Journal of Acute Disease

Case Report

doi: 10.4103/2221-6189.268411 jadweb.org

Dorsal midbrain syndrome secondary to pineal gland tumours: case series and review on manifestations, management and outcome

Wendy Ong Chin Feng[1,4], Logandran Vijaya Kumar[1,4], Mohd Ezane Aziz[2,4], Faezahtul Arbaeyah Hussain[3,4], Wan-Hazabbah Wan Hitam[1,4]✉

Department of Ophthalmology[1], Radiology[2], Pathology[3], School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, 16150 Kelantan, Malaysia

[4]Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia

ARTICLE INFO

Article history:
Received 5 August 2019
Revision 5 September 2019
Accepted 20 September 2019
Available online 1 October 2019

Keywords:
Dorsal midbrain syndrome
Parinaud syndrome
Pineal gland tumour

ABSTRACT

Dorsal midbrain syndrome or Parinaud syndrome is a supranuclear brainstem syndrome involving the vertical gaze centre. These are case series with three patients who were diagnosed with dorsal midbrain syndrome secondary to pineal gland tumours. The prognosis varied depending on tumour types, age of presentation and treatment received. All of them were presented with life-threatening obstructive hydrocephalus. Our first patient was successfully treated with emergency surgery followed by radiotherapy. He regained normal visual acuity and full recovery of his ocular movement. Second and third patients had undergone surgery for raised intracranial pressure. Both had an inoperable pineal gland tumour. As for our second patient, we detected a worsening of vertical gaze during his four years follow-up. However, his bilateral good visual acuity was preserved. The third patient passed away as a result of uncontrolled enlarging tumour. We also briefly reviewed the clinical presentation, diagnosis, and therapeutic approach of the three patients. One of the caveats is that urgent radiological study is crucial to differentiate the tumour type via the pathognomonic features and to delineate the tumour extension. The preferable treatment options vary among each tumour type. A multidisciplinary approach is crucial in early detection, in addition to treatment initiation and long term follow up to achieve a better outcome.

1. Introduction

The vertical gaze centre is in proximity to the superior colliculus, with some of the main nuclei being the interstitial nuclei of Cajal and the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF). Neurons pass via the riMLF to the oculomotor and trochlear nerve nuclei to control the vertical gaze. The suggested locations of a full syndrome are lesion of the dorsal midbrain, bilateral lesions of the pretectal region or a large unilateral tegmental lesion[1,2]. We presented three cases of pineal gland tumour with dorsal midbrain syndrome. These cases are mainly highlighted from ophthalmology point of view as it is rarely being discussed in other literature.

✉Corresponding author: Wan-Hazabbah Wan Hitam, Department of Ophthalmology, School of Medical Sciences, Health Campus, Universiti Sains Malaysia, Kubang Kerian, 16150 Kelantan, Malaysia; Hospital Universiti Sains Malaysia, Kubang Kerian, Kelantan, Malaysia.
Tel: +609-7676362; +6012-9833535
E-mail: hazabbah@usm,.my; hazabbah@yahoo.com
Fax: +609-7653370

How to cite this article: Feng WOC, Kumar LV, Aziz ME, Hussain FA, Hitam Wan-Hazabbah W. Dorsal midbrain syndrome secondary to pineal gland tumours: case series and review on manifestations, management and outcome. J Acute Dis 2019; 8(5): 208-214.

2. Case reports

2.1. Case 1

The informed consent was obtained in a written form. Approval was obtained from the local ethics committee (Approved number is HUSM2019/B575258).

The first case is of a 21-year-old male patient who complained of persistent double vision for 2 months. The symptom was associated with right-sided throbbing headache. His visual acuity in the right eye was 6/7.5 and 6/6 in the left eye. Both pupils were equal and reactive to light. There was no relative afferent pupillary defect (RAPD). Both eyes were unable to elevate. Both anterior segments were normal. Fundoscopy showed bilateral normal optic discs and macula. Humphrey visual field (HVF) and Hess test results were also normal. Systemic examination was unremarkable. Computerised tomography (CT) scan of the brain suggested pineal gland tumour compressing the tectal plate. There was also dilatation of third and temporal horns of bilateral lateral ventricles. Based on the outcomes of the tests mentioned earlier, patient was then diagnosed as having incomplete dorsal midbrain syndrome.

