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Case Report

Adrenocorticotropic hormone Secreting Olfactory Neuroblastoma producing Ectopic Cushing's Syndrome

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Abstract

Olfactory neuroblastoma is a rare sinonasal tumour of neuroendocrine type arising from olfactory neuroepithelium. Cushing`s syndrome is a clinical entity occurring due to elevated serum cortisol levels which is commonly due to exogenous steroids. Ectopic ACTH giving rise to endogenous Cushing's syndrome requires vigilant evaluation in recognition of ectopic site. This syndrome gives rise to multitude of metabolic derangements with high morbidity which warrants early evaluation and management.

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Introduction

Olfactory neuroblastoma is a rare neuroendocrine sinonasal tumour (accounting for 3-10%)[1] having a variable prognosis depending on the pathological grading, arising from the olfactory neuroepithelium. Ectopic Cushing's syndrome results in metabolic derangements with significant morbidity caused by secretion of adrenocorticotropic hormone (ACTH) from a site other than the pituitary gland and accounts for less than 15% of endogenous Cushing's syndrome[2]. The commonest site for ectopic ACTH secreting tumour is a lung cancer. Even though categorized as a neuroendocrine tumour, Olfactory neuroblastoma can cause secretion of hormones and is a rare case as presented here.

Case Report

A 40-year-old previously healthy female patient with a past history of gestational diabetes presented to a tertiary care centre with osmotic symptoms. Evaluation revealed severe hyperglycaemia and insulin was commenced to achieve glycaemic control. Weeks later she presented to National Hospital of Sri Lanka (NHSL) with an altered level of consciousness at which time she was detected to have severe hypoka1aemia with a serum potassium (K^+) level of 1.6mmol/L. During the same admission she developed focal seizures with secondary generalization that worsened to give rise to status epilepticus. Biochemical evaluation revealed a hypokalaemic alkalosis (1.8 mmol/L) with normoglycaemia while other electrolytes were normal.

The patient underwent imaging of the brain with a non-contract CT as well as MRI which failed to recognize a focal pathology. The combination of symptoms with metabolic derangements pointed towards Cushing's syndrome and was investigated accordingly. Even though there were no obvious cushingoid features clinically except for the generalized eruption of monomorphic acne.

Ectopic ACTH syndrome was diagnosed using serum 9am cortisol levels, overnight dexamethasone suppression test (ODST) (820nmol/L), low dose Dexamethasone suppression test (LDST) (632 nmol/L) and serum ACTH levels. High dose dexamethasone suppression (HDST) test showed suppression of serum cortisol levels whilst the cortisol burden was more than 2000 nmol/L.

Imaging studies performed to recognize an ectopic focus of ACTH Secretion (contrast enhanced CT of chest, abdomen, pelvis) turned out to be negative. MRI brain was repeated with pituitary protocol which showed a polyp in the right nasal cavity (arising medial to the middle turbinate from the septum) with no abnormality in brain or pituitary (Figure 1).

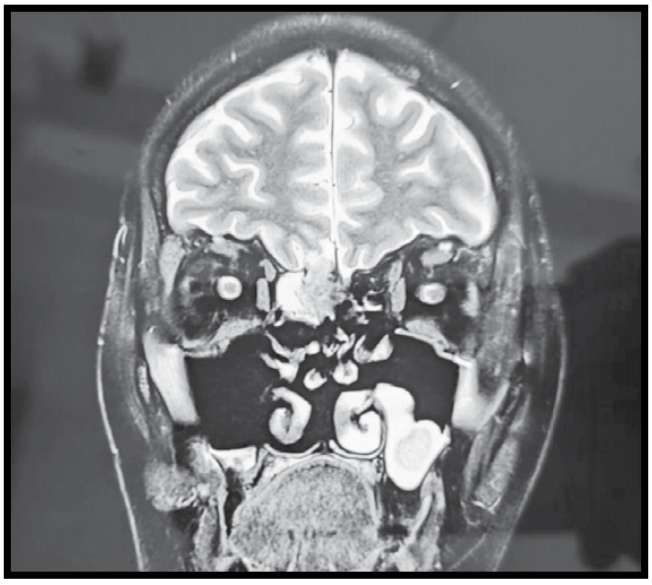

Figure 1. MRI scan of brain (pituitary protocol)

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FDG PET/ CT (Fluorodeoxyglucose - Positron Emission Tomography with Computed Tomography) was performed which revealed the right nasal polyp to be FDG avid (SUV 3.4) (Figure 2). The polyp was measured 1.6cm X 1.1cm. Further inquiry from the patient did not reveal any nasal or orbital symptoms.

