

Endocrine Abstracts

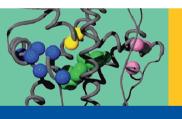
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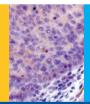


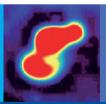
ESE Young Endocrinologists and Scientists (EYES) 2022

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Objectives

Evaluate the contribution of NDN and MAGEL 2 in HPA physiology and response to stress

Methods

We investigated NDN expression in the adrenal and under several genetic and pharmacologic stimulations. We then submitted Ndn-/- Magel2-/- mice to mild stress and explored the HPA physiology through measurement of peptides and steroid hormones.

Results

We found expression of NDN restricted to the zG in the adrenal and negatively regulated by ACTH via PKA signalling. We show that even though NDN and MAGEL2 loss does not lead to morphological changes, their deletion induces blunted stress response and leads to accumulation of ACTH precursor Pomc in the

We can conclude that NDN and MAGEL2 are important actors of proper response to stress. Conditional models targeting the pituitary will lead to better understanding of the mechanisms at stake.

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AP2

Autoimmune polyglandular syndrome type 1 in siblings: assembling the jigsaw puzzle

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Background

Autoimmune polyglandular syndrome type 1 (APS-1) is a rare autosomal recessive, monogenic disease, that could be presented as a group of various symptoms, but clinical diagnosis requires existence of minimum two of three leading disorders: chronic mucocutaneous candidiasis, hypoparathyroidism, and primary adrenocortical insufficiency.

We report the clinical cases of two siblings with APS-1, one 28-year-old male and one 25-year-old female. He is presenting at the age of 3.5 years with Addison's disease, as well as with hypoparathyroidism at the age of 4 years. Meanwhile, at the age of 4 years, onychomycosis, enamel dysplasia and diffuse alopecia were presented in the female, along with hypoparathyroidism. Furthermore, at the age of 11 years, the diagnosis of Addison's disease was made in the female, and at the age of 13.5 years Hashimoto's thyroiditis was diagnosed. The onset of menarche was at the 14 years, but she further developed hypogonadism as a manifestation of the autoimmune oophoritis. Hormonal replacement therapy was initiated for both siblings, including hydrocortisone and fludrocortisone, as well as levothyroxine and levonorgestrel-ethynyl estradiol to the female. Because of hypoparathyroidism, alfacalcidol with calcium supplement were established for both siblings. Since hypercalciuria was confirmed with recurrences of deep hypocalcemia episodes in the female, hydrochlorothiazide was also introduced into the therapy. Moreover, gastrointestinal endoscopy showed chronic atrophic pangastritis with active Helicobacter pylori (H. pylori) infection and chronic duodenitis, enteritis and colitis. H. pylori first-line eradication therapy was initiated. Values of fecal calprotectin, anti-transglutaminase antibodies IgA, fecal PMN-elastase and bile acids were unremarkable. Genetic testing detected a homozygous c.769C > T (R257X (p.Arg257X)) AIRE mutation in both siblings.

Although this is a rare disease, clinicians should be aware of it, especially in people under 30 years of age with more than one endocrine disorder, because timely diagnosis avoids its life-threatening conditions.

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AP3

Recurrent paraganglioma in patient with aneurysmal disease Ilic S^1 , Popovic B^2 , Ognjanovic S^2 , Gostiljac D^1 , Dimitrijevic Sreckovic V^1 , Marina Lj^5 , Knezevic D^3 , Sladojevic M^4 , Petkovic A^6 & Popovic S^1 ¹Clinic for endocrinology, diabetes and metabolic diseases, University Clinical Center of Serbia, Department for diabetes complications; ²Clinic for endocrinology, diabetes and metabolic diseases, University Clinical Center of Serbia, Department for neuroendocrine tumours; ³Clinic for Digestive Surgery, University Clinical Center of Serbia, Department for hepato-biliopancreatic surgery; 4Clinic for Vascular and Endovascular Surgery, University Clinical Center of Serbia, Department for vascular

surgery; 5Clinic for endocrinology, diabetes and metabolic diseases, University Clinical Center of Serbia, Center for infertility and gender endocrinology; ⁶Center for radiology and magnetic resonance, University Clinical Center of Serbia, X knife department

