PROLACTINOMAS IN CHILDREN AND YOUNG ADULTS:

10 year experience in a Tertiary Regional Paediatric – Young Adult – Neuroendocrine Surgical Centre

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Introduction

Pituitary adenomas are rare in the Paediatric and Adolescent population ~ approx. 2% of CNS tumours. Prolactinomas (PRLoma) account for < 50% of pituitary adenomas. Experience with their management in children is reported in few series/case reports (Refs1,2). We report clinical presentation and response to treatment in 9 patients in our centre (population base ~ 3.6million) in the last 10 years with age at diagnosis < 18 years.

Patients and Methods

9 patients (4 male) were diagnosed with **PRLoma** at 13 – 18 years of age between 2006 and 2016. **4 Micro**PRLoma (Pts1-4); **5 Macro**PRLoma (Pts 5-9).

Assessment: Evaluation of puberty, growth and hypothalamo-pituitary function. Gonadotropin, fT4/TSH, and PRL secretion at baseline + / after GnRH tests.. Somatotropic function was evaluated by Glucagon test and serum IGF-1. Evaluation of pituitary-adrenal axis was assessed by glucagon +/- short Synacthen test. Patients with **Macro**PRLoma underwent sequential testing according to clinical progress.

Management: All patients were initially treated with oral Cabergoline (CBR).

- 5 patients responded to CBR therapy alone
- 4 were resistant or partially resistant to CBR and proceeded to trans-sphenoidal surgery (TSS)
- 1 patient required further treatment with Temozolamide and stereotactic radiotherapy (Ref 3)

Follow up: PRL levels initially monthly, then quarterly and six-monthly; with MRI and visual field examination according to clinical need.

Presentation

Microadenomas: 2ary Ammenorhea and galactorrhea were the first symptoms in females. The male patient presented with gynaecomastia, growth and pubertal delay. All females had normal heights for age and previously normal pubertal progression. Only 1 patient had headaches. All had normal ophthalmology examination.

Macroadenomas: Headache, galactorrhea and hypogonadism (2ary amenorrhea or arrest of puberty) were the presenting symptoms. 3 out of 5 patients had visual field defects and one of these also had reduced visual acuity.

Endocrinology: At presentation, serum PRL concentrations ranged from 2815-5240 miU/L in **Micro**APRLoma. and 3960-129000 mIU/L in **Macro**PRLoma. Impairment of pituitary hormone secretion was found in 2 of 5 patients with **Macro**RLoma at diagnosis (1 with GH and one with GH,TSH, ACTH and gonadotrophin deficiency – haemorrhagic)**.**

Histology: 4 Specimens (TSS patients): Immunohistochemistry showed PRL expression. One had mixed GH and PRL immunopositivity (somatomammotroph adenoma). Mitotic activity Ki67 ranged: 1-4%.

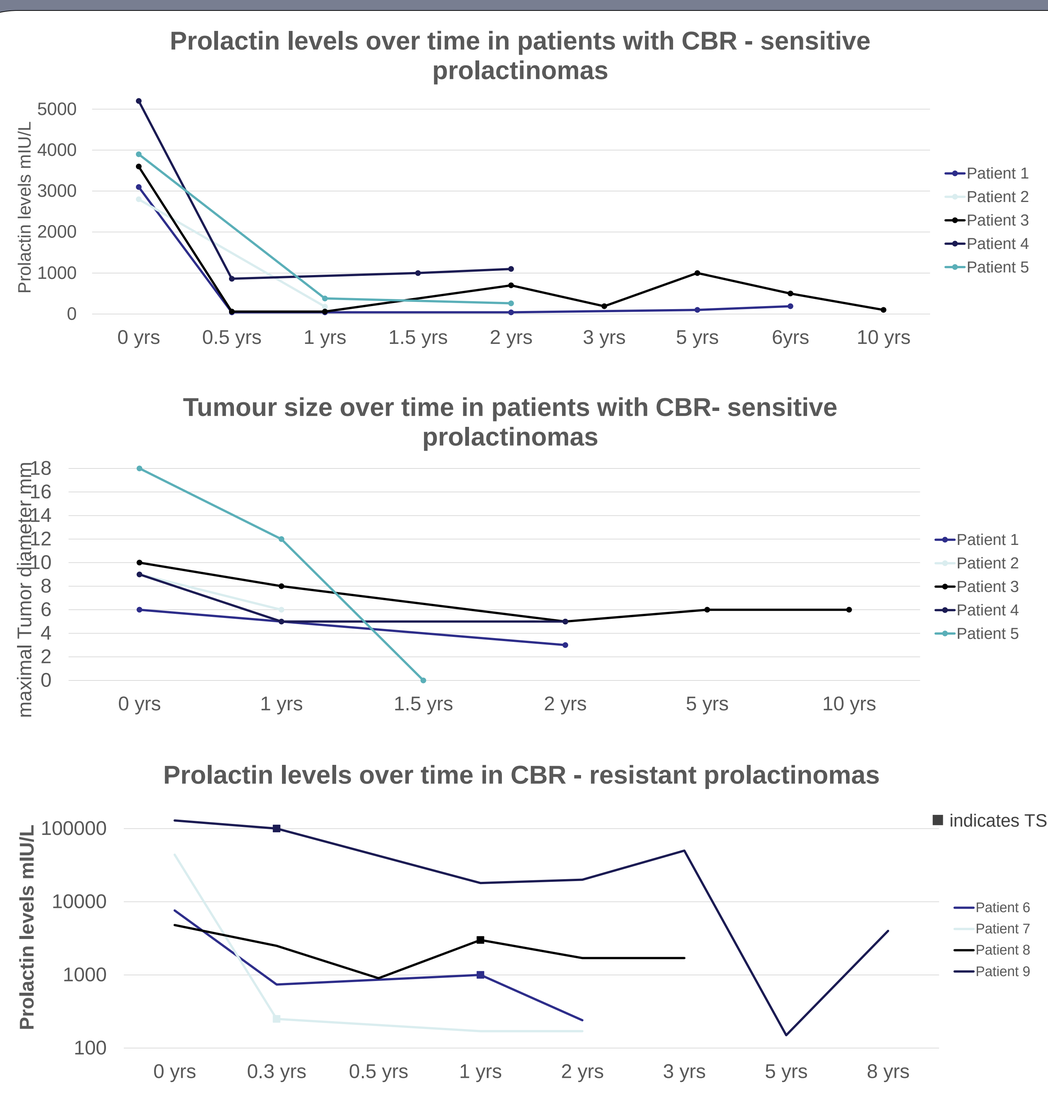
Genetics: No patients had mutations in MEN1 or AIP genes, but the male microadenaoma had h/o maternal aunt with non-functionng pituitary adenoma.

