

Case Study

Title: Parinaud syndrome in association with thalamic infarct in a young person

ABSTRACT

Aim: We report a case of Parinaud syndrome secondary to an acute left posteromedial thalamic infarct in a young person.

Presentation of Case: Patient's main presenting complaints were blurring of vision and diplopia. The main clinical manifestations were that of a severe restriction in upward gaze, and convergence-retraction nystagmus.

Discussion: Vertical gaze palsies have been well associated with midbrain lesions but more rarely associated with seemingly isolated thalamic lesions. This case report further supports current limited literature that suggests that thalamic lesions may also manifest as vertical gaze palsies. In addition, cases of cerebrovascular events are usually first seen in the Emergency Department where diagnoses are made and acute management is given. In this case, the patient was referred to the Eye clinic from the Emergency Department for visual symptoms. Parinaud syndrome was promptly recognised by the ophthalmologist upon examination and the decision for urgent brain imaging with referral to the neurologist was quickly made. Timely management of patient likely contributed to his favourable outcome.

Conclusion: This is a case of Parinaud syndrome secondary to an acute left posteromedial thalamic infarct in a young person without obvious midbrain involvement. This case highlights the important role of ophthalmologists in the early recognition of Parinaud syndrome, which can allow for prompt diagnosis and management. Timely diagnosis of Parinaud syndrome can be crucial to patient's outcome.

Key words: Parinaud syndrome, convergence nystagmus, supranuclear palsy

INTRODUCTION

30 Parinaud syndrome, now better known as dorsal midbrain syndrome, is a supranuclear
31 paralysis of the vertical gaze resulting from damage to the mesencephalic tectum. It consists
32 of abnormalities of eye movement and pupil dysfunction, namely vertical gaze palsies,
33 convergence-retraction nystagmus, convergence bias with horizontal saccades, light-near
34 dissociation, corectopia, spastic-paretic accommodation and pathological lid retraction. It
35 results from direct or compressive injury to the dorsal midbrain, and can arise from a variety
36 of causes, such as pineal, midbrain or 3rd ventricle tumors, aqueductal stenosis, multiple
37 sclerosis, arteriovenous malformations, encephalitis, obstructive hydrocephalus, uncal
38 herniation, and cerebrovascular disorders.¹⁻¹¹ While lesions of the mesencephalic reticular
39 formation are known to produce vertical gaze palsies, herein, we report an interesting case of
40 Parinaud syndrome which manifested in a young patient with thalamic infarction.

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43 CASE REPORT

44

45 We report an interesting case of a 35-year-old Indian male who was referred by the
46 Emergency Department to the Department Of Ophthalmology and Visual Sciences, Khoo
47 Teck Puat Hospital, Singapore, for an acute onset of bilateral painless blurring of vision
48 associated with diplopia of 3-day duration. His symptoms first started when he was seated
49 down and having his breakfast. They were persistent and did not improve or worsen with
50 time. He had no history of trauma or fall. There was no associated focal numbness or
51 weakness, headache, nausea or vomiting. The patient was a smoker of 8.5 pack years, and
52 was diagnosed with diabetes mellitus type 2 three years ago. He was followed up by a private
53 general practitioner and was taking oral hypoglycemic agents. However, there was no record
54 of his glycaemic control available and patient was also not sure of his diabetic control. He
55 denied previous hypoglycemic episodes. He had no other known ischemic risk factors such
56 as hypertension, ischemic heart disease or hyperlipidemia, and no prior ocular history.

