. If we get it right, in six months the patient has the disease under control, but if not, this period is

much longer," explains Puig, the principal investigator of the study.

The speed of controlling the disease also gains relevance in terms of its cure. In this sense, although acromegaly is only cured with surgery, this is often carried out with more guarantees when done in a deferred manner; that is, first controlling the patient hormonally with the pertinent drug treatment before intervening.

The study, called ACROFAST and recently published in *The Journal of Clinical Endocrinology & Metabolism*, was conducted between 2018 and 2023 in 21 tertiary reference centers in Spain. In 11 of these, the classic treatment was administered to around forty patients, while in the remaining centers, 40 more patients received personalized treatment thanks to the use of these predictive biomarkers.

In conclusion, the latter controlled the effects of the disease better and earlier, something relevant if, as mentioned, many months can pass until a patient with acromegaly finds the appropriate therapy.

More information: Montserrat Marques-Pamies et al, Personalized medicine in acromegaly: The ACROFAST study, *The Journal of Clinical Endocrinology & Metabolism* (2024). DOI: 10.1210/clinem/dgae444

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