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Not a usual sight: A rare case of pineal gland tumor associated with Down syndrome presenting with absence of ophthalmologic signs: A case report

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Abstract

We describe a 24-year old man diagnosed with Down syndrome who developed intracranial germinona located at the pineal region who presented with no ophthalmologic signs on neurologic examination on admission. However, after external ventricular device (EVD) insertion, the patient developed upward gaze palsy and convergence retraction nystagmus.

INTRODUCTION

Pineal gland tumors are rare and make up less than 1% of all intracranial neoplasms, with the majority being of germ cell tumors (GCTs). It accounts for 50% of tumors found in the pineal region and most patients diagnosed are 20 years or younger at the time of evaluation.[1] It is much common in males.[2] They are commonly diagnosed with cerebrospinal fluid tumor markers with elevated beta-human chorionic gonadotropin (b-HCG) and normal alpha feto protein (AFP). The patients can present with findings of increased intracranial pressure and/or hydrocephalus: headache, nausea, vomiting, papilledema, lethargy, and somnolence. Parinaud syndrome can be found in patients with pineal GCTs and is characterized by paralysis of upward gaze in addition to convergence retraction nystagmus, and pupillary hyporeflexia.

Among patients with Down syndrome, solid brain tumors are rarely reported and their behavior is not well known. In a study by Ehara *et al*. (2011) looking into the benign and malignant tumors among 1,514 pediatric patients with Down syndrome, hematopoietic malignancies predominated representing 83.7% of tumors[3], where 16.3% of cases were solid tumors, of which, brain tumors consisted only of 0.2%.[4] However, there is paucity of data on brain tumors among adult patients with Down syndrome. To date, only two reported cases of a brain tumor in a patient with Down syndrome has been written presenting with an intracranial germinona in the pineal gland.[5]

CASE REPORT

A 24-year old male with developmental delay and Down syndrome presented with a 6-month history of holocranial and progressive headache, occurring at night, non-radiating, and relieved by rest and with no other accompanying signs and symptoms. During the episodes of headache, the patient's mother noticed intermittent medial deviation of the left eye which spontaneously resolve after few hours, and occurred two to three times a day. At times, the mother also observed the same medial deviation on the right eye. The patient complained of double vision described as seeing things side by side when looking on his right and left. He also started to have altered sleeping patterns described as having long afternoon naps lasting for 3 to 4 hours, and with multiple awakenings at dawn where he was seen wide awake and active. There were no other accompanying symptoms such as vomiting, focal numbness or weakness, stiffening of extremities, and loss of consciousness. Interval history showed progression of headache, now accompanied by vomiting, and worsening of sleep pattern disturbances described as longer sleeping time from 5 to 6 hours to 8 to 10 hours.

The patient was born from a Gravida 1 Para 1 mother via normal spontaneous delivery at the age of 27 years old, delivered at a hospital, with no known fetomaternal complications. The mother had no maternal sickness during pregnancy, exposure to radiation, or illicit drug use. He had a history of generalized onset seizure

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at two years old described as stiffening of both upper and lower extremities followed by jerking movements which lasted for 5-10 seconds, no head veering, with no post-ictal bowel and bladder incontinence but was seen asleep after the seizure episode. Consultation with a child neurologist was done where work-ups showed abnormal EEG findings, and an unremarkable Cranial MRI. The patient was prescribed with Phenobarbital. EEG was repeated after two years showing normal result. Phenobarbital was then discontinued with no reported seizure occurrence. Recall of developmental milestones of the patient showed a global delay of about 3 months to 3 years, with a language delay of about 6 months to 1 year. He underwent cleft palate repair in 2001 with subsequent speech therapy. He was also diagnosed to have perforated tympanic membrane in 2014 due to recurrent otitis media on the left ear. The patient had no other co-morbidities. Pertinent family history showed that the mother underwent hysterectomy with findings of endometrial carcinoma, stage 1A.