57

58 On examination, distant Snellen visual acuity was 6/15 for both eyes, best corrected with
59 pinhole to 6/12 in the right eye and 6/9 in the left eye. Refraction was not performed. Patient

60 did not have a history of wearing glasses or contact lens. Direct and consensual pupillary light
61 reflexes were normal. There was no relative afferent pupillary defect. His lenses were clear.
62 Intraocular pressure was normal. Anterior and posterior segments were unremarkable.
63 However, patient had a severe restriction in upward gaze and a mild restriction in downward
64 gaze. There was also convergence-retraction nystagmus on attempted upward gaze. Doll's
65 head maneuver elevated the eyes. Eye movements were otherwise full in lateral gazes.
66 Binocular vertical diplopia was present for both far and near vision. There was convergence
67 bias with horizontal saccades. He did not have light-near dissociation, corectopia or Collier's
68 sign. Bell's phenomenon and skew deviation were not investigated. Figure 1 shows the
69 clinical pictures of patient's eyes in different directions of gazes. However, we recognize that
70 the data shown in pictures do not always correlate with the clinical examination.
71
72 On further examination, patient had normal cranial nerve function, full power in all limbs, and
73 intact sensation. However, he had unsteady gait and was unable to perform tandem gait.
74 Patient had complained that he was feeling too giddy to do so. Glasgow Coma Scale was 15.
75
76 Based on these findings, a provisional diagnosis of Parinaud syndrome was made. Possible
77 causes included brain tumors in the pineal gland, such as intracranial germinomas, as well as
78 multiple sclerosis, arteriovenous malformation and stroke. Patient was admitted on the same
79 day and magnetic resonance imaging (MRI) and angiography of the brain confirmed an acute
80 infarct in the left posteromedial thalamus, extending slightly into the left cerebral peduncle.
81 Figures 2, 3 and 4 show various cuts of the MRI performed. A neurologist further confirmed
82 the diagnosis. The patient's systolic blood pressure was noted to range from 100 to
83 120mmHg while his diastolic blood pressure had ranged from 70 to 80mmHg. Lipid panel
84 revealed total cholesterol of 5.13 mmol/L, triglycerides of 1.92 mmol/L, high-density
85 lipoprotein (HDL) of 0.81 mmol/L, low-density lipoprotein (LDL) of 3.88 mmol/L, and a
86 cholesterol to HDL ratio of 6.33, which essentially put the patient at a high risk for
87 cardiovascular diseases. His diabetic control was unacceptable with a glycated HB of 9.2%
88 (77 mmol/mol). Thyroid, liver and renal function tests were unremarkable. Calcium panel and
89 magnesium level were within normal range. Full blood counts, peripheral blood film,

90 prothrombin time, international normalized ratio, and activated partial thromboplastin time
91 were normal. A young stroke work-up comprising of anti-nuclear antibody, anti-double-
92 stranded-DNA antibody, lupus anticoagulant and anti-cardiolipin antibodies were negative.
93 Homocysteine, anti-thrombin III, activity profiles of protein C and S were normal too.
94 Ultrasound Doppler of carotid arteries was unremarkable.
95
96 Patient was started on aspirin 100mg once every morning, and simvastatin 20mg once every
97 night. To improve control of his diabetes, physicians made adjustments to his oral
98 hypoglycemic agents, and provided dietary and lifestyle advice. Patient was also given
99 counselling on smoking cessation.

100

101 Over the course of his 4-day inpatient stay, patient experienced symptomatic and clinical
102 improvement, with resolving giddiness and diplopia as his restriction in upward gaze
103 improved. He was subsequently able to ambulate well prior to discharge.

104

105 **DISCUSSION**

106

107 Vertical gaze palsy has been reported to be caused by lesions involving bilateral rostral
108 interstitial nucleus of medial longitudinal fasciculus (riMLF) or unilateral posterior commissure,
109 while convergence nystagmus is usually caused by a lesion near or within the dorsal
110 mesencephalon.^{12,13} Later reports demonstrated that vertical gaze palsy and convergence
111 nystagmus can result from unilateral riMLF lesion.¹⁴⁻¹⁷ Each riMLF contain burst neurons for
112 both upward and downward movements.¹⁸ A unilateral lesion of the riMLF may occasionally
113 cause combined upgaze and downgaze palsies, perhaps by disrupting bilateral upward gaze
114 excitatory and inhibitory inputs and unilateral downgaze excitatory inputs.¹⁹ Fibres
115 responsible for upward gaze cross rostrally and posteriorly between the riMLF nuclei (near
116 the pineal body) through the posterior commissure and are subject to interruption before
117 descending and terminating in the contralateral oculomotor nuclei. On the other hand,
118 pathways for downward gaze project directly downward from the riMLF to the oculomotor
119 complex. This may be a reason for the dissociation of the upward and downward gaze

