CASE REPORT

Olfactory bulb agenesis with normal sexual hormones

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SUMMARY

An 18-year-old Caucasian man presented with a lack of sense of surrounding smell. The problem was first noticed when a family member discussed the smell of the food, which he had no idea what it was. The patient had normal development and sexual function, no history of trauma, surgery, chemical exposure or infection. Physical examination revealed no significant abnormalities. Smell threshold test using phenyl-ethyl-alcohol revealed bilateral anosmia. MRI showed bilateral aplastic olfactory bulbs and tracts associated with absent cortical growth of the olfactory sulci and asymmetrical gyrus rectus. Circulating hormones including cortisol, growth hormone, insulin-like growth factor 1, adrenocorticotrophic hormone, thyroid hormones, follicle-stimulating hormone, luteinizing hormone, prolactin and testosterone were within normal ranges. Doppler ultrasound showed normal testis with bilateral suprastesticular varicoceles. Given the loss of warning smell sensation, counselling for daily living precautions especially those related to gas, fire and rotten food was given.

BACKGROUND

Congenital or primary anosmia is a rare condition which, if exists, would be secondary to genetic disorders. This patient was brought to our attention by his mother because she noticed his lack of smell sensation of the food during a family gathering. Although genetic disorders especially Kallmann's Syndrome (prevalence 1 in 10 000 men) would have been the most likely differential diagnosis, they were excluded because of the otherwise normal investigative findings including the sex hormones. As this patient did not have any delayed sexual development, the diagnosis was not made until he reached the age of 18 without anosmia-related injury.

CASE PRESENTATION

An 18-year-old Caucasian man presented with a lack of sense of surrounding smell. The problem was first noticed when a family member discussed smelly food, which he had no idea what it was. The patient had normal development and sexual function: had morning erection about once a week and ejaculation once in 2–3 weeks. He had no history of trauma, surgery, chemical exposure or infection.

Physical examination was within normal limits including normal cranial nerves other than cranial nerve 1, intact sensory functions, normal visual field, no focal weakness, intact finger-to-nose test, negative Romberg test, no breast enlargement, normal growth (body mass index 23.87 kg/m²), no

hair loss and normal penis but relatively small both testes (10 mL).

Social history was not significant; no smoking or alcohol use. He has been doing well academically, currently attending high school.

INVESTIGATIONS

Smell threshold test using phenyl-ethyl-alcohol (PEA) was 'top-out' (could not sense the strongest smell level proposed) which is suggestive of bilateral anosmia. Unlike ammonia, the PEA is a rose-smelling pure aromatic odorant that has minimal propensity to stimulate intranasal free nerve endings from the trigeminal nerve.¹

Axial and coronal T1W, T2W, 3D T2W thin slice olfactory bulb/tract MRI showed bilateral aplastic olfactory bulbs and tracts associated with absent cortical growth of the olfactory sulci and asymmetrical gyrus rectus (figure 1). Several small non-specific hyperintense T2W/Fluid Attenuated Inversion Recovery at subcortical white matter of both frontal lobe were detected. Myelination was within normal range for age. No parenchymal lesion or abnormal fluid collection was identified. Asymmetrical prominence of the right lateral ventricle relatively to the left side was noted. The rest of the ventricles and sulci were normal in size and configuration. There was no midline shift, mass effect or acute infarction. The visualised major intracranial vessels appeared patent. The posterior fossa structures were normal. The cerebellar tonsils terminated above the level of the foramen magnum. Both maxillary sinuses had mucosal thickening.

Hormone studies: Growth hormone <0.05 ng/mL; insulin-like growth factor 1 228 ng/mL; luteinizing hormone 3.28 mIU/mL, follicle-stimulating hormone 3.52 mIU/mL; prolactin 14.19 ng/mL; testosterone 8.00 ng/mL; cortisol 13.35 µg/dL, adrenocorticotrophic hormone 24.9 pg/mL; free thyroxine 1.03 ng/dL, thyroid stimulating hormone 0.814 nU/mL

Doppler ultrasound of testes: Small right varicocele at suprastesticular region; large left varicocele extending from left suprastesticular region to inferior pole of left testis. Otherwise, structures are unremarkable

Whole abdominal ultrasound: Normal liver, biliary tract, gallbladder, pancreas, kidneys, spleen, aorta, urinary bladder and prostate gland (14 g).

Chest X-ray: Normal lung volumes, no abnormal pulmonary opacity, no effusion or pneumothorax, normal heart size, unremarkable mediastinal contour and normal bony structures.