In view of the early sign of obstructive hydrocephalus, patient was counselled for surgical intervention and biopsy. However, patient was undecided and was discharged. After 4 months, patient came to the hospital complaining of worsening headache and projectile vomiting. He also had progressively reduced vision in both eyes for a month. Upon examination, patient appeared to be drowsy. Visual acuity in the right eye was 6/60 and the left eye was 6/120. Both pupils were equal but sluggish. Extraocular muscle movement was both restricted up-gaze (-2) and abduction (-4). Other gazes were normal. Fundoscopy revealed grade 2 papilloedema due to compressive optic neuropathy. Urgent magnetic resonance imaging (MRI) was performed. The MRI showed that the pineal gland tumour had increased in size (Figure 1). In view of deteriorating consciousness level and increasing size of the tumour, an emergency right burr hole with endoscopic third ventriculostomy and biopsy was performed. Histopathological examination results turned out to be pineal gland germinoma (Figure 2). After which patient underwent radiotherapy for 3 months.

One-month after treatment, patient's visual acuities had improved (RE 6/30, LE 6/45) with preserved optic nerve function on both eyes. A remnant of up-gaze palsies (-2) with a resolved horizontal gaze palsies were also observed. A year after surgery, a follow up was conducted. Outcome of the follow-up revealed that patient had regained both his visual acuity to 6/9 bilaterally. However, both his visual field were constricted. His up-gaze recovered completely with full ocular movement. MRI of the brain also showed significant reduction of pineal tumour size (Figure 3).

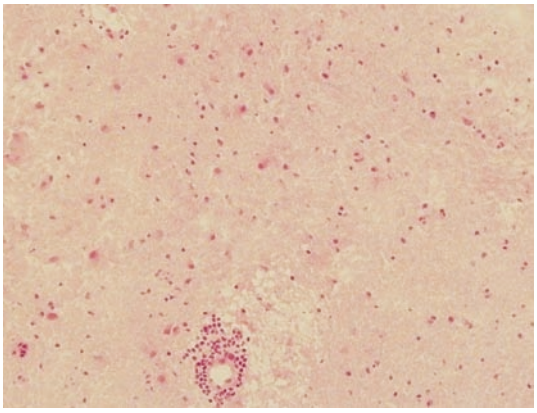

Figure 2. Frozen section of pineal gland tumour (H&E 200). Section of glial tissue exhibits an increased number of astrocytes with the presence of scattered neurons. A blood vessel with perivascular lymphocytes infiltrate is also present.

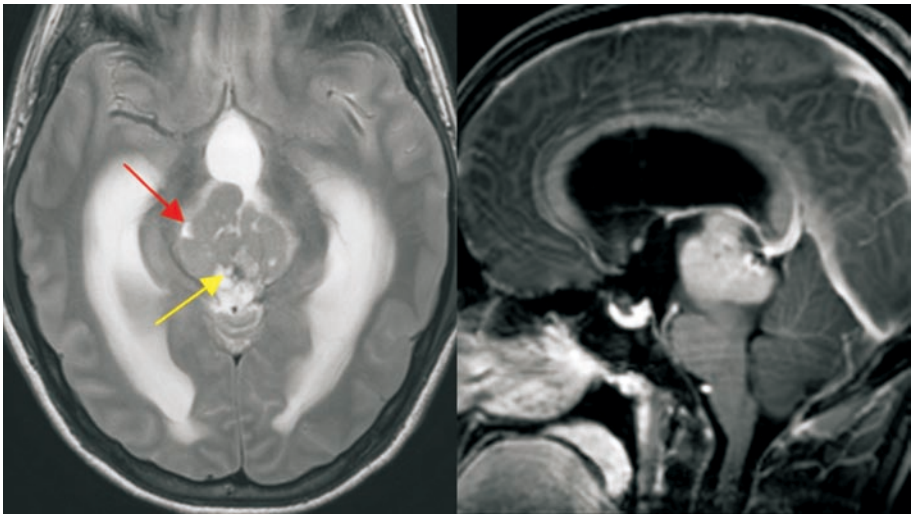

Figure 1. Urgent magnetic resonance imaging shows that the pineal gland tumour had increased in size. Axial and sagittal T2 MRI exhibits isointense to grey matter with areas of cyst formation shown by red arrow. Low signal intensity in the posterior part of the mass represents calcification shown by yellow arrows. The pineal gland tumour compressed the aqueduct of Sylvius causing hydrocephalus. The MRI features suggested of germinoma.