120 palsies, and the reason why upward gaze appears to be affected more than downward
121 gaze.²⁰ There have been a few anatomo-clinical cases which demonstrated that supranuclear
122 palsies of the downward gaze were related to paramedian lesions of the rostral
123 mesencephalon involving the riMLF, the nucleus of Cajal, and/or their afferent and/or efferent
124 pathways, while supranuclear palsy of the upward gaze was related to lesions of the posterior
125 commissure.¹²

126
127 Lesions of the mesencephalic reticular formation including the nucleus of Darkschewitsch, the
128 rostral interstitial medial longitudinal fasciculus, the interstitial nucleus of Cajal, and the
129 posterior commissure, are known to produce vertical gaze palsies.²¹ In general, vertical gaze
130 palsies have been attributed to associated lesions of vertical eye movement control centres in
131 the rostral midbrain rather than the thalamic injury. The frequent coexistence of both midbrain
132 and paramedian thalamic infarct is related to their vascular supply; a single vessel arising
133 near the top of the basilar may branch to supply both the paramedian region of the thalamus
134 and the rostral medial mesencephalon.²² There have been only a few cases with MRI-
135 documented medial thalamic infarctions without midbrain involvement who presented with
136 vertical gaze palsies.^{21,23} In our case, patient had vertical gaze palsy and was found to have
137 an acute infarct in the left medial thalamus. There was no obvious midbrain involvement on
138 the imaging studies. It could be that microinfarcts in the dorsal mesencephalic structures
139 sharing a common vascular supply were too small to be detected,^{21,24} or that the supranuclear
140 inputs were interrupted,²¹ possibly by the surrounding edema resulting from the infarct.
141 Perhaps serial brain imaging done over a space of time could have provided more
142 information.

143
144 Convergence-retraction nystagmus is believed to be a saccadic disorder rather a nystagmus
145 because the primary adductive movements are asynchronous adducting saccades.²⁵ It is not
146 a true nystagmus because there is no slow phase. Convergence and globe retraction occurs
147 when attempting upward saccades. Limitation of upward gaze as well as defective upward
148 saccades and pursuit are always present. Globe retraction occurs as a result of co-
149 contraction of the medial rectus muscles. It is often best elicited by down-moving optokinetic

150 nystagmus stimulus since upward movement of the eyes is replaced by convergence
151 retraction movement. Convergence-retraction nystagmus has been reported as a classic
152 finding in extensive and bilateral lesions of the dorsal midbrain, which are usually neoplastic
153 and signal poor prognosis.²⁶ However, in our case, while the patient did have convergence-
154 retraction nystagmus, he did not have extensive or bilateral lesions of the dorsal midbrain and
155 had experienced instead, a good functional recovery. Doll's head maneuver could elevate the
156 patient's eyes as it was a supranuclear vertical gaze palsy. In this case, patient's Bell's
157 phenomenon would have been preserved since there was no lower motor neuron palsy. The
158 patient was having diplopia possibly from a skew deviation, or a subtle hypertropia or
159 hyperphoria. Unfortunately, these signs were not investigated and picked up clinically.
160
161 Benign course with favourable outcome has been reported for cerebrovascular events with
162 conservative management.^{26,27} On the other hand, surgical treatment such as transpositions
163 and inferior rectus recessions have also demonstrated improvement in upgaze limitation and
164 convergence-retraction nystagmus.²⁸ Parinaud syndrome associated with brain tumors in
165 pineal gland or midbrain is seen more frequently in younger patients, while in older patients, it
166 is more commonly associated with cerebrovascular disorders such as hemorrhage, ischemia
167 and infarct. In our case study, although the patient was young, he had a few ischemic risk
168 factors such as diabetes and a smoking history. Hyperlipidemia was only detected after
169 investigations. He had no autoimmune or thrombophilic disorders. He experienced
170 symptomatic and clinical improvement with non-invasive and conservative management.
171
172 Prognosis for Parinaud syndrome depends on the causative factor. Parinaud syndrome has
173 been classically associated with young patients with brain tumors in the pineal gland or
174 midbrain, with intracranial germinomas being the most common lesion. Generally, intracranial
175 germinomas have excellent prognosis due to their sensitivity to radiotherapy.²⁹ Parinaud
176 syndrome can also manifest in patients with multiple sclerosis, or following stroke of the upper
177 brainstem, like the patient in this case. Factors that led to his favourable outcome likely
178 included his young age, lack of existing co-morbidities and the fact that the infarct was not

