Secondary resistance to Cabergoline — pitfalls and challenges of managing macroprolactinoma with high dose dopamine agonist therapy

Dr A Abdalaziz1, Dr S Nag1, Dr B Dhakshinmoorthy1
1. James Cook University Hospital, Middlesbrough

❖ Introduction:

✓ Dopamine agonists (DA) are first line therapy for Prolactinoma which normalises prolactin (PRL) level in 80% of cases at a median weekly dose of 1mg.
✓ An accepted criterion of pharmacological resistance to DA is failure to normalize PRL levels.
✓ Failure to normalize PRL levels is seen in 24% of those treated with bromocriptine, 13% of those treated with pergolide and 11% of those treated with cabergoline.
✓ Although most patients who respond to dopamine agonists with a normalization of PRL levels have substantial tumour size reduction not all do and vice-versa.
✓ We report a case of aggressive macroprolactinoma that required 7mg of Cabergoline to reduce prolactin despite radiological evidence of tumour shrinkage.

❖ Case Summary:

o A 42 year old male presented with a bitemporal field defect and his imaging confirmed an invasive macroprolactinoma.
o His biochemical profile showed elevated PRL level of 91,760 mU/L and hypogonadotropic hypogonadism (FSH-3.3 u/L, LH-2.5 u/L; testosterone- 6.2 nmol/L).
o The patient was started on 500 mcg of Cabergoline per week and the dose was titrated to 1 mg/week.
o After 6 months there was marked reduction in the size of the tumour which was accompanied by a fall in prolactin to 10,6050 mU/L.
o Thereafter, prolactin level remained static and the dose of Cabergoline was progressively titrated to a maximum of 7mg weekly.
o Repeat MRI scan showed complete shrinkage of macroprolactinoma however, the prolactin remained persistently elevated at 1,826 mU/L.
o There was associated with adverse effects and the dose of cabergoline was reduced gradually to a maintenance dose of 500 mcg weekly.
o Prolactin remains slightly elevated at 2037mU/l but is stable with no associated increase in tumour size.

❖ Summary:

▪ Resistance to dopamine agonists can be defined with respect to failure to normalize PRL levels and failure to decrease tumor size by ≥50%.
▪ This case highlights marked secondary resistance to Cabergoline following an initial favourable response.
▪ Secondary resistance to DA occurs rarely but this case demonstrates that effective tumour shrinkage can be obtained with higher doses of cabergoline with careful monitoring of adverse effects.
▪ Once tumour shrinkage has been achieved the dose of cabergoline should be reduced to the lowest effective dose that maintains a stable prolactin level.
▪ Complete normalisation of prolactin may not be feasible or indicated in the majority of cases.

Conflicts of interest
1. The authors declare no relevant conflict of interest

Acknowledgments
1. Patients and the endocrine team at James Cook University Hospital