Title
SAT-LB18 A Randomized Controlled Trial of Vosoritide in Children With Achondroplasia

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28.7 pmol/l ref. 1.50-9.30 pmol/l; phosphorus 0.89 mmol/l ref. 0.80-1.45 mmol/l). Sestamibi & US of the neck revealed no clear parathyroid adenoma. Two incidental thyroid nodules were benign on FNA cytology.
The patient underwent neck exploration & a single enlarged parathyroid gland was removed. Pathology showed an enlarged hypercellular gland. Her calcium & PTH normalized after surgery but recurrence was documented a year later. Her family history was significant for PHPT in two brothers & a history of kidney stones in a third brother. Multi-gene panel testing (CASR, CDC73, CDKN1B, MEN1, RET, Invitae Corp.) revealed a pathogenic variant (PV) in *CDKN1B* (c.215delG). The patient underwent a 2 ½ parathyroidectomy with subsequent normalization of her calcium & PTH. Further work-up showed a 4.5mm non-secreting pituitary adenoma. Plasma metanephrines & NE were intermittently elevated. Serum gastrin was also mildly elevated 83 pmol/l (<53 pmol/l). A Ga68-DOTATATE PET scan was negative. Her 23-year-old daughter tested positive for the familial PV. She is asymptomatic & has normal calcium & PTH; pituitary function is normal except for an elevated IGF-1 at 63.9 nmol/l (ref 13.3- 42.6 nmol/l) with borderline growth hormone during OGTT (0.40 ug/l). Her pituitary MRI was normal. One brother with history of prostate cancer, PHPT & partial parathyroidectomy has tested positive for the familial *CDKN1B* variant. A second brother was also found to carry the familial variant & was clinically asymptomatic.Endocrinological workup has revealed he has PHPT, elevated chromogranin A at 196.2 ng/ml (ref <=82), calcitonin at 25 ng/l (normal <=9 ng/l), IFG1 (35.3 nmol/L ref. 13-21) but normal plasma metanephrines. An MRI of the sella shows an 8mm hypoenhancing lesion. On CT, a retroperitoneal hyperenhancing 4cm mass adjacent to the left ilio-psoas was seen, in keeping with a paraganglioma; additionally, he has a congenital left atrophic kidney & ureter. Two additional brothers; one with history of non-Hodgkin's lymphoma, PHPT & partial parathyroidectomy & a second brother, also with prostate cancer & recurrent renal stones, have yet to be tested.
Conclusions: A new MEN4 family is described here which expands the spectrum of clinical manifestations of this syndrome. Of great interest in our cases is the presence of paraganglioma, urological malformation, & pre-clinical GH/IGF1 elevation.

Pediatric Endocrinology

PEDIATRIC GROWTH AND ADRENAL DISORDERS

A Randomized Controlled Trial of Vosoritide in Children With Achondroplasia

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Background: Achondroplasia is a disorder caused by specific mutations in the gene encoding the fibroblast growth factor receptor 3 (*FGFR3*) protein. Open-label, phase 2 trials in children with achondroplasia showed that administration of vosoritide, an analogue of C-natriuretic peptide, resulted in sustained increases in annualized growth velocity. **Methods:** This international, randomized, double-blind, phase 3 trial compared once-daily subcutaneous administration of vosoritide, at a dose of 15 µg per kg of body weight, with placebo in children with achondroplasia aged 5 to <18 years. Eligible patients had participated, for at least 6 months, in an observational growth study in order to calculate their baseline annualized growth velocity. The primary efficacy endpoint was the change from baseline in annualized growth velocity at week 52 of treatment. The primary analysis of the change from baseline in annualized growth velocity was performed using an ANCOVA model. **Results:** A total of 121 patients were randomized, with 60 assigned to receive vosoritide and 61 to receive placebo. A total of 119 patients completed the 52-week trial. The adjusted mean difference in annualized growth velocity between patients administered vosoritide and those administered placebo was 1.57 cm per year in favor of vosoritide (95% CI: [1.22, 1.93], two-sided p-value <0.001). A total of 119 patients experienced at least one adverse event (vosoritide group, 59 [98.3%], placebo group, 60 [98.4%]). **Conclusions:** Daily, subcutaneous administration of vosoritide to children with achondroplasia resulted in a significant increase in mean annualized growth velocity and similar incidence of adverse events compared to placebo.