On physical examination, the patient had low set ears, perforated tympanic membrane on the left, and short neck. A simian crease was evident with short and broad hands and curved fingers, which are presenting features of down syndrome. Patient was subjected for genetic testing however not done due to financial constraints.

On neurologic examination, the pertinent findings were: fundoscopy showed a red orange reflex, clear media, arteriovenous ratio of 2:3, indistinct disc borders, and no hemorrhages, suggestive of papilledema. The patient had a primary gaze at midline with full and equal extraocular muscle movements with pupils 2-3 mm equally and briskly reactive to light (Figure 1). There was decrease hearing on the left ear, with a findings of a conductive type of hearing loss. The patient had symmetrical muscle distribution with normal muscle tone, no atrophy or fasciculation with 5/5 motor strength in all extremities, intact sensory, and normoactive reflexes. There were no cerebellar, frontal, parietal, and long tract signs noted.

Cranial MRI with contrast showed a heterogeneously enhancing mass centered in the pineal gland with consideration of a germinoma, and obstructive hydrocephalus (Figure 2).

Due to the presence of hydrocephalus, the patient underwent external ventricular device (EVD) insertion where CSF tumor markers were obtained and showed elevated b-HCG of 33.06 mIU/ml (normal value:0-1.1 mIU/ml) and normal AFP of 4.62 ng/ml (normal value: <7 ng/ml). Post-operatively, on neurologic examination, the patient developed Parinaud's syndrome presenting with upward gaze palsy and convergence nystagmus. On repeat cranial CT scan, taken 8 days post operative, noted shunt tip at the frontal horn of the right lateral ventricle with resultant decrease in the degree of the dilatation of the lateral and third ventricles and resolution of transependymal

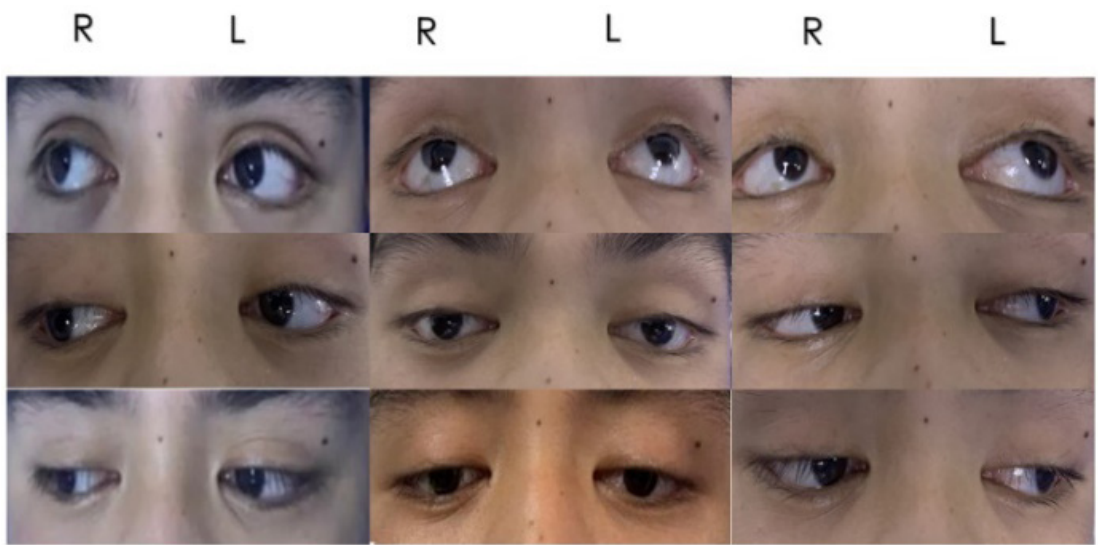

Figure 1. Extraocular muscle movement during admission
Test of ocular motility. E: Primary gaze at midline; A, G: Patient can do lateral upward and downward gaze to the right; C, I : lateral upward and downward gaze to the left; D,F: test for horizontal eye movement; B, H: test for vertical eye movement

