Hyperprolactinemia >1000

HOSP #		WARD	Neurosurgery
CONSULTANT	Dr. Jody Rusch	DOB/AGE	10 year female

Abnormal Result

Prolactin >1000 ug/L

Presenting Complaint

Patient presented at 7 years of age with galactorrhea and visual field defects.

History

Patient had a craniotomy for debulking of the adenoma. This was opposed to the usual transsphenoidal more non-invasive route of pituitary adenoma surgery. She was initiated on Cabergoline 1 g twice weekly for suppression of the tumour size.

It was also noted during surgery that the tumour was extremely vascular with much bleeding and the neurosurgeons struggled to mobilize it to adequately get it separated from the optic chiasm. Some portion of the tumour was left in situ during surgery as this was too big a risk for trying to excise.

A biopsy was also taken.

Examination

Patient subsequently developed severe intracranial edema after surgery in the ICU.

Laboratory Investigations

Collection date time Requisition number Status	*Reference range unit*	2020-03-11 12:48 713553140	2020-03-13 09:45 713555581	2020-11-26 00:00 713573116	2020-11-26 13:07 713573113	2020-12-03 05:43 713573635	2020-12-21 15:38 713578670	2020-12-21 15:43 713578671	**2021-02-03 15:10 713583689**
BIOCHEMISTRY									
LIPAEMIC		1+		ABSENT		ABSENT		ABSENT	ABSENT
ICTERIC		ABSENT		ABSENT		ABSENT		ABSENT	ABSENT
HAEMOLYSIS		ABSENT		ABSENT		ABSENT		ABSENT	ABSENT
S-SODIUM	136-146 mmol/L	137		136		141		141	138
S-POTASSIUM	3.5-5.1 mmol/L	3.7		3.8		4.4		3.4 L	3.8
S-CHLORIDE	101-109 mmol/L	105		98 L		105		104	99 L
S-BICARBONATE	21.0-31.0 mmol/L	25.0		25.0		30.0		28.0	31.0
ANION GAP	3-15 mmol/L	7		13		6		9	8
S-UREA	2.1-7.1 mmol/L	4.8		2.2		3.6		3.0	2.2
S-CREATININE	23-68 umol/L	48		40		38		48	
C-REACTIVE PROTEIN	< 5.0 mg/L	3.6		2.8					
S-TOTAL PROTEIN	57-80 g/L	76		76		66		72	72
S-ALBUMIN	35-52 g/L	46		44		38		39	39
GLOBULIN	21-35 g/L	30		32		28		33	33
ALB./GLOB. RATIO	0.9-2.7	1.5		1.4		1.4		1.2	1.2
S-TOTAL BILIRUBIN	5-21 umol/L	5		9		4 L		6	5
S-CONJ. BILIRUBIN	< 3.4 umol/L	1		2		1		1	1
UNCONJ. BILIRUBIN	2-17 umol/L	4		7		3		5	4
S-ALK. PHOSPHATASE	51-332 IU/L							129	135
S-ALK. PHOSPHATASE	69-325 IU/L	144		149		111			
S-gamma GT	4-22 IU/L	10		9		9		7	10
S-ALT	< 35 IU/L	15		11		23		12	12
S-AST	15-60 IU/L	28		29		33		16	18
P-GLUCOSE RANDOM	mmol/L		3.7						
ENDOCRINOLOGY									
INSULIN-LIKE GROWTH FACTOR 1	57-277 ng/mL			32.40 L					
INSULIN-LIKE GROWTH FACTOR 1	80-233 ng/mL		93.70						
FREE T4	7.2 - 16.4 pmol/L	5.8*L		8.3		8.1		14.5	13.7
FREE T3	3.88 - 8.02 pmol/L	3.44*L		2.43*L		2.42*L		3.31*L	
S-TSH	0.79 - 5.85 mIU/L	0.96		1.52				0.02*L	0.01*L
PROLACTIN	3.3 - 26.7 ug/L	613.5*H		1892.1*H		948.2*H		726.4*H	
FSH	0.03 - 3.9 IU/L	1.2		0.7					
LH	0.7 - 6.7 IU/L	0.4 L		0.8					
17B OESTRADIOL (E2)	< 60 pmol/L	< 55		< 55					
CORTISOL RANDOM*	nmol/L			126					
CORTISOL 08H00	184 - 618 nmol/L		85*L						
ACTH	1.6 - 13.9 pmol/L		2.7	1.4 L					