179 extensive. Patient's long-term outcome would likely be dependent on his control of his
180 cardiovascular risk factors.
181
182 Cases of cerebrovascular events are usually first seen by the Emergency Department where
183 diagnoses are made and acute management is given. In this case, the patient was referred to
184 the Eye clinic from the Emergency Department for visual symptoms. Parinaud syndrome was
185 promptly recognised by the ophthalmologist upon examination and the decision for urgent
186 brain imaging with referral to the neurologist was quickly made. Timely management of
187 patient likely contributed to his favourable outcome. Patients presenting with symptoms such
188 as vertical gaze palsies and convergence-retraction nystagmus should prompt physicians to
189 perform neuroimaging studies quickly, especially if risk factors for cerebrovascular events are
190 present.

191

192 CONCLUSION

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194 This is a case of Parinaud syndrome secondary to an acute left posteromedial thalamic infarct
195 which extended slightly into the left cerebral peduncle. This further supports current literature
196 which suggests that Parinaud syndrome can manifest in thalamic infarctions even without
197 obvious midbrain involvement. Patient's main presenting complaint was diplopia with blurring
198 of vision, and the main clinical manifestations were that of a severe restriction in upward
199 gaze, and convergence-retraction nystagmus. This case highlights the important role of
200 ophthalmologists in the early recognition of Parinaud syndrome, as it may be the sole
201 manifestation of cerebrovascular events. Early recognition can allow for timely referral and
202 prompt imaging for diagnosis and subsequent management. This can be crucial to patients'
203 outcome.

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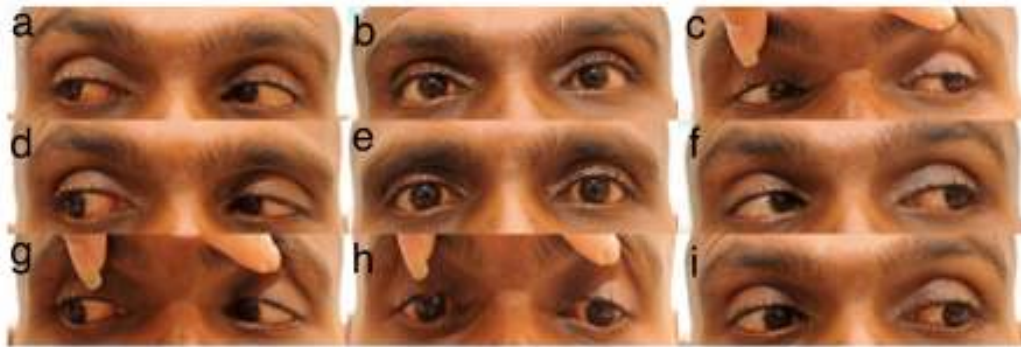
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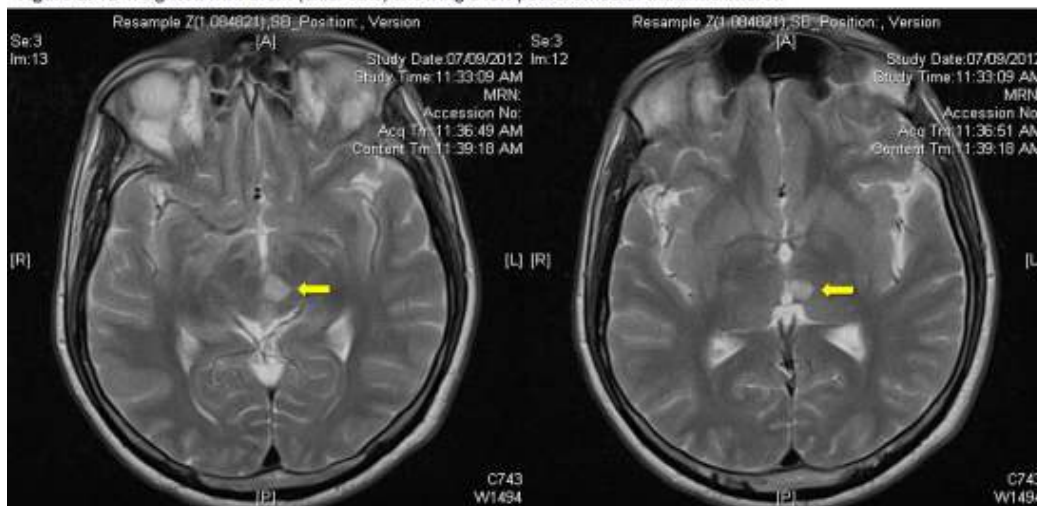
274 FIGURES