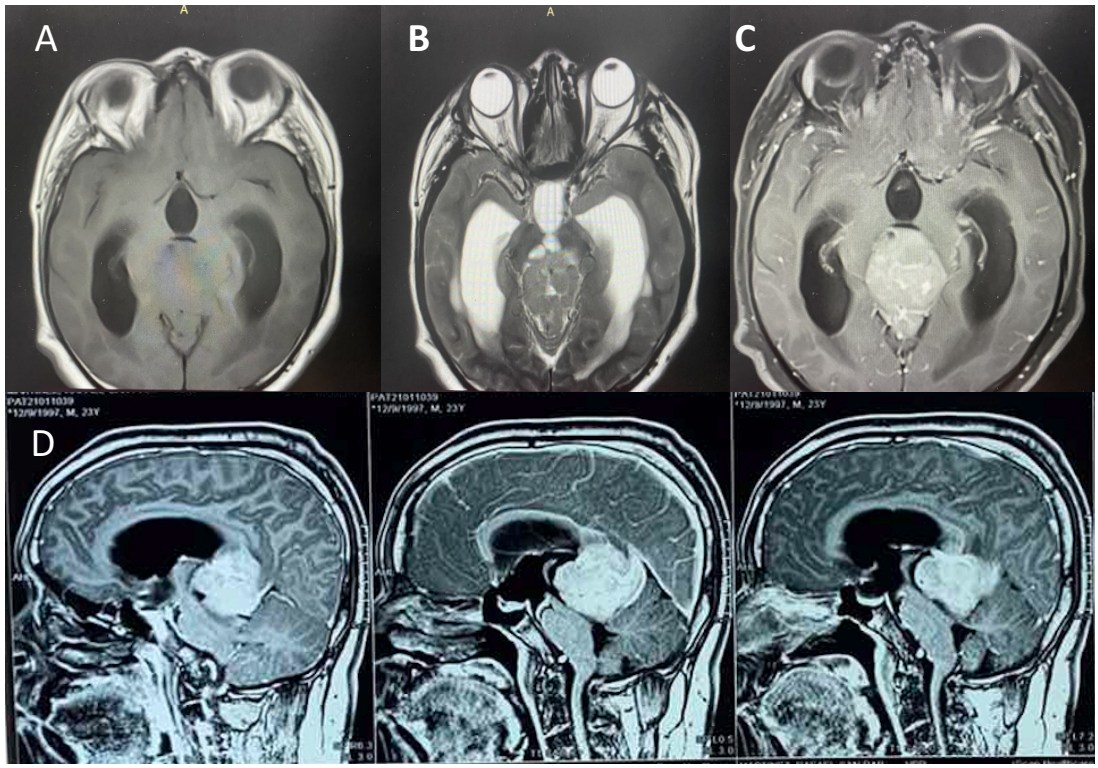

Figure 2. Pre-operative Cranial MRI with contrast: A. T1 axial, B. T2 axial, C. T1 with contrast, axial D. with sagittal view

edema. The patient then went for chemotherapy with bleomycin, etoposide, and cisplatin. After chemotherapy, patient will be referred to radiation oncologist for radiation therapy.

DISCUSSION

Solid tumors including intracranial tumors are rare among adult patients diagnosed with Down syndrome. Most of these patients present with hematopoietic malignancies. The decreased incidence of solid tumors in Down syndrome patients as compared to the general population is due to the potential tumor-suppressive role for trisomy 21 in non-hematological malignancies.[6]

At the time of diagnosis, most malignant pineal gland tumors present with hydrocephalus and ophthalmological involvement such as vertical gaze palsy (100%), convergence-retraction nystagmus (87.5%), and light-near dissociation (65%).[7] Seventy-five percent of patients had partial or complete Parinaud's syndrome, while papilledema can be found in 69% of patients.[8] In patients with germinomas in the pineal region where tumor biopsy and conservative treatment were done, symptoms remained at the pre-operative level with no progression of oculomotor and pupillary functions.[9]