Collection date time Requisition number Status	Reference range unit	2021-02-10 05:35 713583939	2021-02-10 13:38 713584112	2021-02-19 11:43 713585065	2021-03-15 00:00 712530075	2021-03-16 00:15 713586569	2021-03-16 00:15 713586570	2021-04-08 21:40 713588757	2021-04-08 21:40 713590857
Biochemistry									
LIPAEMIC		ABSENT	ABSENT	ABSENT		ABSENT			ABSENT
ICTERIC		ABSENT	ABSENT	ABSENT		ABSENT			ABSENT
HAEMOLYSIS		ABSENT	ABSENT	ABSENT		ABSENT			ABSENT
S-SODIUM	136-146 mmol/L	136	136	142		141			138
S-POTASSIUM	3.5-5.1 mmol/L	4.8	4.1	4.4		3.8			3.8
S-CHLORIDE	101-109 mmol/L	101	99 L	105		104			102
S-BICARBONATE	21.0-31.0 mmol/L	30.0	30.0	28.0		31.0			28.0
ANION GAP	3-15 mmol/L	5	7	9		6			8
S-UREA	2.1-7.1 mmol/L	3.8	4.7	3.5		3.1			3.2
S-CREATININE	23-68 umol/L	40	38			44			48
S-CALCIUM (total)	2.20-2.70 mmol/L					2.39			2.24
CALCIUM (corrected)	2.20-2.70 mmol/L					2.49			2.34
S-PHOSPHATE	1.20-1.80 mmol/L					1.48			1.51
S-OSMOLALITY	280-295 mOsm/kg	294				299 H			292
U-OSMOLALITY	mOsm/kg	545			91				
C-REACTIVE PROTEIN	< 5.0 mg/L								5.4 H
S-TOTAL PROTEIN	57-80 g/L					77			67
S-ALBUMIN	35-52 g/L					36			36
GLOBULIN	21-35 g/L					41 H			31
ALB./GLOB. RATIO	0.9-2.7					0.9			1.2
S-TOTAL BILIRUBIN	5-21 umol/L					5			4 L
S-CONJ. BILIRUBIN	< 3.4 umol/L					1			1
UNCONJ. BILIRUBIN	2-17 umol/L					4			3
S-ALK. PHOSPHATASE	51-332 IU/L					124			109
S-gamma GT	4-22 IU/L					8			8
S-ALT	< 35 IU/L					10			10
S-AST	15-60 IU/L					14 L			16
Endocrinology									
VITAMIN D (25 OH)	ng/mL					23			
FREE T4	7.2 - 16.4 pmol/L								12.6
FREE T4	8.5 -15.7 pmol/L					13.6			
FREE T3	4.3 - 6.8 pmol/L								3.0 L
S-TSH	0.79 - 5.85 mIU/L					<0.01*L			
PROLACTIN	4.0-23.0 ug/L					1055.2*H			791.2*H
FSH	0.03 - 3.9 IU/L								0.3
LH	0.7 - 6.7 IU/L								< 0.2 L
17B OESTRADIOL (E2)	< 60 pmol/L								< 55
PARATHYROID HORMONE	1.6-6.9 pmol/L					0.3 L			
PARATHYROID HORMONE	15.2-65.7 pg/mL					2.9 L			

Other Investigations

Histology

Frozen section – pituitary adenoma. GROSS DESCRIPTION: Specimen labelled tumour. Specimen consists of 2 fragments of tissue, larger measuring 4x3mm. HISTOLOGY: Sections show tumour tissue composed of nests of monotonous cells with intervening fibrous septae. The cells have round nuclei and abundant eosinophilic cytoplasm. The nuclei have stippled chromatin with inconspicuous nucleoli. No mitotic activity or necrosis is seen. Immunohistochemistry: Synaptophysin:Positive Prolactin: Positive LH: Negative FSH: Negative GH: Negative

TSH: Negative ACTH: Negative CONCLUSION: Pituitary, mass, excision: – Pituitary adenoma with an immunohistochemical profile compatible with a prolactinoma.

Final Diagnosis

Pituitary Macroadenoma

Take Home Message

Cabergoline, sold under the brand name Dostinex among others, is a dopaminergic medication used in the treatment of high prolactin levels, prolactinomas, Parkinson's disease, and for other indications. It is taken by mouth. Cabergoline is an ergot derivative and a potent dopamine D_2 receptor agonist.

Lactotroph adenomas (prolactinomas) are more amenable to pharmacologic treatment than any other kind of pituitary adenoma because of the availability of dopamine agonists, which usually decrease both the secretion and size of these tumors. For the minority of lactotroph adenomas that do not respond to dopamine agonists, other treatments must be used. Hyperprolactinemia due to nonadenoma causes should also be treated if it causes hypogonadism.