Figure 1. Clinical pictures of patient's eyes in different directions of gazes



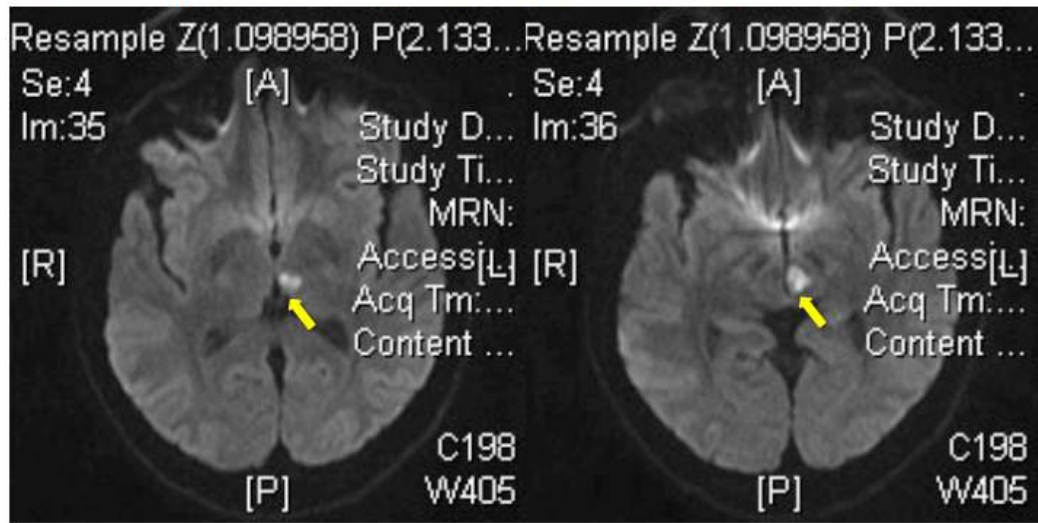
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Figure 2. T2-weighted MRI brain (axial cuts) showing a left posteromedial thalamic infarct.



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Figure 3. Diffusion MRI brain (axial cuts) showing the left thalamic infarct.



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Figure 4. T2 FLAIR MRI brain (coronal cut) showing the left thalamic infarct.