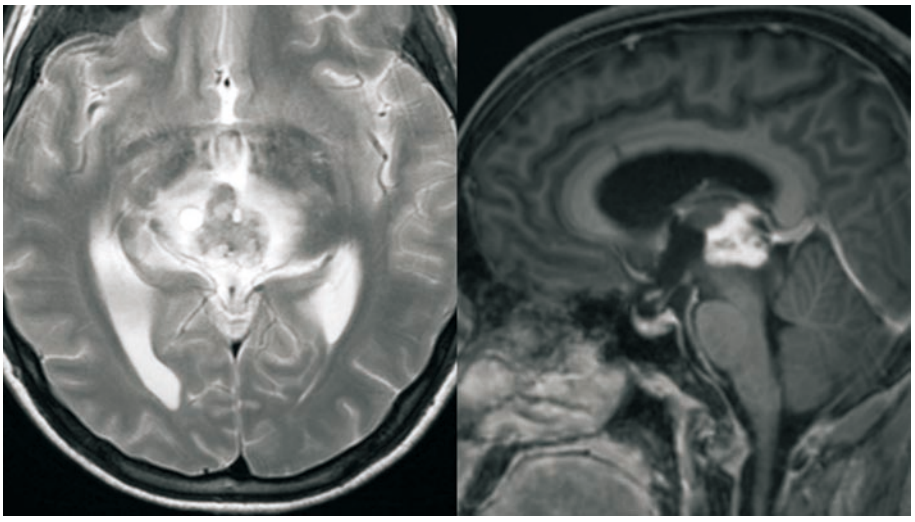

Figure 3. Axial and sagittal T2 weighted MRI images show a significant reduction in the size of pineal gland mass with less of hydrocephalus.

2.2. Case 2

The informed consent was obtained in a written form. Approval was obtained from the local ethics committee (Approved number is HUSM2019/B575258).

This is a case involving a 6-year-old male patient who experienced intensive fatigue and sleepiness for 2 months. The symptoms were associated with vomiting and double vision. The initial ocular examination showed both visual acuities were 6/9. There was restriction in the abduction and Grade 3 papilloedema. His anterior segment and intraocular pressure were normal. We then discovered the presence of false localising sign with bilateral abducent nerve palsy. An urgent CT brain showed an enlargement of pineal gland causing obstructive hydrocephalus and cerebral oedema (Figure 4). Patient underwent ventriculoperitoneal shunt and endoscopic biopsy for obstructive hydrocephalus. Intraoperatively, the tumour appeared to be multilobulated, glistening white in colour and firm inconsistency. Tuff of hair within the tumour capsule is mixed with yellowish substance were present. HPE revealed pineal gland mature teratoma (Figure 5). Alpha-fetoprotein (AFP) and the beta subunit of the gonadotrophic chorionic hormone were normal. Postoperatively, his vision remained good. His best-corrected visual acuity result was right eye 6/6 and left eye 6/7.5. There was no RAPD. The eye movement was normal in both eyes. The anterior and posterior segments in both eyes were unremarkable. MRI postoperatively showed resolving hydrocephalus (Figure 6).

After a month, the patient's mother started to notice that he had an abnormal head posture. The patient tends to turn his face towards his right side while reading and writing. Upon examination, we discovered that his up-gaze movement in both eyes were completely restricted. At the same time, we detected convergence retraction nystagmus and pupil light near dissociation. He was diagnosed as having complete Parinaud syndrome. Tests of optic nerve function, other cranial nerves and peripheral nerves all showed normal results. Urgent MRI of the brain showed enlargement in the size of the tumour. The patient was scheduled for craniectomy and tumour excision, but the operation was abandoned in view of the severely oedematous brain.

