

Olfactory Neuroblastoma Presented as an Ectopic ACTH Syndrome: Usefulness of gallium-68 DOTATOC PET

¹연세대학교 세브란스병원 내과, ²연세대학교 세브란스병원 신경외과

*이승연¹, 구철룡¹, 김의현²

Olfactory neuroblastoma is a rare sinonasal tumor that invades paranasal sinuses, anterior skull base and adjacent brain tissue. Cushing's syndrome is occasionally resulted from other than pituitary gland or adrenal gland, so called ectopic ACTH syndrome. A few had described the olfactory neuroblastoma is an ectopic source of ACTH secretion: only less than ten cases were reported worldwide. A 46-year old man visited local clinic for general weakness and hyposomnia. There were also vague Cushingoid feature including skin pigmentation, weight gain started from one month before. Endocrinologic workup showed high serum cortisol(38.2 µg/dL), plasma ACTH(174.5 pg/mL) level. And low does dexamethasone suppression test(serum cortisol 39.9µg/dL, plasma ACTH 218.90pg/mL), high dose dexamethasone suppression test(serum cortisol 34.8µg/dL, plasma ACTH 159.1pg/mL) were not suppressed. These results suggested ACTH dependent Cushing's syndrome. Sellar MRI revealed no pituitary enlargement instead of heterogeneous large scale nasal cavity tumor. However, inferior petrosal sinus sampling (IPSS) was centralized which suggested the pituitary gland as an origin of ACTH hypersecretion. (Peak IPS/P was 2.9, Basal IPS/P was 2.4). Based on the discordant results between MRI and IPSS, Gallium-68 DOTATOC PET-CT was performed to find neuroendocrine tumors secreting ACTH. Gallium-68 DOTATOC PET scan showed significant activity in nasal cavity, which coincides correctly with brain MRI lesion. Taken together, imaging studies revealed that there was a kind of neuroendocrine tumor, olfactory neuroblastoma. Surgery was performed after finding lesions through the above examinations. Combined transcranial and endonasal endoscopic resection of tumor was successful. Serum cortisol and plasma ACTH level were normalized after surgery. The pathologist confirmed that it was consistent with olfactory neuroblastoma which expressed neuron specific enolase, synaptophysin, chromogranin A, CD-56, and ACTH. In this case, olfactory neuroblastoma may be the cause of ectopic Cushing, and if brain MRI and IPSS are discordant, gallium 68 DOTA PET-CT may be useful in establishing a diagnosis and treatment plan.

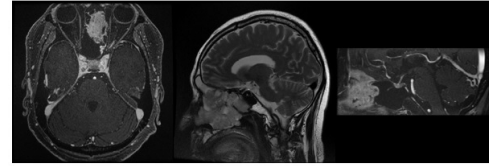


Image 1. Sella MRI

Tumor from sinonasal cavity origin, with intracranial extension, r/o olfactory neuroblastoma.

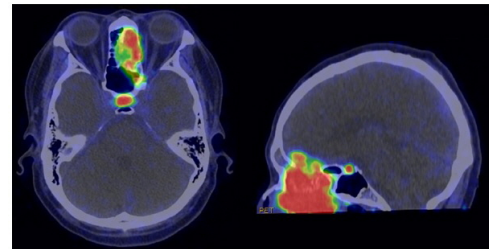


Image 2. PET-CT Ga-68 DOTATOC

Intense DOTATOC uptake in the left nasal cavity mass, suggesting neuroendocrine neoplasm such as olfactory neuroblastoma.

Insulin-Deficient Diabetes Associated with Pembrolizumab

울산의대 서울아산병원 내과

*김휘승, 이우제

Background: Pembrolizumab is a humanized IgG4 monoclonal antibody used in cancer immunotherapy. It targets the programmed cell death-1 (PD-1) receptor which is important in maintaining self-tolerance. Therefore, while pembrolizumab is able to fight cancer, at the same time it also can trigger autoimmune-like manifestations in different organ systems, generally referred to as immune-related adverse events (irAEs). Endocrine dysfunctions including insulin-deficient diabetes are rare irAEs that have been reported in clinical trials with pembrolizumab. There has been no report of pembrolizumab-induced diabetes in Asian populations. **Case Report:** A 80 year-old man with no history of diabetes attended a diabetes outpatient clinic with lethargy and thirst. Ten months before the visit, he had started pembrolizumab injection to treat malignant melanoma with multiple metastases. At that time, his HbA1c was 6.2% and he did not use any glucose-lowering agent. At first visit to the diabetes clinic, HbA1c level was 10.3%. Anti-GAD antibody was negative and serum C-peptide level was 0.59ng/ml. Glucocorticoid or other glucose-elevating agents were not used. The patient was prescribed oral hypoglycemic agents. However, his blood glucose levels were not reduced. After 3 months, HbA1c was 10.4% and serum C-peptide level was 0.1 ng/ml. He was diagnosed with pembrolizumab-associated insulin-deficient diabetes. To date, the patient controls his glucose with basal-bolus insulin therapy. **Conclusion:** Here, we report the first case of an Asian patient who developed insulin-deficient diabetes after ten months of pembrolizumab treatment. Given the increasing use of immune checkpoint inhibitors in clinical practice and the life-threatening nature of endocrine dysfunction if not promptly recognized, regular glucose monitoring to early detect diabetes in patients who use pembrolizumab is suggested.

