Radiological latency in pineal germinoma; a case report and literature review

Siu Chi Hin Ivan
Division of Neurosurgery, Department of Surgery,
Prince of Wales Hospital

Male / 23 / good past health

Presented to ophthalmology with 3 months history of diplopia (since late 2017)

Assessment at the time revealed dorsal midbrain signs;

Pupillary light-near dissociation bilaterally
Convergence retraction nystagmus on vertical saccades
Upgaze palsy

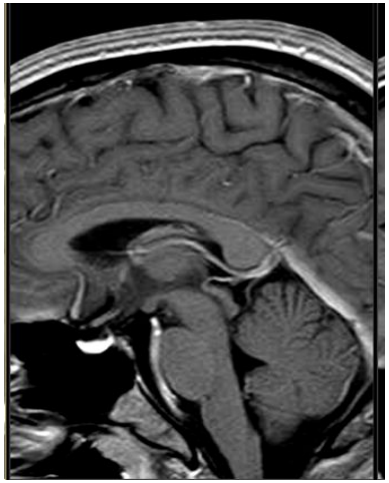
1/2018 MRI brain with contrast:
No lesion

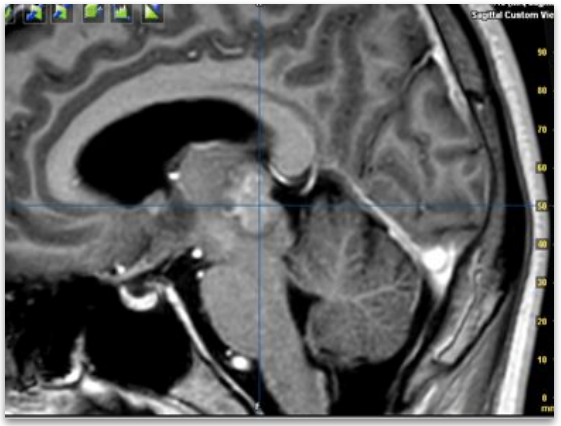
↓

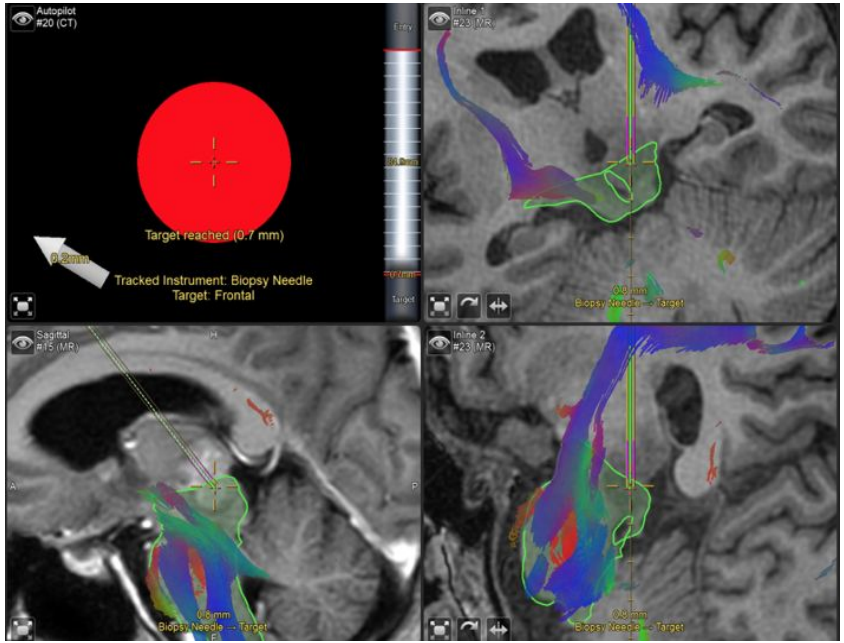
Worsening diplopia on follow up in 2019

↓

6/2020 MRI brain with contrast:
Pineal region tumour







On admission to Neurosurgery, also noted:

Polydipsia + polyuria → consistent with DI
Also noted low fT4

Serum and CSF tumour markers (AFP, alpha fetoprotein, human chorionic gonadotropin):
Normal

Varioguide frameless stereotactic biopsy of pineal region tumour performed

Pathology:
Pineal germinoma

...So what?

→ *Focal signs in the absence of radiological evidence*

→ *Latency of radiologically discrete lesion*

This phenomenon also seen in some patients with *suprasellar germinoma,* presenting with symptoms of diabetes insipidus *prior* to radiological evidence of discrete lesions, as reported in literature...