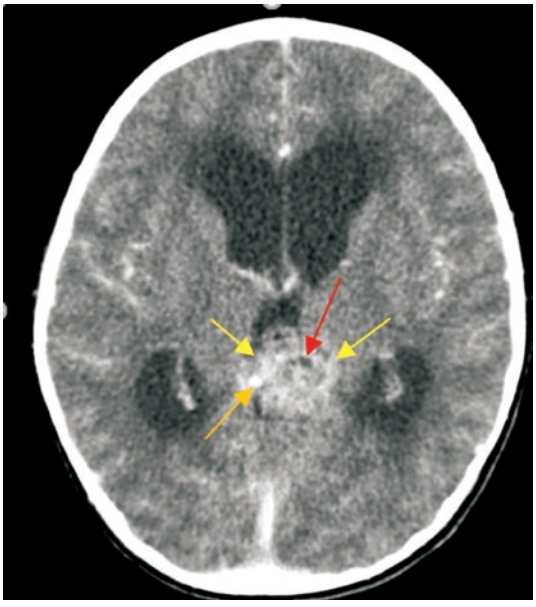

Figure 4. Urgent CT scan of the brain. It shows an enlargement of pineal gland causing obstructive hydrocephalus and cerebral oedema. Contrast-enhanced CT scan of the brain exhibits a heterogeneously enhancing, lobulated, mixed solid and cystic mass at pineal gland region shown by yellow arrows. Peripheral calcification is shown by orange arrows and cystic region shown by red arrow consistent with pineal teratoma. It also shows the presence of hydrocephalus and cerebral oedema evidenced by generalised effacement of the cerebral sulci.

The patient, who is currently ten years old, had undergone 4 years of regular follow-up at the hospital. Thus, patient remains clinically stable and asymptomatic. During the follow-up sessions, we discovered the presence of restriction in ocular movement involving the down-gaze in addition to up-gaze palsies

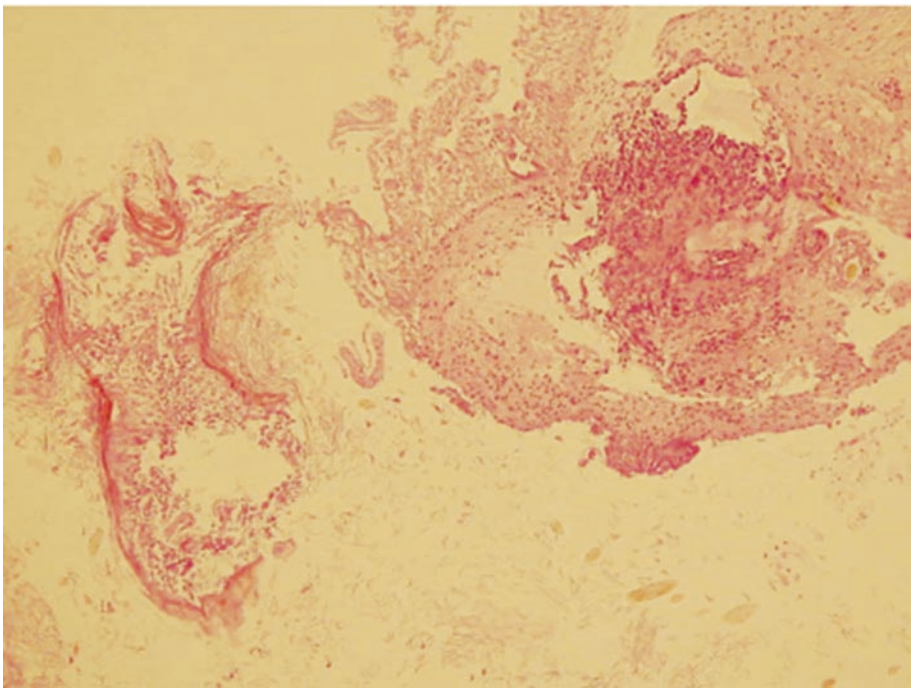

Figure 5. Section of pineal gland tumour showing fragments of stratified squamous epithelium admixed with hair follicles with scattered mature lymphocytes.

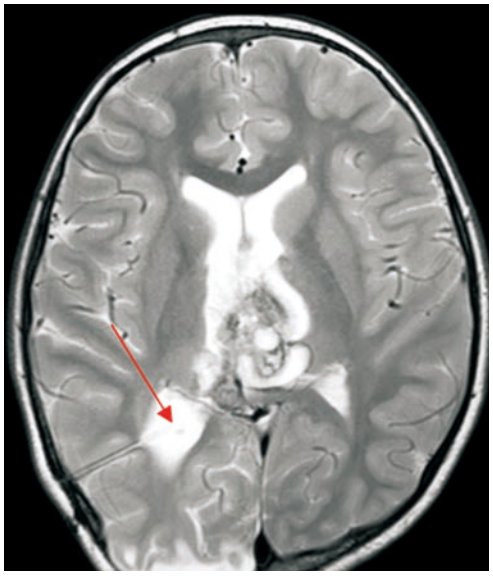

Figure 6. T2 weighted MRI image in axial view post VP shunt placement through the right temporal region. The tip within the occipital horn of the right ventricle is shown by red arrow. There is a reduction in hydrocephalus.

bilaterally. There were also other signs such as convergence defect, convergence retraction nystagmus and pupil light near dissociation present. Although both his optic discs were pale temporally, his visual acuity remained at 6/9. Humphrey visual field test result was not considered due to low test reliability. There is no further plan for tumour excision or radiotherapy. This is in view of the high risk of complications arising during surgery as well as radiotherapy treatment. As such, the patient was recommended to have a regular follow up.