There are two principal reasons why patients with hyperprolactinemia may need to be treated: existing or impending neurologic symptoms due to the **large size** of a lactotroph adenoma, and **hypogonadism** or other symptoms due to hyperprolactinemia, such as galactorrhea.

A third indication is in women with mild hyperprolactinemia and normal cycles who are trying to conceive as they may have subtle luteal phase dysfunction.

Rapidly decreasing Prolactin result

HOSP #		WARD	Endocrinology Clinic
CONSULTANT	John Stanfliet	DOB/AGE	36 y Female

Abnormal Result

A low prolactin result was obtained in a patient in whom a macroadenoma was suspected:

Prolactin: 1.3 mIU/L

Presenting Complaint

The patient presented with headache and decreased visual acuity (more specifically peripherally).

History

There were bilateral galactorrhoea, amenorrhoea, and as noted above, headache and visual disturbances.

The patient had received Cabergoline (a dopamine receptor agonist on D2 receptors) for the past 4 months.

Examination

As above

Laboratory Investigations

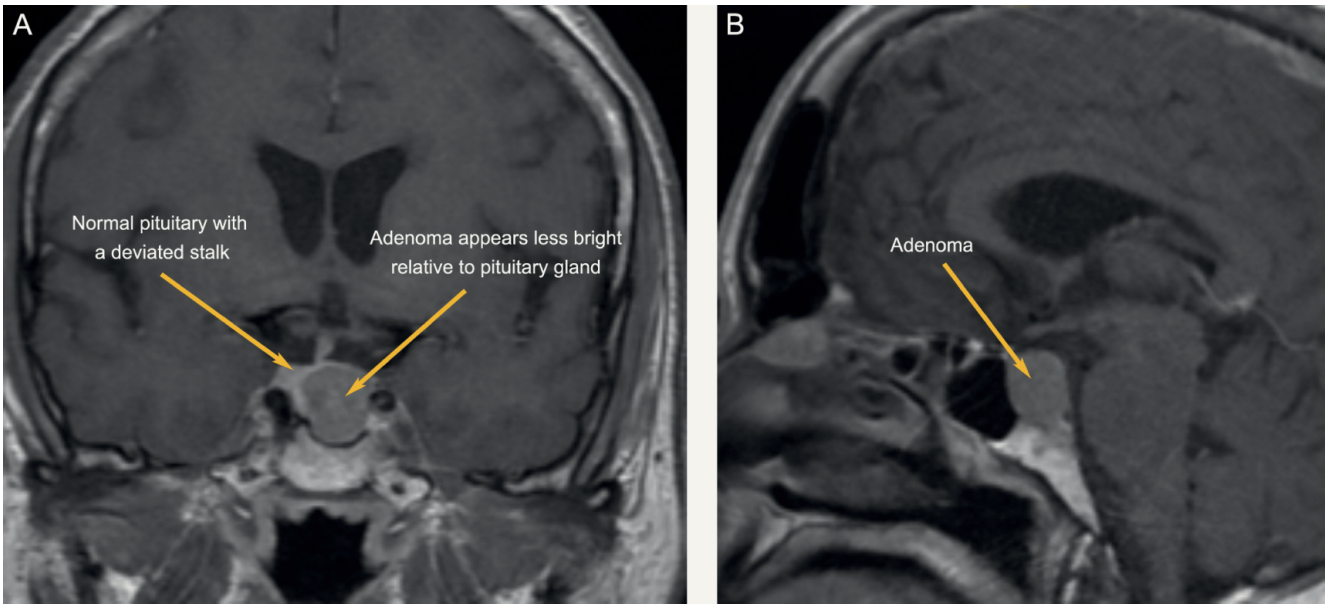
Date	**Prolactin** (mIU/L)
02/2019	106 (Recovery of 80% following PEG precipitation)
05/2019	135
06/2019	85
08/2019	1.3 (1.59 with a 1:10 dilution; 3.94 with a 1:50 dilution)

Prolactin Results

Other Investigations

MRI Head was booked for the following week. Interestingly, even in prolactin secreting tumours, the correlation between tumour size and prolactin level is limited. MRI head remains a vital investigation.