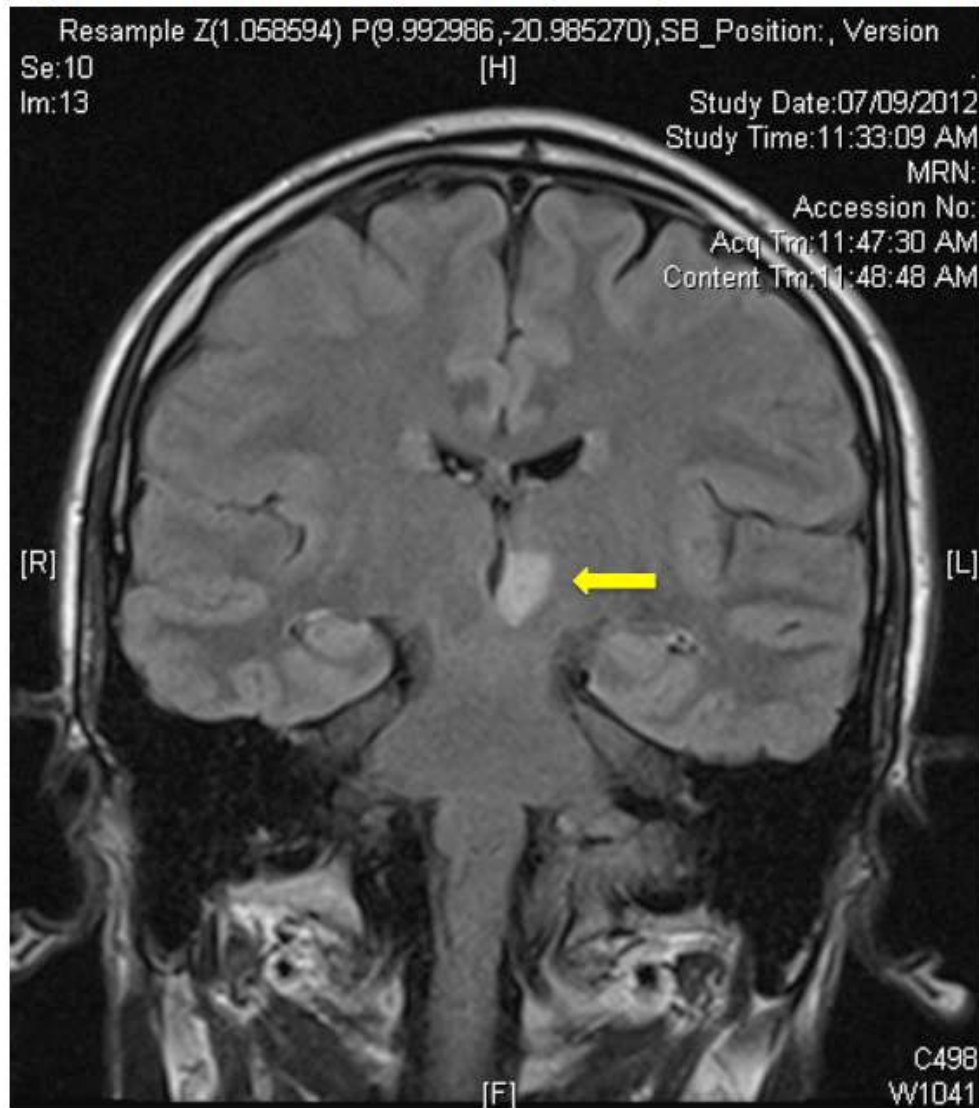


FIGURE LEGEND

Figure 1 shows the clinical pictures of patient's eyes in different directions of gazes. **Figure 1b** shows a severe restriction in upward gaze while **Figure 1h** shows a mild restriction in downward gaze.

Figure 2 shows T2-weighted MRI of the patient's brain in axial cuts. The yellow arrows point to the acute left posteromedial thalamic infarct.

289 **Figure 3** shows diffusion MRI of the patient's brain in axial cuts. The yellow arrows point to
290 the acute left posteromedial thalamic infarct.
291
292 **Figure 4** shows T2 FLAIR MRI of the patient's brain in a coronal cut. The yellow arrow points
293 to the acute left medial thalamic infarct.
294