2.3. Case 3

The informed consent was obtained in a written form. Approval was obtained from the local ethics committee (Approved number is HUSM2019/B575258).

This is a case involving a 15-year-old boy who had headache for 3 weeks. The symptom was associated with diplopia, nausea and vomiting. Patient had good vision in both eyes. He was alert and conscious. There was no peripheral neurological deficits or cerebellar sign. A bilateral sixth cranial nerve palsy was also detected. CT scan of the brain showed a pineal gland tumour causing obstructive hydrocephalus and cerebral oedema (Figure 7). The patient underwent right stereotactic frontal burr hole and ventriculoscopic biopsy and endoscopic third ventriculostomy. HPE result showed undefined malignant tumour cells. Both alpha-fetoprotein (47.53) and beta human chorionic gonadothopin (1 477) were raised. One-month after operation, the patient noticed that his diplopia was deteriorating despite resolving headache. Repeat CT scan of the brain showed the pineal gland tumour had increased in size with worsening obstructive hydrocephalus, intratumor bleed surrounding the oedema (Figure 8).

Further ocular examination showed that visual acuity in the right eye was 6/9 and left eye was 6/6. There was no RAPD. Extraocular muscle movement was restricted on up-gaze (-4) and downgaze (-2) in both eyes with convergence defect. There was no convergence retraction nystagmus or diplopia. Confrontation and visual field tests were also normal. Both anterior segments were normal with intraocular pressure of 18 mmHg. Swelling

of patient's optic discs on both eyes had subsided. Based on the outcome of the tests results conducted, we diagnose the patient as having incomplete Parinaud syndrome. He was scheduled for radiotherapy treatment. Unfortunately, he passed away as a result of progressive enlarging inoperable pineal gland tumour.

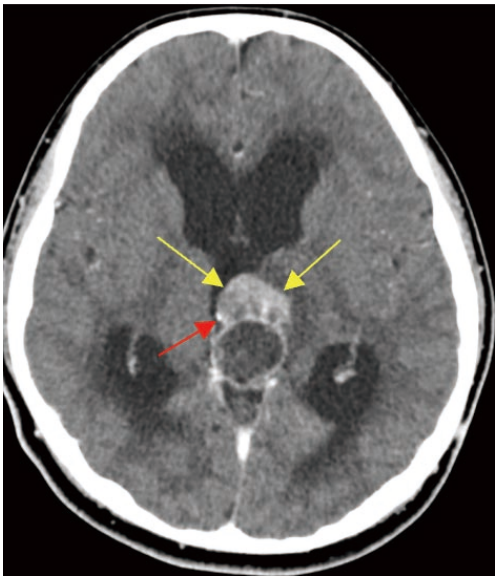

Figure 7. Preoperative contrast CT scan of the brain shows a heterogeneously enhancing, mixed solid cystic mass at pineal gland region (yellow arrows) with peripheral calcification (red arrow) consistent with pineal gland tumour causing obstructive hydrocephalus and cerebral oedema.

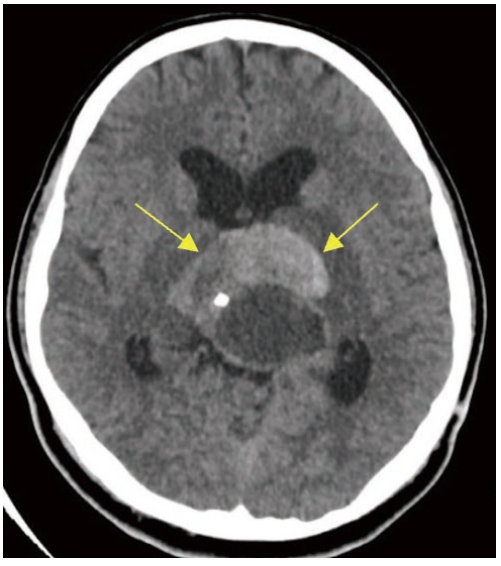

Figure 8. Post-operative plain CT scan of the brain in axial view showing an increase in size and intra-tumour bleed.