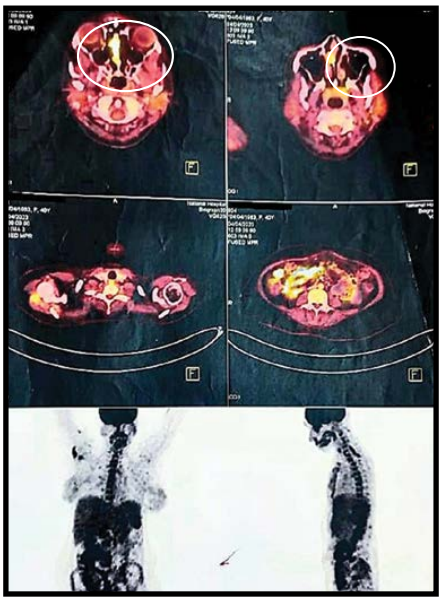

Figure 2. FDG PET CT showing FDG avid nasal polyp

Rigid nasal endoscopy revealed vascularized smooth polyp in the right olfactory groove which was attached to right middle turbinate while septum was intact. Excision biopsy was performed and specimen sent for histology. Histopathological evaluation revealed a small round blue cell tumour in a myxoid stroma. Few rosettes were seen focally. Immunohistochemistry showed positivity for synantophysin, chromogranin A and ACTH. The features were compatible with an olfactory neuroblastoma (Hyams Grade II).

Repeated CT of nose and paranasal sinuses revealed residual tumour of Kadish C in the right cribriform area with base of skull erosion and further complete surgical excision was planned. There was no obvious residual tumour in nasal cavity. Accordingly anterior skull base was exposed by anterior and posterior ethmoidectomy and excision of middle turbinate flush from skull base. This revealed an anterior bony skull base defect in right cribriform area with exposed dura and small area of residual tumour. Complete excision done with the involved dura. CSF leak was successfully repaired using synthetic dural material. Histology confirmed the dura positive for tumour cells.

Patient's hypokalaemia improved following surgical interventions and potassium levels became normal without replacement. Repeat assessment of cortisol burden was reduced significantly. Severity of hyperglycaemia was reduced significantly and overnight dexamethasone suppression test which was repeated showed successful suppression. She was discussed at a multi-disciplinary team (MDT) meeting where the oncologist agreed to provide her with further chemo radiation. Subsequently, she underwent 3 cycles of weekly intravenous Cysplatin and radiotherapy by IMRT (Intensity modulated radiation therapy) of 60 Gy in 30 fractions.

Imaging done following treatment completion revealed of post-surgical changes with no residual tumour. Patient is currently normokalaemic without supplementation and achieves glycaemic control with oral hypoglycaemics. She does not have any CSF rhinorrhoea or surgical complications and is currently being followed up at National Hospital of Sri Lanka.

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Discussion

Olfactory neuroblastoma also known as esthesioneuroblastoma is a rare sinonasal malignancy first described by Berger and Luc in 1924. It accounts for less than 10% of sinonasal tumours and less than 0.3% of all upper aerodigestive tract malignancies[3]. Arising from olfactory neuroepithelium, this tumour is locally aggressive and can metastasize rarely.

Common clinical presentation is by local symptoms of sinonasal disease. Ectopic ACTH syndrome due to secretory cells in the tumour is a rare occurrence (around 20 published cases[4]) which produce metabolic derangements as in the case discussed. Nasal endoscopy may reveal unilateral, poloidal, soft reddish grey mass with intact mucosa. Imaging with CT will show unilateral mass in the olfactory groove which may be associated with bony erosions. MRI will provide better discrimination between tumour and accumulated secretions and confirm the extent of the disease. The staging is by Kadish classification (from A to C with addition of D in a modified staging).

Ectopic ACTH secretion is evaluated by a biochemical panel including ODST, LDST, HDST and confirmed by inferior petrosal sinus sampling. To localise the ectopic site, FDG PET/CT can be used but ^{68}Ga-DOTA-conjugated octreotide PET has a better sensitivity and specificity[4].

Diagnosis is by histopathological examination of tissues which will show small round blue cells characteristic of neuroendocrine tumours with formation of true or pseudo rosettes. Graded according to Hyams grade I to IV according to pathological features including polymorphism and mitoses. Immunohistochemical analysis will show positivity for neurone specific enolase, synaptophysin, chromogranin A, CD 56, beta tubulin couple of which were positive in the index case.

Management is mainly by open or endoscopic surgical resection depending on the staging and chemoradiation plays a role in adjuvant setting. Occasional cases are treated with single modality with either surgery or radiation depending on stage and grade of the tumour.

Good prognosis is reported in cases of Hyams grade I and II with variable prognosis in grades III and IV.

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