



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

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❖ 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.

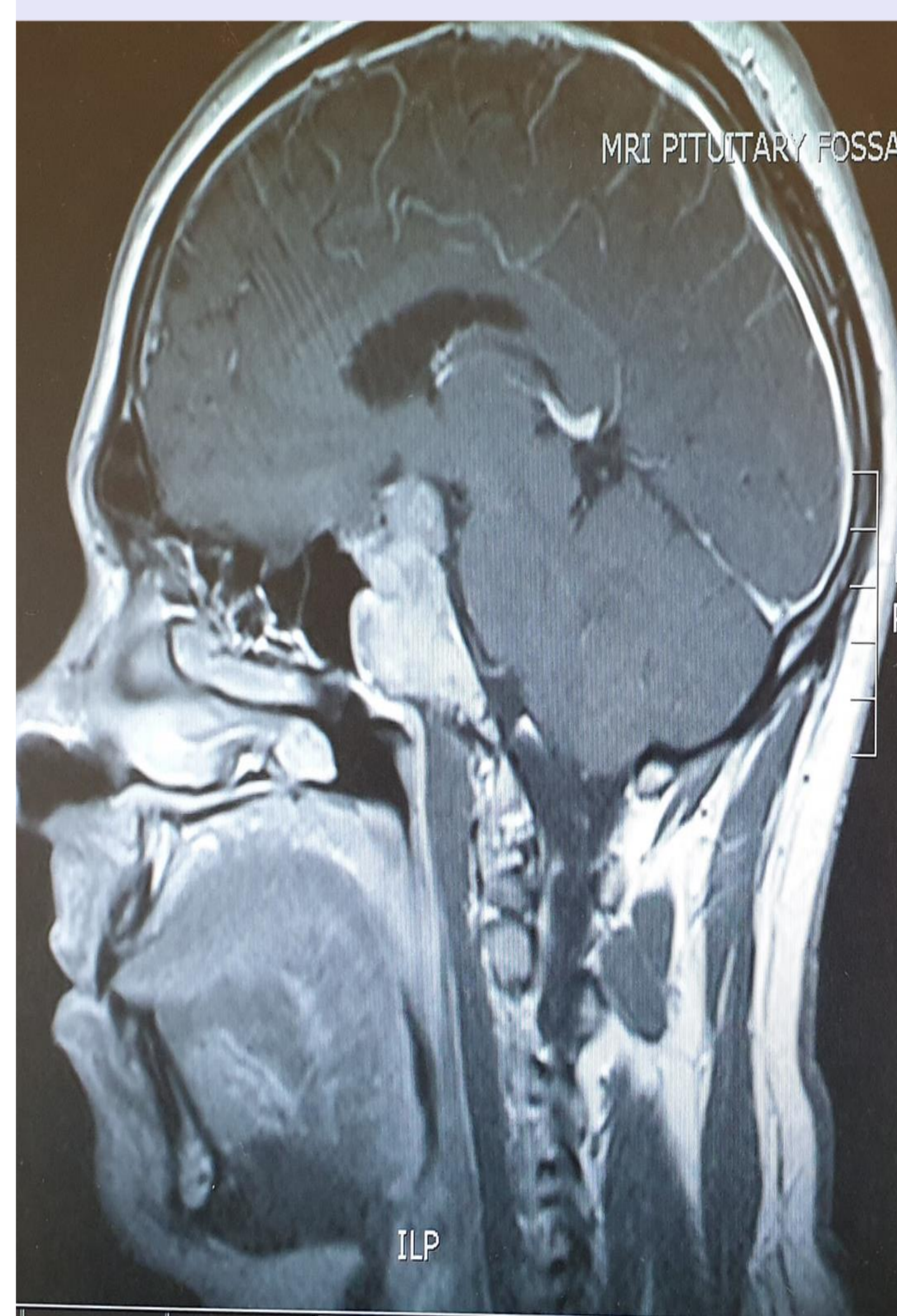
❖ Case Summary:

- A 42 year old male presented with a bitemporal field defect and his imaging confirmed an invasive macroprolactinoma.
- 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).
- The patient was started on 500 mcg of Cabergoline per week and the dose was titrated to 1 mg/week.
- 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 .
- Thereafter, prolactin level remained static and the dose of Cabergoline was progressively titrated to a maximum of 7mg weekly.
- Repeat MRI scan showed complete shrinkage of macroprolactinoma however, the prolactin remained persistently elevated at 1,826mU/l.
- This dose was associated with adverse effects and the dose of cabergoline was reduced gradually to a maintenance dose of 500 mcg weekly.
- Prolactin remains slightly elevated at 2037mU/l but is stable with no associated increase in tumour size.

