Hyperprolactinaemia: Secondary Development of Cabergoline Resistance

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A 32 year-old Emirati woman presented in 2007 with an 8-month history of oligomenorrhoea and secondary infertility. A microprolactinoma had been diagnosed 7yrs earlier (prolactin 293.1ng/ml) and she had transsphenoidal resection after an unsatisfactory response to Cabergoline (prolactin 54.6ng/ml). Pathology confirmed an adenoma, positive for prolactin on immunohistochemistry. Post-operatively her prolactin normalised (9.2ng/ml) with no evidence of residual adenoma on MRI. However, she developed primary infertility 3yrs later and her prolactin levels were again elevated. She resumed Cabergoline, conceived and was able to breastfeed after discontinuing her medication. Since then, her hyperprolactinaemia persisted despite on-going Cabergoline and trials of Bromocriptine; her menstrual cycle returned but she was unable to conceive.

Her repeat pituitary MRI showed a normal residual gland. The Cabergoline was titrated gradually to 4.5mg per week however her prolactin levels remained high. Cabergoline suppression test (see Table 1) demonstrated no reduction in her prolactin levels in response to Cabergoline. Two months later, she conceived spontaneously, off all medication.

Table 1: Cabergoline Suppression Test – showing response of prolactin to 4 days of Cabergoline dosing.

	beta-HCG	Initial Prolactin (mIU/L)	Cabergoline dose	Prolactin - post cannula 20min (mIU/L)
Day 1	<1mIU/ml	1255	0.5mg at 12:17	1280
Day 2		1268	0.5mg at 10:20	1363
Day 5		1469	0.5mg at 11:07	1579
Day 6		1596	0.5mg at 10:55	1476

Although Cabergoline resistance is well described, developing secondary resistance after an initial response to Cabergoline is not common. Such cases are assumed to be due to non-compliance. The mechanism of secondary resistance is not known. It is thought to be associated with reduced D_2 receptor gene transcription resulting in a decline in the number of D_2 receptors available on the cell membrane.