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# No Respond to Growth Hormone Treatment: What is the Next Step?

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## Abstract

When we have a patient with clinical history compatible with growth hormone deficiency (GHD), associated with delay bone age, no respond to two hormone stimulating tests, with or without changes in brain MRI, we conclude that the patient showed all criteria of GHD and will start GH treatment. The first year treatment is the time that the growth velocity (GV) increase more, around 9 - 11 cm in most cases. But when the GV is less than 2 - 3 cm, we need to find others causes that are responsible for this non-response. If the patient showed beside short stature, anorexia, mild anemia, thinness, even with no others signs like abdominal pain or chronic diarrhea, we need to exclude inflammatory bowel disease (IBD), like Crohn disease (CD). Treatment with prednisolone, mesalazine, azathioprine, will restart growth in these patients, with no need to use GH at the same time because there is a resistance to GH treatment in CD, secondary to LPS, TNF, IL-1 and IL-6 that reduces growth hormone receptors and IgF1 messenger RNA levels.

***Keywords:*** *Growth Hormone Resistance; Crohn Disease*

When we have a patient with short stature, growth velocity less than 4 cm/year, associated with delay bone age of 3 or more years, we suspect of growth hormone deficiency (GHD).

If this patient is a girl, we do a karyotype to exclude Turner syndrome, even when the phenotype is normal.

We perform growth hormone (GH) stimulating test to see the respond of GH activity. Is consensus that we need to have two tests with low respond to consider GHD. We use mainly clonidine and L- dopa to stimulate GH respond. We also check for IgF1 levels that can be low or normal in GHD.

Finally, we study if the patient has hypoplasia of hypophysis, by performing the brain MRI.

With clinical history compatible with GHD, associated with delay bone age, no respond to hormone stimulating tests and with or without changes in brain MRI, we conclude that the patient showed all criteria of GHD and we will start GH treatment.

After we start the treatment with GH, we follow up the patient clinically to see if the stature showed catch up growth, if the growth velocity increase, the bone age start to recover to near the chronologic age. The first year treatment is the time that the growth velocity increase more, around 9-11 cm in most cases.

This is the normal evolution of the patient with GHD after start treatment with GH.

But sometimes this respond is not like this, with only growth of 2 - 3 cm in the first year of treatment.

First of all, before we start to exclude any other cause behind this non-respond, we need to check if the device is functional, if the GH is well injected by the patient or family, if the treatment is really done at home and if the patient has hypothyroidism as one of the side effects of the treatment.

After confirm that everything is correct, we need to exclude other diseases that can interfere with the GH respond.

If the patient showed beside short stature, anorexia, mild anemia, thinness, even with no others signs like abdominal pain or chronic diarrhea, we need to exclude inflammatory bowel disease (IBD), like Crohn disease [1-4].

If we treat these patients with prednisolone, mesalazine, azathioprine, after confirmation of Crohn disease, we can find catch up growth, with no need to use GH at the same time. In this case, there is a resistance to GH treatment (Figure 1).

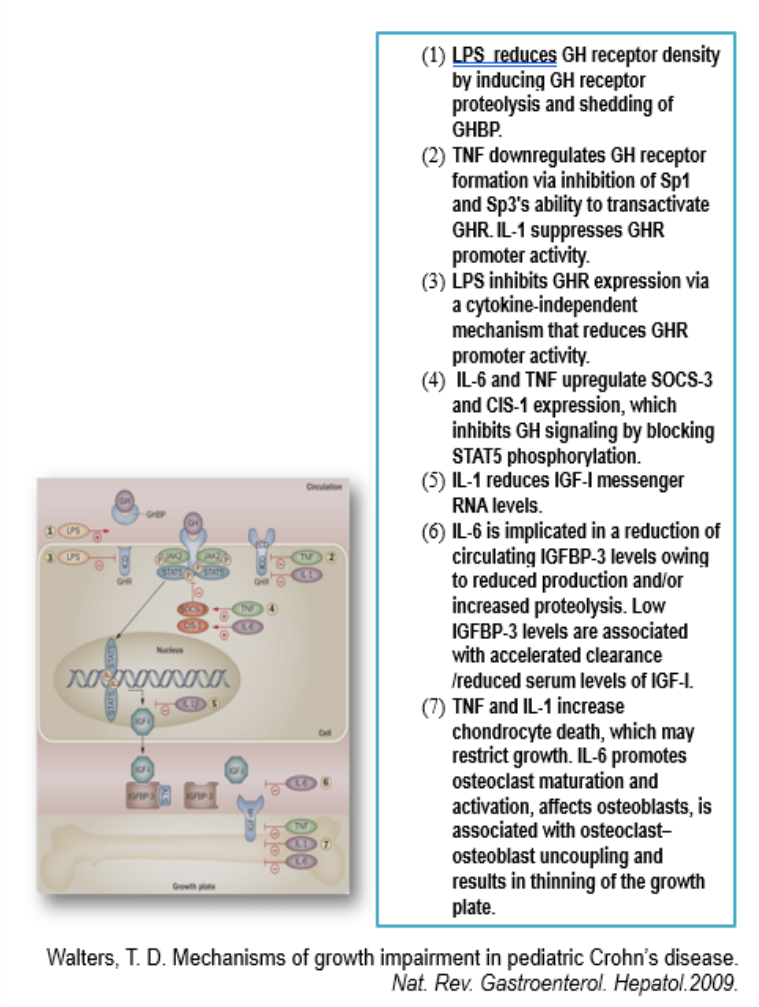


***Figure 1:*** *Crohn disease-mechanism of resistance to GH.*

## Conclusion

In conclusion, in patients with all criteria of GHD, but without a good respond on his growth velocity and catch up growth after we start the treatment with GH, we need to consider IBD as a primary cause of his short stature. Growth retardation or delay puberty can be the first sign of the disease.

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