Final Diagnosis



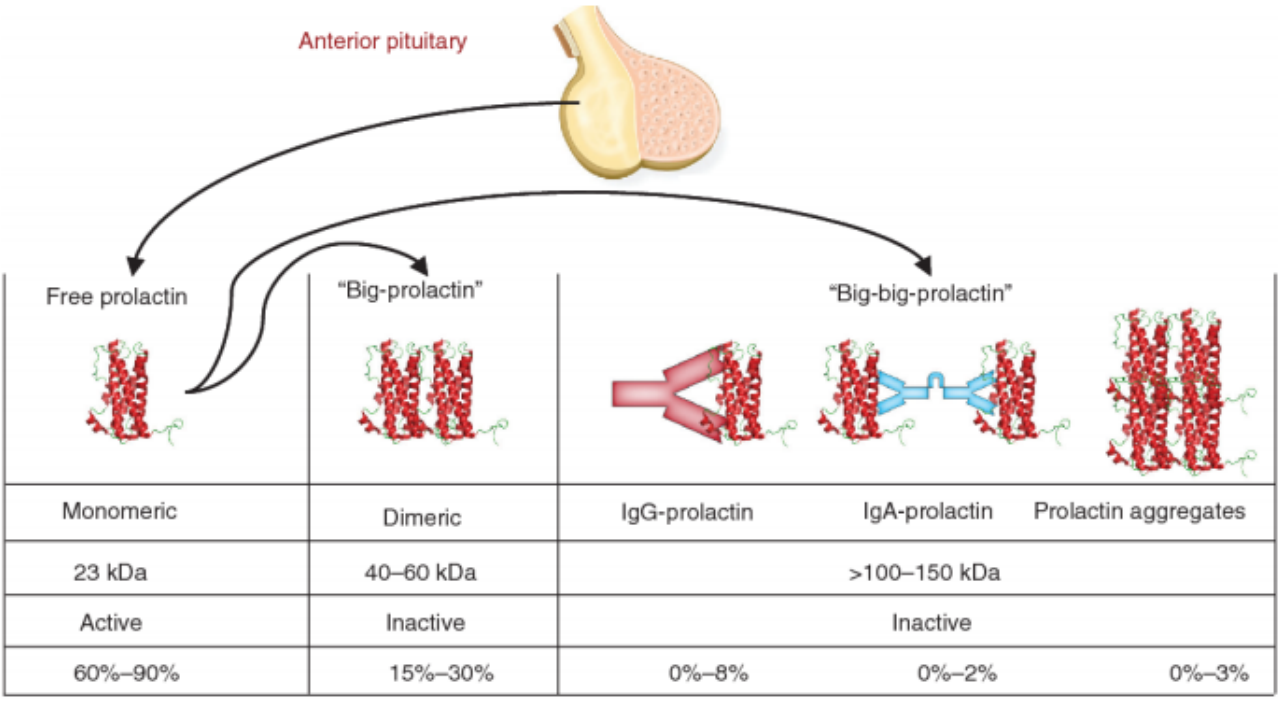
Pituitary Macroadenoma

Take Home Message

During pregnancy the concentration of prolactin rises under the influence of elevated estrogen and progesterone production. The stimulating action of prolactin on the mammary gland leads post partum to lactation. Hyperprolactinemia (in men and women) is the main cause of fertility disorders. The determination of prolactin is utilized in the diagnosis of anovular cycles, hyperprolactinemic amenorrhea and galactorrhea, gynecomastia and azoo-spermia. Prolactin is also determined when breast cancer and pituitary tumors are suspected. As in this case, a pituitary tumour was suspected, hence the repeated prolactin results.

As was noted in another short case, our assay on the Roche platform does measure all forms of prolactin, and when a high result is obtained (above the gender-specific reference range) it is recommended to measure the recovery after PEG precipitation.

Roche Prolactin Package Insert (2013)Download
Clin-Biochem-Rev-2018_Prolactin-Biology-and-Lab-MeasurementDownload
Clin-Chem-2008-Macroprolactin-Reference Intervals-after-PEGDownload



Monomeric	Dimeric	IgG-prolactin	IgA-prolactin	Prolactin aggregates
23 kDa	40–60 kDa	>100–150 kDa		
Active	Inactive	Inactive		
60%–90%	15%–30%	0%–8%	0%–2%	0%–3%

Figure 1. Structure of monomeric prolactin, "big-prolactin" and "big-big prolactin". Figure 1 adapted from reference 9 with permission.

Figure 1

Dr. John Stanfliet (pathologist at Pathcare) repied to the above case with very valuable comments:

- We use Beckman Coulter DxI, an immunoassay that is not affected by macroprolactin (I've include an article that shows this).
- Even in prolactin secreting tumours, the correlation between tumour size and prolactin level is limited. MRI head remains a vital investigation.
- Some prolactin secreting tumours also secrete other pituitary hormones such as growth hormone.
- I would ascribe the reduction in PRL to the Carbegoline and wonder whether the dose has been increased.
- Dr. Pete Berman would often suggest a mixing study: find a sample with high PRL, mix it 50/50 with this sample, and measure it to see whether there is some interferant in this sample.

[The-Beckman-DxI-800-prolactin-assay-demonstrates-superior-specificity-for-monomeric-prolactinDownload]