3. Discussion

The classic triad of Parinaud syndrome includes up-gaze palsy, pupillary light-near dissociation and convergence retraction nystagmus. These symptoms are usually found in 65% of patients with Parinaud's syndrome[3]. Other symptoms include accommodation spasm, lid retraction (Collier's sign) and loss of convergence. The up-gaze palsy occurs when the vertical gaze centre is affected. However, down-gaze is typically presented in such cases. It has been suggested that difference in the affected gaze is due to the pathways. The downward gaze is not affected because it is directed medially from the riMLF, whereas, the fibres for upward gaze are directed more laterally. Therefore, the up-gaze fibres are more predisposed to pressure effect from the surrounding lesion. Reverse Parinaud syndrome is rare where down-gaze instead of up-gaze palsy may be detected[3].

In addition, it is observed that patients with near dissociation to light, the pupils responded briskly with convergence but poorly to light. This could be attributed to pupillary light reflex pathway that the near reflex fibres which is located more ventrally than the light reflex fibres. As a result of the anatomical location of light reflex fibres, patients are more susceptible to the external compressive effect of mass lesions. Meanwhile, the convergence-retraction nystagmus is jerky associated with convergence and retraction of both eyes. This can be observed when the patient makes an attempt to look upwards. This is a clear sign to locate a lesion arising from dorsal midbrain. On the other hand, the postulated pathogenesis is caused by damage to the supranuclear fibres that has an inhibitory effect on the convergence and divergence neurons. This might lead to sustained neuronal discharge from the extraocular muscles[3].

The aetiology of Parinaud syndrome differs with ages. Neoplastic causes are more common in children and young adults, while vascular causes are more common in the middle-aged and elderly[2]. Parinaud syndrome is a well-known complication of pineal gland tumour (30%) that causes the pressure on the reflex centres in dorsal midbrain[3]. Pineal gland tumours account for 0.5% of all central nervous system tumours in adults, 1% in young adults (aged 20-34 years), and 2.7% in children (aged 1-12 years)[4]. Pineal tumours can be classified as germ cell tumours (50%-75%), pineal parenchymal tumours (14%-27%), gliomas, atypical rhabdoid/teratoid tumours, or other tumours such as papillary tumours of the pineal region. Histologically, tumours of germ cell origin with increasing malignancy include mature or benign teratoma, germinoma, immature or malignant teratoma, embryonic carcinoma, yolk sac tumour, choriocarcinoma[5,6]. Germinomas develop in the midline and are most common in the pineal gland (50%-65%). They affect males more than females (3:1), but in the pineal region, the ratio becomes 12:1. In addition, mean age at diagnosis is 10-12 years, with 90% under 30[7,8]. Most of the pineal gland tumours were found to be germinoma, followed by mature teratoma. Others include pilocytic astrocytoma, atypical teratoid rhabdoid tumour, mixed germ cell tumour, pineoblastoma and malignant teratoma[2].

Likewise, a case series done by Mary Ellen *et al.*[9], found that 51% of patients with pineal gland tumour suffered Parinaud syndrome. Majority of the subjects that ranging from 5 months old to 20 years old was suffered from pineoblastoma (37%) followed by germinoma (34%) and mixed germ cell tumour (14%). For the clinical outcome, 47% of patients remained static, 41% improved

clinically and only 12 % experienced a complete resolution.

Henceforth, to further understand the pineal gland tumours related Parinaud syndrome, we did a literature search from Pubmed with keywords such as pineal gland tumour, germ cell tumours, germinoma, teratoma, Parinaud syndrome, we found several papers on pineal gland tumours related Parinaud syndromes from the year 1995 till 2018. There are altogether 5 related case reports[10-14]. It was reported in the research papers that all the five patients were male with age ranging from 9 to 33 years old. All of them had symptoms of raised intracranial pressure as seen in our patients. Menon *et al.*[10] from India reported a case who presented with reversed Parinaud syndrome where there is a total loss of downward eye movement rather than an upgazed palsies that typically found in Parinaud syndrome. Other features of Parinaud syndrome include bilateral upper lid retraction, light near dissociation and convergence insufficiency. Compressive optic neuropathy was detected in 2 patients[12,13] as a result of raised intracranial pressure. Most importantly, though reading the 5 different research study, we found similarities in terms of symptoms of the 5 patients and our 3 case studies. The most significant is the compressive optic neuropathy which appears during the acute presentation of the illness. However, their visual outcome was good as prompt surgical intervention was carried out to relieve the raised intracranial pressure. Four out of those five patients mentioned in the research papers were diagnosed to be having pineal gland germinoma. There are various methods employed in the treatment of tumours which is also dependent on whether it is operable or inoperable. When dealing with operable tumour, surgical removal of the tumour is recommended followed by adjuvant radio-chemotherapy[10,11]. On the contrary, for a more extensive inoperable tumour, radiotherapy or a chemotherapy is the first line of treatment[12,13].