TABLE 3. Imaging profile

Patient no.	Sex	Age	Original head MRI interpretation	Retrospective evaluation	Interval[a]	Follow-up	Biopsy results
1	M	2 yr 8 m	Thick stalk	Thick stalk	6 m	Increased stalk thickening	Pending
2	F	5 yr 8 m	Normal	Normal	8 m	Thick stalk, full pineal	Germinoma
3	M	8 yr 2 m	Normal	Thick midstalk	9 m	Normal stalk and pineal	Not done
4	F	10 yr 5 m	Normal	Normal	3 m	Thick, nodular stalk	Germinoma
5	M	10 yr 8 m	Thick stalk	Thick stalk	12 m	Suprasellar and infundibular mass	Germinoma
6	M	11 yr 4 m	Thick stalk and small pituitary	Thick stalk and small pituitary	3 m	Reduced stalk thickening	Inflammation[b]
7	F	11 yr 8 m	Thick stalk (no contrast)	Thick stalk	11 m	Extensive enhancement	Germinoma[c]
8	F	13 yr	Normal	Thick stalk	14 m	Enhancement of 3rd ventricular floor	Germinoma
9	F	18 yr	Thick stalk and abnormal enhancement	Thick stalk	8 m	Normal scan status post-bx and tx	Germinoma

m, Months; bx, biopsy; tx, therapy.
[a] Interval from presentation to first follow-up MRI with a notable change.
[b] Mononuclear inflammatory cells.
[c] First biopsy was of inflammatory cells; second biopsy was germinoma (see text).

Mootha et al [1] reported in a study of nine children, clinical latency between appearance of symptoms to a biopsy-proven diagnosis of germinoma based on initial MRI findings as seen in the table above

In our series, 44.4% of patients with suprasellar GCTs received an initial diagnosis of idiopathic central DI because the tumour was not detectable in the initial MRI. In these patients, the mean time elapsed from the onset of symptoms with normal MRI findings to the evidence of suprasellar tumour in MRI was 21 months, which was consistent with

In another retrospective review of intracranial germ cell tumours by Carpio et al [2], a similar phenomenon was observed

What about pineal germinoma?

Table 1 Summary of 17 patients with intracranial GCT and delayed diagnosis

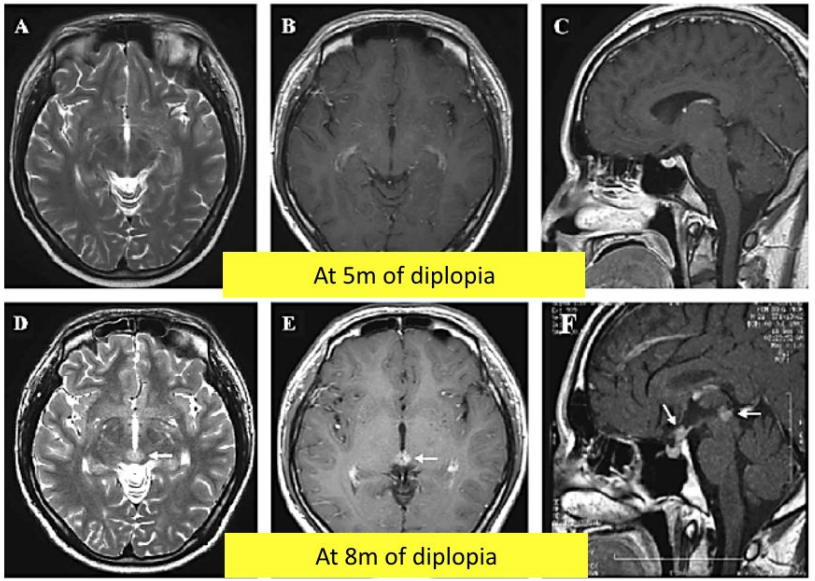
	Case no.	Sex	Age at diagnosis (yr)	Initial symptom	Initial MRI	Initial serum β-HCG[a]	Initial serum AFP[b]	Prodrome I (mo)	Prodrome II (mo)	Number of MRI before diagnosis	MRI at diagnosis	Serum β-HCG at diagnosis[c]	Serum AFP at diagnosis[d]	Biopsy	Diagnosis	Final status	OS (mo)
Suprasellar group	1	M	12	CDI	Normal	NA	NA	64	64	3	Suprasellar mass	15	<5	Endo	GE	Alive	85
	2	F	8	CDI	Loss of HSPH	NA	NA	11	5	2	Suprasellar mass	<3	<5	TSA	GE	Alive	139
	3[e]	M	14	CDI	Loss of HSPH	NA	NA	10	7	2	Bifocal masses	<3	<5	Endo	GE	Dead	50
	4[e]	M	15	CDI	TPS (equivocal)	<3	9	31	24	4	Bifocal masses with seeding	<3	8	Endo	GE	Alive	72
	5	F	8	CDI	TPS (equivocal)	<3	<3	33	24	3	Suprasellar/stellar mass	3.1	1.3	Open	GE	Alive	49
	6	F	12	CDI	TPS (overt)	NA	NA	7	4	3	No change	5	<3	Open	GE	Alive	162
	7	M	13	CDI	TPS (overt)	NA	NA	12	10	3	TPS more prominent	<5	<3	Open	GE	Alive	168
	8	F	17	CDI	TPS (overt)	<3	<5	44	21	4	Suprasellar mass	5	<3	TSA	GE	Alive	68
	9[e]	M	29	Blurred vision	TPS (equivocal)	NA	NA	9	8	2	Bifocal masses	31	580	No	Mixed GCT	Alive	12
Basal ganglia group	10	M	15	Vomiting, hiccup	BG type I	NA	NA	22	13	4	Bilateral BG masses with seeding	<3	<5	ST	GE	Alive	73
	11	M	9	Hemiparesis	BG type I	NA	NA	16	9	4	BG mass	6	<5	ST	GE	Dead	25
	12	M	13	Hemiparesis	BG type I	NA	NA	41	30	2	Right BG mass/ left subtle lesion with seeding	92	<5	ST	Mixed GCT	Dead	47
	13	M	17	Hemiparesis	BG type I	8	<5	28	22	5	BG mass	<3	<5	ST	GE	Dead	86
	14	M	18	Hemiparesis	BG type I	NA	NA	10	9	5	No change	<3	<5	ST	GE	Alive	12
	15	M	15	Hemiparesis	BG type II	<1	<1	48	15	5	No change	2.7	1.1	ST	GE	Alive	45
Pineal group	16	M	8	Precocious puberty	Normal	46	<5	10	10	3	Pineal mass with bleeding	11,510	<5	Resection	Chorioca	Alive	118
	17	M	13	Precocious puberty	Normal	<3	<3	86	26	2	Pineal mass	13.2	62.6	Endo	ImT	Alive	52

