

# Bromocriptine or cabergoline-induced cerebrospinal fluid rhinorrhea: A life-threatening complication during management of prolactinoma

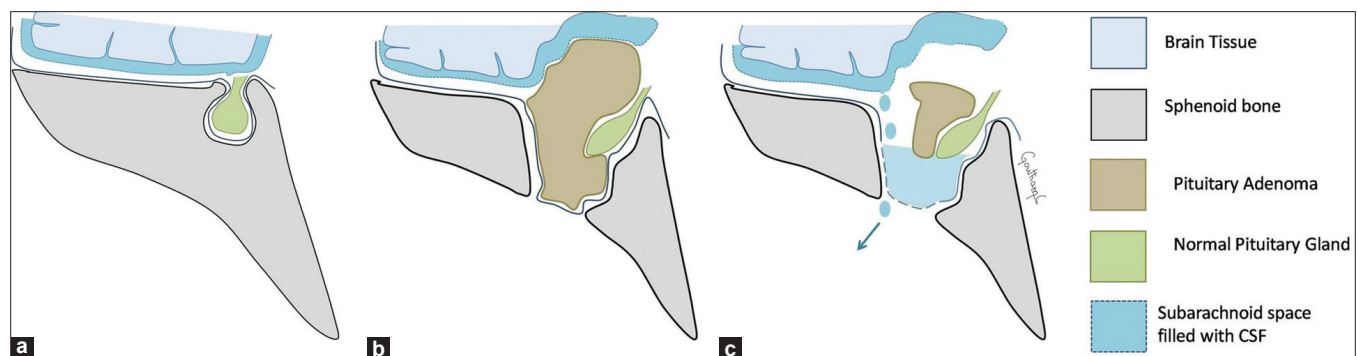
Sir,

Prolactinomas are the most common pituitary tumors accounting for 45% of all pituitary tumors. Its prevalence is around 60–100 cases per million.<sup>[1]</sup> Prolactinoma occur more commonly in females than males in younger population compared with middle age group.<sup>[1]</sup> Microprolactinoma (<10 mm) and macroprolactinoma (>10 mm) are the most common causes of hyperprolactinemia.<sup>[1]</sup>

Hyperprolactinemia is found in 15%–20% of females presenting with secondary amenorrhea or oligomenorrhea, in around 30% galactorrhea or infertility, and in 75% both with amenorrhea and galactorrhea.<sup>[1]</sup>

Prolactinomas are one of the common causes of infertility in both males and females.<sup>[1,2]</sup> Most of the prolactinomas can be managed medically with bromocriptine or cabergoline, which are largely used as primary treatment or treatment of first choice for prolactinomas, including large and invasive prolactinomas.<sup>[2,3]</sup> They normalize serum prolactin levels and induce reduction in the tumor size, promoting restoration of gonadal function, cessation of galactorrhea, and improvement in visual defects in the majority of patients.<sup>[2,4]</sup> A large invasive prolactinoma can invade the skull base, widely erode the sellar floor, and often extend into the sphenoid sinus [Figure 1a,b].<sup>[3]</sup> In the patient who is having large invasive prolactinoma and started on bromocriptine or cabergoline, there is high possibility of development of spontaneous drug induced cerebrospinal fluid (CSF) rhinorrhea.<sup>[3,5-8]</sup> Presumably, it is caused by unplugging of an eroded area in the skull base as a result of tumour shrinkage under the influence of bromocriptine or cabergoline [Figure 1c].<sup>[4]</sup> Bromocriptine-induced CSF rhinorrhea is a rare but life-threatening complication and carries a fairly high risk of ascending meningitis.<sup>[3,5-8]</sup> Its onset can be early within the first few weeks or late after several months of treatment.<sup>[3]</sup> Presumably it can be unknowingly misdiagnosed by clinician with allergic rhinitis or other nasal discharge condition, which can lead to life-threatening catastrophic complications of ascending meningitis.<sup>[5]</sup> CSF rhinorrhea can be easily differentiated from allergic rhinitis or other nasal discharge conditions by biochemical analysis of fluid for sugar (usually more than 30 mg/dL) and beta-2 transferrin, which is present in CSF-containing fluid.<sup>[2]</sup>

These reports point toward the possibility of bromocriptine



**Figure 1:** Schematic diagram showing bromocriptine/cabergoline-induced CSF rhinorrhea. (a) Normal sella, pituitary (green), sphenoid sinus (grey), and CSF spaces (blue). (b) Widening of the sella due to erosion by the pituitary tumor (brown). (c) Shrunken tumor after bromocriptine/cabergoline therapy resulting in CSF rhinorrhea

or cabergoline-induced cerebrospinal fluid rhinorrhea, which should be kept in mind when a patient is started on bromocriptine or cabergoline for the treatment of prolactinomas and if the patient develops watery discharge from nose or has salt-like taste in the throat.<sup>[3,5-8]</sup> Fluid should be sent for biochemical analysis for sugar and beta-2 transferrin.<sup>[2]</sup> If sugar level is more than 30 mg/dL or beta-2 transferrin is positive, the patient should be referred to neurosurgical care for further management of CSF rhinorrhea. Careful follow-up is required when treatment with bromocriptine or cabergoline is attempted for prolactinoma in reproductive medicine clinic for infertility management in male and female patients.

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