Pineal gland tumour can be diagnosed and monitored by neuroimaging. In view of the possibility that biopsy might leads to mortality and severe morbidity, many studies have tried to determine the pathognomonic neuroimaging findings to differentiate each histological type. One of the studies done by Ryuji *et al.*[15]. found that local calcification was seen mostly in germ cells tumours, consisting of up to 70% while scattered calcifications were more commonly found in pineal parenchymal tumours. Besides that, germinoma usually has thick peritumoral oedema and bithalamic extension. Cystic components within the tumour were suggestive of non-germinomatous germ cell tumours such as teratoma shown in our second patient. For the monitoring purpose, patients may predispose to irradiation if a repeated sequential radio imaging is performed. From the ophthalmological point of view, the presence of worsening of Parinaud syndrome might be a warning sign of disease progression. As evidenced by our second patient, after a long-standing pineal gland tumour, the patient presented with an additional down-gaze palsy in the absence of symptoms of raised intracranial pressure (due to the presence of functioning VP shunt). We believe this to be a spectrum of Parinaud syndrome.

Conclusively, besides using neuroimaging to monitor the disease progression, clinicians also employ the use of Hess chart. However, the test has a limitation for children, as children usually have difficulties in comprehending and following the instructions during the test. Unfortunately, children are most vulnerable and more likely to suffer from this disease. In addition, up-gaze palsy is the most common sign of Parinaud syndrome. A proper vertical gaze monitoring should be carried out to confirm the diagnosis. A digital video camera monitoring can be useful for assessing and monitoring eye movements as recommended by Oguro *et al.*[16]. Besides that, tumour markers also play a crucial role in the disease monitoring. In pineal gland tumour, beta subunit of the gonadotrophic chorionic hormone is the characteristic of choriocarcinoma, AFP of yolk sac tumours, placentar alca- line phosphatase of germinoma.

Likewise, the symptoms of raised intracranial pressure such as headache, nausea, vomiting, diplopia, even reduced conscious level are life-threatening, because of the false localizing sign of abducent nerves palsy. Two of our patients presented with intense drowsiness that draws immediate attention. Papilloedema is also found in 2 of our patients. Urgent surgical decompression is therefore inevitable for life-saving. Endoscopic tumour biopsy with simultaneous endoscopic third ventriculostomy has emerged as a minimally invasive and highly effective strategy for initial management. This is due to the fact that it addresses the issue of tissue diagnosis and offers a solution for the associated hydrocephalus that frequently occurs among these patients[17]. Moreover, the cerebral spinal fluid that obtained intraoperatively, can be sent for tumour marker analysis to confirm the diagnosis. Three of our patients had undergone the initial endoscopic surgery and their biopsy was taken. One of them was implanted with ventriculoperitoneal shunt. In a study done by Oppido et al. stated that only 10% of the tissue diagnosis remained inconclusive, this is due to insufficient samples as the neuro-endoscopic biopsy is limited by a small size samples as compared to open surgery[18]. The third patient had an undetermined histopathological result as the of the biopsy was taken from the adjacent reactive brain tissue rather than the tumour itself. This is most likely due to limited view as well as limited working space with the endoscopic technique. Complications of endoscopic procedure including bleeding intraoperatively might obscure the view for precise and affect accurate biopsy, and lead to transient memory loss and risk of hemiparesis[19]. Extensive surgical removal can offer a cure in most benign tumours and provide a better outcome for malignant tumour with adjuvant therapy[20]. Radiotherapy is the first-line treatment for germinomas. However, the optimal radiation dosage is undetermined. Craniospinal radiation and adjuvant chemotherapy are indicated in the presence of cerebral spinal fluid seeding regardless of tumour type[21].

In conclusion, the factors affecting outcome of pineal gland tumour are multifactorial. The outcome depends on the age of patients, tumour type, duration of disease and treatment. Early diagnosis and proper treatment could help patients to have better outcomes. Most importantly, a multidisciplinary approach can save patients' life, and prolong and improve the quality of life of patient diagnosed of Parinaud syndrome.