Complete blood count: Total white blood cells 9700/µL, neutrophil 72.9%, lymphocyte 19.6%,

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Figure 1 Bilateral aplastic olfactory bulbs and tracts associated with absence cortical growth of the olfactory sulci and asymmetry on gyrus rectus. Non-specific bilateral frontal subcortical white matter lesions. Asymmetrically prominent right lateral ventricle. Mild chronic bilateral maxillary sinusitis.

monocyte 6.6%, eosinophil 0.7%, basophil 0.2%, red blood cell $5.29 \times 10^6/\mu\text{L}$, haemoglobin 16.0 g/dL, hematocrit 45.0%; platelet count 214 000/ μL .

Blood chemistry: Fasting blood sugar 82 mg/dL; uric acid 5.4 mg/dL; alkaline phosphatase 121 μL , aspartate aminotransferase 23 μL , alaline aminotransferase 18 μL ; creatinine 0.83, estimated glomerular filtration rate $>60 \text{ mL/min/1.73 m}^2$; total cholesterol 174 mg/dL, triglycerides 88 mg/dL, high density lipoprotein 43 mg/dL, low density lipoprotein 118 mg/dL.

DIFFERENTIAL DIAGNOSIS

- ▶ Kallmann syndrome (KS): isolated gonadotropin-releasing hormone (GnRH) deficiency with anosmia which is predominantly male but should also have underdeveloped sexual characteristics and other affected organs and systems.
- ▶ Hatsfield syndrome: a mild form of holoprosencephaly with olfactory bulb agenesis and ectrodactyly but the patient has normal physical appearance.
- ▶ Septo-optic-pituitary dysplasia (de Mosier syndrome) which has hypoplastic olfactory bulbs but the MRI showed no significantly abnormalities of the optic tracts and septum.
- ▶ Agenesis of the corpus callosum which is usually accompanied by agenesis of the anterior commissure but the MRI findings.
- ▶ Waardenburg syndrome: autosomal dominant inherited pigmentary disorder possibly with arrhinencephaly but the patient did not have patchy depigmented areas such as white forelock of hair nor did he have sensorineural hearing loss.
- ▶ Congenital insensitivity to pain with anhidrosis or Hereditary sensory and autonomic neuropathy type 4: an autosomal recessive disorder with profound loss of pain sensitivity leading to injuries and/or self-mutilation but the olfactory bulbs and tracts are still intact.
- ▶ Head injury is unlikely because he had no history of head trauma as far as he can recall.
- ▶ Viral-induced anosmia is possible but unlikely because of no preceding cold symptoms before the onset of anosmia. As he might become anosmia after viral rhinitis that might have happened when he was still too young to recognise and describe the loss of smell, it was a differential diagnosis before receiving the MRI findings.
- ▶ Allergic rhinitis and sinusitis could lead to occasional smell loss but were unlikely in this patient who had persistent anosmia with no other symptoms related to the two diseases.
- ▶ Occupational exposure is also unlikely as the patient had no history of strong-smell chemical substance exposure.

TREATMENT

No curative treatment was available. Given the loss of warning smell sensation, counselling for daily living precautions especially those related to gas, fire and rotten food was given.

OUTCOME AND FOLLOW-UP

The patient has been doing well.

DISCUSSION

The incidence of olfactory bulb agenesis or 'arrhinencephaly' is estimated at 700 per 100 000 births² and has usually been found with other primary malformations.^{3,4} KS, isolated GnRH deficiency with anosmia, is a common differential diagnosis for patients with underdeveloped sexual characteristics and other affected organs and systems.⁵ A number of KS cases have been reported since its first introduction by Kallmann *et al* in 1944⁶ with estimated prevalence of 1 in 8000 men and 1 in 40 000 women.⁵ For example, Shetty *et al* reported a 17-year-old woman who presented with primary amenorrhoea and later revealed on questioning that she was not appreciative of smell from childhood.⁷ Another recently reported case was a 23-year-old man who primarily presented with a lifelong lack of erection and ejaculation.⁸

Our patient is a very rare case of isolated congenital anosmia that was brought for medical attention. In addition to an appreciation of food and surroundings, smell sensation is essential for detecting environmental hazards. Without the careful observation and suspicion by his mother, the patient might have presented with an injury or food poisoning instead. Hence, counselling for daily living precautions especially those related to gas, fire and rotten food should be given. Also, the compensatory mechanism such as an increased ability to detect fear or disgust facially expressed by others should be evaluated in a patient with congenital or long-lasting acquired anosmia.⁹

Learning points

- ▶ Isolated congenital anosmia with normal sexual characteristics is more difficult to be detected.
- ▶ Anosmia is commonly found as part of the Kallmann's Syndrome—a rare genetic disease with isolated gonadotropin-releasing hormone deficiency.
- ▶ Given the loss of warning smell sensation, counselling for daily living precautions especially those related to gas, fire and rotten food should be given.
- ▶ The compensatory mechanism for their inability to detect environmental hazards through olfactory sensation such as the detection of facial expression by others should be evaluated.

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