Microprolactinomas (n=4)

Features	Male	Female
Number of patients	1	3
Mean age at diagnosis	14	15.7
Range		14-18
Mean duration of symptoms	2 years	1 year
Range		6m – 24m
Max tumor dimension @ diagnosis	6mm	9.5mm
Range		9-10mm
Presenting symptoms		
Headaches	0	1
Galactorrhea	0	2
Amenorrhea	0	3
Gynecomastia	1	0
Pubertal arrest	1	0
Growth failure	1	0
Mean prolactin at diagnosis mU/L	3119	3860
Range		2815- 5240

Macroprolactinomas (n=5)

Features	Male	Female
Number of patients	3	2
Mean age at diagnosis	14	14.5
Range	13-15	14 and 16
Mean duration of symptoms	9m	1 year
Range	3m -24m	1 week - 2 years
Max tumor dimension @ diagnosis	58 mm	
Range	17 – 58 mm	17mm / 18mm
Presenting symptoms		
Headaches	3	0
Galactorrhea	0	2
Amenorrhea	0	2
Gynaecomastia	0	0
Pubertal arrest	1	0
Growth failure	0	0
Mean prolactin at diagnosis mIU/L	59600	7600 and 3960
Range	4840 – 129400	
Visual defects	2	1



Treatment and Follow up

CBR sensitive group: includes all patients with **Micro**PRLoma and 1 patient (#5) from the **Macro**PRLoma group. All had normal serum PRL levels within 6–12 months, complete resolution of symptoms and variable, but significant, tumour shrinkage. In most pts CBR was well tolerated without side effects. Pt 3 (**MicroPRL**oma) experienced "dizziness", leading to poor compliance and discontinuation of CBR, later restarted in view of relapse of symptoms reflected in the swinging PRL levels ~ graph 1). In one patient (male, **Micro**PRLoma) treatment was stopped after involution of tumour on MRI and remains tumour free to date (3 years later).

CBR resistant group: Includes 4 of 5 patients with **Macro**PRLomas. CBR treatment induced PRL normalisation and significant tumour shrinkage in only 1 patient, although this was followed by tumour expansion. Three had either modest or no significant change in tumour size, modest reduction in PRL levels and ongoing symptoms eventually requiring TSS. Near complete excision was achieved in 2 pts with substantial debulking in 2 to protect optic tracts. One patient had substantial residual tumour mass and high PRL levels leading to further treatment with Temozolamide (3 yrs post-TSS,) and Radiotherapy (5 yrs post-TSS) to achieve stable clinical condition (now 9 yrs post-diagnosis). All patients are still on CBR treatment.

Disease related chronic morbidity:

Microadenoma Group: None observed.

Macroadenoma Group: 2 patients have residual hemianopia. One has isolated GH deficiency and 3 have multiple pituitary hormones impairment in different combinations and are on long term replacement. 1 Pt has co-existing Growth hormone secretory excess without symptoms. None had diabetes insipidus. One patient has chronic troublesome headaches following tumour excision the nature of which to date remains unclear. The haemorrhagic **Macro**PRLoma involuted to leave normal pituitary function.

Conclusion

The spectrum of Prolactinomas in children and young adults requires combined expertise of a MultiDiscipline Team to provide comprehensive resources to manage these patients through a transition period.

References :

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