Conflict of interest statement

The authors report no conflict of interest.

References

[1] Leigh RJ, Zee DS. *The neurology of eye movements*. New York: Oxford University Press, USA; 2015.

[2] Daroff RB, Jankovic J, Mazziotta JC, Pomeroy SL. *Bradley's neurology in clinical practice*. Elsevier Health Sciences; 2015.

[3] Feroze K, Bhimji S. *Parinaud syndrome*. StatPearls Publishing; 2017.

[4] Dolecek TA, Propp JM, Stroup NE, Kruchko C. CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2005-2009. *Neuro–oncology* 2012; **14**(5): v1-v49.

[5] Rousselle C, des Portes V, Berlier P, Mottolese C. Pineal region tumors: clinical symptoms and syndromes. *Neurochirurgie* 2015; **61**(2-3): 106-112.

[6] Villano JL, Propp JM, Porter KR, Stewart AK, Valyi-Nagy T, Li X, et al. Malignant pineal germ-cell tumors: an analysis of cases from three tumor registries. *Neuro–oncology* 2008; **10**(2): 121-130.

[7] Reddy MP, Saad AF, Doughty KE, Armstrong D, Melguizo-Gavilanes I, Cheek BS, et al. *Intracranial germinoma*. Proceedings from Baylor University Medical Center Proceedings; 2015.

[8] Gregory ME, Rahman MQ, Cleary M, Weir CR. Dorsal midbrain syndrome with loss of motor fusion: a rare association. *Strabismus* 2012; **19**(1): 17-20.

[9] Hoehn ME, Calderwood J, O'Donnell T, Armstrong GT, Gajjar A. Children with dorsal midbrain syndrome as a result of pineal tumors. *J Am Assoc Pediatric Ophthalmol Strabismus* 2017; **21**(1): 34-38.

[10] Menon V, Khokhar S, Tondan R. Reverse parinaud's syndrome due to pineal tumour. *Ind J Ophthalmol* 1995; **43**(1): 31.

[11] Miškovská V, Usakova V, Vertakova-Krakovska B, Mrinakova B, Lehotská V, Chorváth M, et al. Pineal germ cell tumors. *Klinicka onkologie: casopis Ceske a Slovenske onkologicke spolecnosti* 2013; **26**(1):19-24.

[12] Ahmad K, Ansari S, Dhungel K, Gupta MK, Rauniyar RK, Mishra N. Pineal germinoma presenting with Parinaud's syndrome. *Heal Renaissance* 2013; **11**(3): 276-278.

[13] Burgueño-Montañés C, Santalla-Castro C, Peña-Suárez J. Parinaud "plus" syndrome in a patient with dysgerminoma. *Archivos de la Sociedad Española de Oftalmología* 2016; **91**(7): 341-345.

[14] De Los Reyes FV, Rivera ID, Santos HM, Carlos RM. Mature teratoma of the pineal region in the paediatric age group: A case report and review of the literature. *Malaysian J Pathol* 2018; **40**(2):175-183.

[15] Awa R, Campos F, Arita K, Sugiyama K, Tominaga A, Kurisu K, et al. Neuroimaging diagnosis of pineal region tumors-quest for pathognomonic finding of germinoma. *Neuroradiol* 2014; **56**(7): 525-534.

[16] Oguro H, Okada K, Suyama N, Yamashita K, Yamaguchi S, Kobayashi S. Decline of vertical gaze and convergence with aging. *Gerontology* 2004; **50**(3): 177-181.

[17] Azab WA, Nasim K, Salaheddin W. An overview of the current surgical options for pineal region tumors. *Surg Neurol Int* 2014; **5**: 39.

[18] Oppido PA, Fiorindi A, Benvenuti L, Cattani F, Cipri S, Gangemi M. Neuroendoscopic biopsy of ventricular tumors: a multicentric experience. *Neurosurg Focus* 2001; **30**(4): E2.

[19] Ferrer E, Santamarta D, Garcia-Fructuoso G, Caral L, Rumia J. Neuroendoscopic management of pineal region tumours. *Acta Neurochirurgica* 1997; **139**(1): 12-21.

[20] Bruce JN, Stein BM. Surgical management of pineal region tumors. *Acta Neurochirurgica* 1995; **134**(3-4): 130-135.

[21] Blakeley JO, Grossman SA. Management of pineal region tumors. *Curr Treatment Options Oncol* 2006; **7**(6): 505-516.