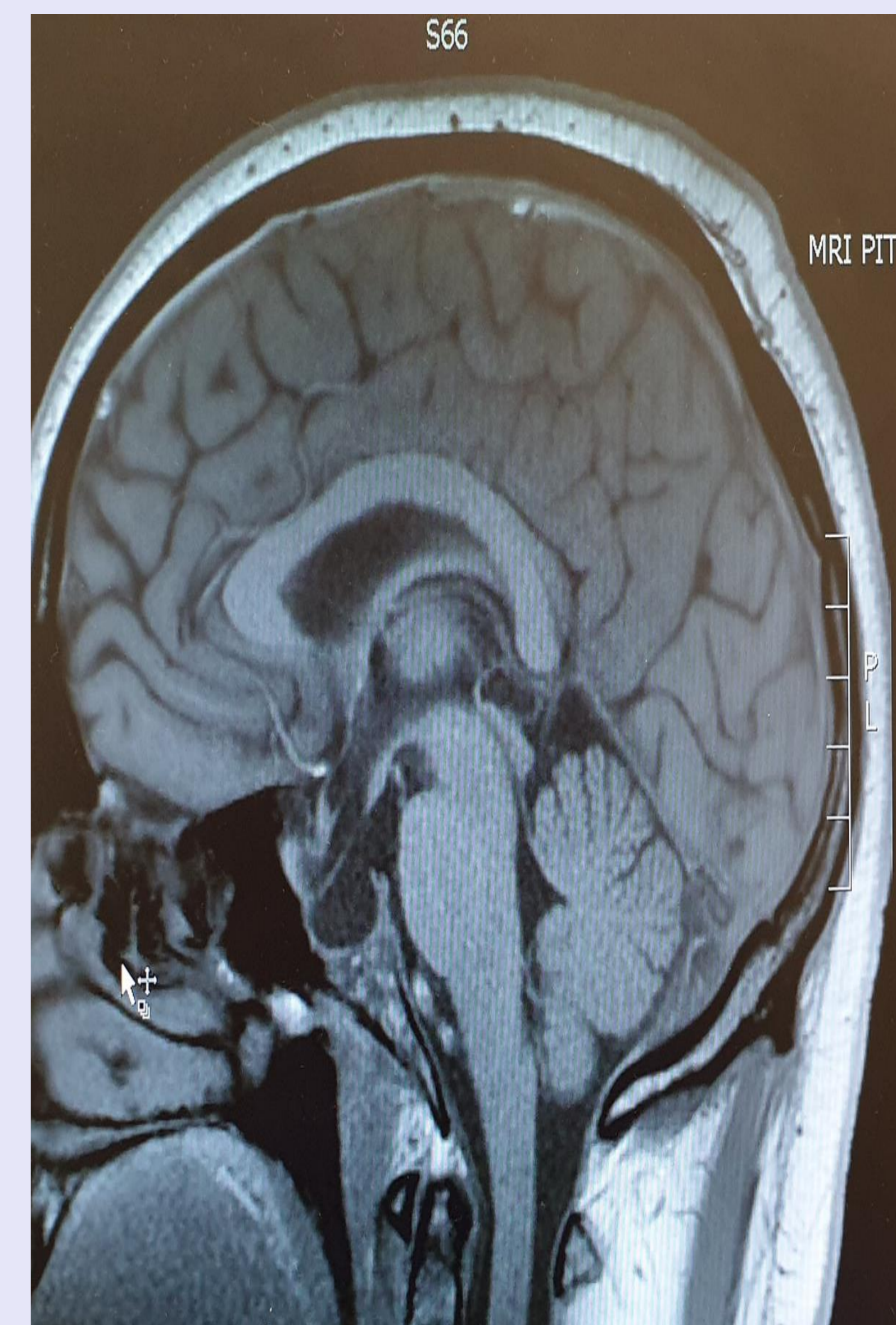
Conflicts of interest

1. The authors declare no relevant conflict of interest

MRI scan images (Pre & post Cabergoline)



(A) Initial MRI.



(B) post Cabergoline

❖ Summary:

- Resistance to dopamine agonists can be defined with respect to failure to normalize PRL levels and failure to decrease tumor size by $\geq 50\%$
- 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.

Acknowledgments

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