A retrospective cohort study by Phi et al [3] of 181 patients with intracranial germ cell tumour, 17 patients had a delayed diagnosis of more than 90 days since initial MRI imaging.

2 of these patients who presented with precocious puberty, went on to develop ***pineal region germinoma.*** Both ***initially had normal MRI*** scans

Another case report [4] of a 21 year old man who developed enhancing suprasellar and pretectal masses on ***subsequent MRI*** brain scans, presumed to be germinomas

Much like our patient, presented with a ***normal*** initial MRI, but florid ophthalmological signs including ***pupillary light-near dissociation, convergence-retraction nystagmus, and up-gaze palsy***



Moon SY, Kim JS, Choi KD, Park SH, Hwang JM, Park M. Isolated vertical diplopia as the initial manifestation of presumed pretectal and anterior hypothalamic germinomas. J Neuroophthalmol. 2005 Jun;25(2):105-8

The phenomenon of "radiological latency" is well documented in patients with suprasellar germinoma, but the literature documenting this same phenomenon in patients with pineal region germinomas is sparse.

Indeed the evidence exists and well demonstrated in select studies / case reports, and our case characterizes this phenomenon clearly
In fact, through a review of the literature, this phenomenon can be seen in intracranial germ cell tumours of other regions as well, including the basal ganglia

Clinical implications?

High index of suspicion in the absence of initial radiological evidence should the patient present with symptoms of diabetes insipidus, or ophthalmological signs such as those characterizing Parinaud syndrome

Adopt a follow up MRI protocol for suspected cases eg. **follow up scan every 6 months** in order to minimize time to diagnosis

References

1. Mootha SL, Barkovich AJ, Grumbach MM, Edwards MS, Gitelman SE, Kaplan SL, Conte FA. Idiopathic hypothalamic diabetes insipidus, pituitary stalk thickening, and the occult intracranial germinoma in children and adolescents. J Clin Endocrinol Metab. 1997 May;82(5):1362-7.
2. Cormenzana Carpio M, Nehme Álvarez D, Hernández Marqués C, Pérez Martínez A, Lassaletta Atienza A, Madero López L. Tumores germinales intracraneales: revisión de 21 años [Intracranial germ cell tumours: A 21-year review]. An Pediatr (Barc). 2017 Jan;86(1):20-27.
3. Phi JH, Kim SK, Lee YA, Shin CH, Cheon JE, Kim IO, Yang SW, Wang KC. Latency of intracranial germ cell tumors and diagnosis delay. Childs Nerv Syst. 2013 Oct;29(10):1871-81.
4. Moon SY, Kim JS, Choi KD, Park SH, Hwang JM, Park M. Isolated vertical diplopia as the initial manifestation of presumed pretectal and anterior hypothalamic germinomas. J Neuroophthalmol. 2005 Jun;25(2):105-8