Genetics inMedicine | CORRESPONDENCE

Response to Hannah-Shmouni and Stratakis

We thank Hannah-Shmouni and Stratakis[1] for their comment on our clinical practice resource on the care of adults with neurofibromatosis type 1 (NF1)[2]. We agree that growth hormone excess resulting in subclinical gigantism or acromegaly is generally underrecognized by clinicians. We also agree that many of the published accounts of growth hormone excess and clinical consequences in NF1 have been reported in children. As noted in the Methods of our clinical practice resource, we focused on common and emerging NF1-related clinical problems and emphasized studies that investigated populations, multi-institution clinic cohorts, and large case series. We could not address all potential comorbidities, such as growth hormone excess in NF1 adults, so we focused on those with a large published reference base and that in our clinical experience are more common.

As the authors note, growth hormone excess in NF1 is particularly intriguing from an endocrine perspective because it can arise from a pituitary or an optic tract tumor. In the latter situation, growth hormone excess may stem from a hypothalamic regulatory defect.[3] In children with NF1, growth hormone excess has been reported to be a transient phenomenon and thus may not need treatment.[4,5] Although gigantism and acromegaly in NF1 are rare, childhood overgrowth secondary to *NF1* microdeletion has been recognized for many years.[6,7] Its pathogenesis may involve other genes (such as *RNF135* or *SUZ12*) at the *NF1* locus and not *NF1* itself.[8,9] As noted in our clinical practice resource,[2] people with an *NF1* deletion are also at increased risk for malignant peripheral nerve sheath tumor and intellectual disability.

The role of growth hormone itself in the etiology of NF1 microdeletion–associated overgrowth, if any, is unknown. Similarly, the reporting of *NF1* genotype (or deletion) in published reports of NF1-associated growth hormone excess, acromegaly, or gigantism is uncommon.[10] In this respect, the report of germline *NF1* genotypes (one missense, one truncating) by Hannah-Shmouni et al. of two patients with NF1 and growth hormone excess is useful, even in abstract form.[11]

In summary, Hannah-Shmouni and Stratakis are correct that growth hormone excess in NF1 is rare, easily overlooked, and merits additional phenotype and genotype investigations.

DISCLOSURE

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