2010년도 대한내분비학회 3월 학술집담회

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- 증례발표 -

제목 : : von Hippel-Lindau disease presenting with pancreatic neuroendocrine tumor
소속 : 서울대학교병원 내분비내과
발표자 : 온정헌

22세 여자 환자가 내원 1개월 전부터 땀이 나고 체중이 감소하는 증상을 주소로 개인 병원에서 시행한 복부 전산화단층촬영에서 췌장과 부신에 종괴가 있어 내원하였다. 가족력에서 외조부가 40대에 췌장암으로 사망하였고, 이모와 어머니가 부신 종괴로 부신절제술 시행받은 병력이 있으며, 이모는 30대에 췌장암으로 사망하였고, 어머니는 췌장에 낭종이 있어 수술한 결과 neuroendocrine tumor로 진단받았다. 내원하여 시행한 복부전산화단층촬영에서 췌장 두부에서 11x6cm 크기의 peripheral hypervascularity with central calcification 을 보이는 종괴와, 양측 부신에 nodular lesion 이 관찰되었다. 호르몬 검사에서 intact PTH와 calcitonin 및 24시간 소변 catecholamine, metanephrine 정상이었으며, 갑상선 초음파도 정상 소견이었다. von-Hippel Lindau disease 의심하여 시행한 유전자검사에서 c.592delC (p.L198WfsX4, frameshift mutation으로 codon 201에서 stop codon을 유발함) 의 돌연변이가 관찰되었다. 안과 검진 및 뇌자기공명영상에서 이상소견은 관찰되지 않았다. 환자는 췌장 전절제술 및 위부분절제술 시행하였고, 병리소견에서 주위 연부조직과 혈관 및 림프관 침윤이 있는 well differentiated endocrine carcinoma(Ki-67 + in 5%, CD56+, Synaptophysin +, Chromogranin +)로 진단되었다. 이후 환자는 췌장 전절제술에 의한 당뇨병으로 인슐린 투약 중이며, 1년 6개월동안 종양의 재발 증거없고 부신 종괴의 크기 변화 및 24시간 소변 catecholamine, metanephrine 의 상승 소견 없이 추적관찰 중이다.

제목 : A case of Fugitive Acromegaly
소속 : 연세의대 내분비내과, 신경외과, 병리과
발표자 : 임정수, 구철룡, 신동엽, 이미경, 김세훈, 김선호, 이은직

Fugitive acromegaly has known to be mostly caused by pituitary acidophil stem cell adenoma, characterized by relatively short clinical history, large and locally invasive tumor, and relatively low hormonal activity. Here we report an unusual case of fugitive acromegaly initially presented as invasive prolactinoma. Abstract termed fugitive AA 48-year-old man with a huge pituitary mass extending to the suprasellar area was referred in December 2007. He had undergone transsphenoidal surgery in November 1999 due to a large invasive prolactinoma. The tumor has grown progressively despite therapy with dopamine agonists. Subtle features of acromegaly were noted and measured serum IGF-1 level was also high (733.0 ng/ml). Oral glucose tolerance test revealed that basal and nadir levels of GH were 1.56 ng/mL and 1.0 ng/mL, respectively. As a therapeutic trial, long-acting octreotide LAR (20 mg IM, monthly) was added. The tumor size was markedly reduced in 6 months on MRI examination. Immunohistochemical staining of the tumor tissue obtained at the surgery in 1999 showed positive staining for GH and PRL. Double immunofluorescence staining showed mixed positivity for GH and PRL in the majority of tumor cells. However, two hormones were co-localized in the minority of tumor cells, indicating that tumors were composed of three different cells (GH, PRL and GH/PRL). This patient was overlooked initially for the diagnosis of fugitive acromegaly due to normal serum GH level and no acromegalic features although histological evidence for GH production was present. IGF-1 measurement would be helpful for the diagnosis of fugitive acromegaly.

- 연구세미나 강의 -

제목 : The role of S6K1 signaling in diet-induced insulin resistance and pancreatic beta-cell size regulation

소속 : 성균관대학교 의과대학 분자세포생물학교실

발표자 : 엄성희

Mice deficient for S6 Kinase 1 (S6K1), an effector of the mammalian target of rapamycin (mTOR) are small at birth, display reduced pancreatic b-cell size and pronounced hypoinsulinimia. Here we show that *S6K1*$^{-/-}$ mice also exhibit severe intrauterine growth retardation (IUGR) and placental deficits, fetal pathologies normally associated with impaired b-cell development and diabetes in later life. Unexpectedly, amelioration of the placental abnormalities and resulting IUGR by tetraploid embryo complementation did not restore b-cell size and insulin levels. However, selective expression of S6K1 in b-cells of *S6K1*$^{-/-}$ mice restored cell size, insulin levels, and glucose tolerance, but had no effect on fat mass, lean mass, energy expenditure or birth weight. Critically, re-expression of S6K1 in b-cells restored 40S ribosomal protein S6 phosphorylation, which has been implicated in the control of b-cell size and insulin homeostasis. These findings indicate that during development reduced S6K1-dependent signaling in b-cells, rather than in the placenta, is the cause of impaired insulin secretion in the adult.