Background

Duration of postoperative follow-up in patients with pheochromocytoma/paraganglioma (PPGL) is still not clearly specified. It is estimated that 5-year risk of a new events (metastatic/recurrent disease) after surgery is 27% in young patients, 25% in those with paraganglioma and around 10% in older patients and those with pheochromocytoma. Arterial aneurysms (AA) accompanying PPGL are described as complication/comorbidity that affects prognosis in these patients. Case Presentation

A 72-year old male patient with five-year history of: hypertensive crises (max 220/130 mmHg), bradycardia to tachycardia (HR 45-120/min), orthostatic hypotension, night sweating and de novo diabetes mellitus, was presented at our Clinic. He had right-side adrenalectomy 18 years before (high risk procedure due to multiple AA), after the same clinical presentation and was diagnosed with composite tumour paraganglioma-ganglioneuroma (PASS 3). In present, catecholamine hypersecretion was confirmed in 24h urine samples - high noradrenaline (6600-12000 nmol/24h) and normetanephrine (11.55-24.40 umol/24h), together with high chromogranine A 974 ng/ml. CT found retroperitoneal interaortocaval tumour 47.9x35.6mm, MIBG scintigraphy was negative, FDG/PET CT showed retroperitoneal mass (SUVmax 35.6) and nodules in mediastinum and left lung (SUVmax 3.9 and 4.8 respectively). Retroperitoneal tumour extirpation was managed, with perioperative complication - left kidney failure, due to a thrombosis of aneurysmatic left renal artery. Pathohistological diagnosis was paraganglioma (PASS 2, Ki67 5.6%). Resolution of all features was observed after surgery, adrenal medulla metabolites were in reference range and lung nodules were CT described as fibrosis. Genetic analyses on MEN2, SDH and VHL are still ongoing.

Current guidelines suggest that patients with PPGL should be followed for at least 10 years after surgery and with extra-adrenal tumour or genetic PPGL should be followed lifelong. Abdominal AA (aorta, renal artery) carry on an additional effect on morbidity and mortality of patients and should be monitored closely and multidisciplinary.

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AP4

Malignant PPGLs - diagnosis and treatment challenges in a developing country-case series presentation Lider Burciulescu S. M. ^{1,2}, Gheorghiu M. L. ^{2,1}, Stancu C¹ & Badiu C. ^{1,2}

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Introduction

Malignant pheochromocytomas and paragangliomas (PPGLs) are rare, and knowledge of the natural history is limited.

Material Methods

Data of 7 (7.6%) (out of 109) patients with malignant PPGLs referred to a Tertiary Centre of Endocrinology from Bucharest, Romania, were retrospectively collected. Follow-up ranged from 2004 to 2022. Demographic data, genetic status, site and size of primary tumor, biochemical activity, metastasis time (synchronous/metachronous), therapeutic approach and outcome were analysed.

Six women and 1 man were included in our analysis. Follow-up duration was 14 \pm 7.2 years. Mean age at diagnosis was 50.2 \pm 14.3 y.o. One patient had RET pathogenic variant, one had Carney-Stratakis Syndrome. For the rest of the patients, we were unable to perform genetic test. Four patients had right PHEO, 2 had bilateral PHEO and 1 had retroperitoneal PGL as the primary tumor. Mean tumor dimensions were 4.3 \pm 2.1 cm. The secreting pattern was noradrenergic in 5 patients and adrenergic in 2 of them. Three patients had metachronous metastatic disease (at 10, 8 and 1 years from the first diagnosis). The rest of four had synchronous metastatic disease. All the patients underwent surgery of the primary tumour. Furthermore, one of them had only MIBG therapy, one had MIBG therapy plus PRRT, one had MIBG plus systemic chemotherapy, one patient had surgery plus chemotherapy and of the rest of three had only surgery. As outcome, two patients with surgery only and the patient with surgery plus chemotherapy were lost to follow-up (probably due to exitus), one patient with surgery only is disease free; the patient with MIBG has biochemical inactive disease, the patient with MIBG+PRRT has biochemical active disease, but without any clinical signs and the patient with MIBG and chemotherapy has active disease.