This patient, diagnosed with Down syndrome, presented with a solid tumor of intracranial origin at the pineal region consistent with germinoma as confirmed by CSF tumor markers. Contrary to published articles, the patient at the time of diagnosis did not present with any ophthalmologic signs supportive of pineal gland tumor. As of this writing, there are only two published case of an adult Down syndrome who had a mass lesion in the pineal, bilateral cerebello-pontine cistern, and spinal cord with marked hydrocephalus.[5] Although intracranial tumors are rare in patients with Down syndrome, careful evaluation is still warranted in cases presenting with increased intracranial pressure or focal neurologic deficits, so as not to miss these pathologies. On the other hand, patients with diagnosed case of pineal gland tumor does not necessarily present with ophthalmologic signs. The compression of the nearby structures can predict the presenting symptoms. Compression on the aqueduct of Sylvius can give rise to increased intracranial pressure with signs of headache, nausea, vomiting, and papilledema. On the other hand, pressure on the corpora quadrigemina, situated caudal and lateral to the pineal gland tumor, can give rise

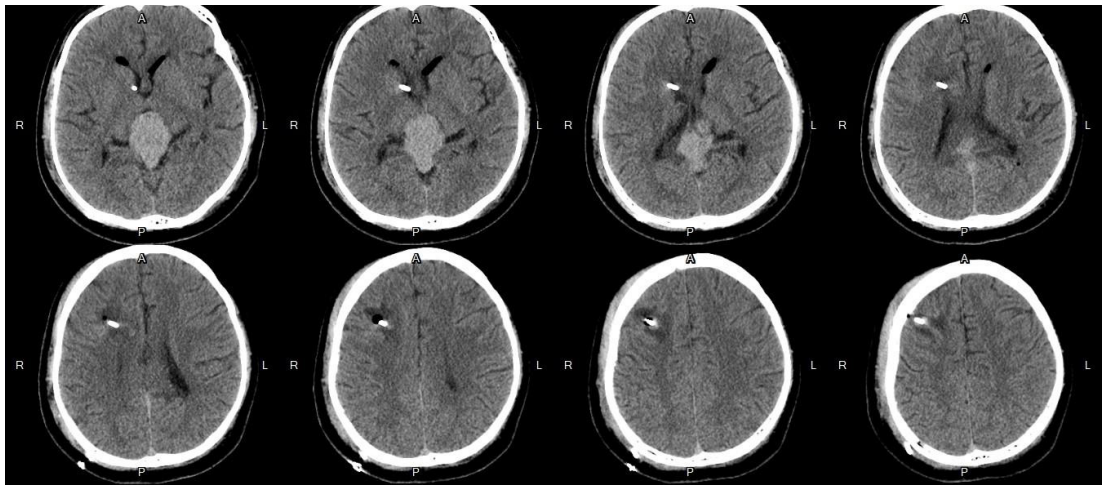

Figure 3. Post operative plain cranial CT scan, post external ventricular device insertion

to eye signs- impaired pupillary reactions and limitations of extra-ocular movements, especially conjugate movements upward. In this case, taking into account the large mass on the pineal gland, pre-operatively, the tumor could have compressed the aqueduct of Sylvius presenting only with signs of increased intracranial pressure, however, post operatively, the resolution of hydrocephalus resulted to a shift in the structures involved such as the corpora quadrigema leading to partial Parinaud's syndrome. Given the location of the tumor and published articles, the patient should have presented with eye signs supportive of pineal gland tumor which can aid on the proper localization of the lesion.[10]

In conclusion, this is a case of a 24-year old, male, diagnosed with Down syndrome who presented with a rare case of solid tumor in the pineal gland area. On admission and presentation, the patient did not present with typical neurologic findings of pineal gland tumor hence localization of the case was challenging. Taking into account the multiple literatures published, intracranial tumors are rare in patients with Down syndrome, careful evaluation is warranted in cases presenting with increased intracranial pressure or focal neurologic deficits, so as not to miss these pathologies. On the other hand, patients with diagnosed case of pineal gland tumor does not necessarily present with ophthalmologic signs, contrary to published literatures.

DISCLOSURE

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Conflict of interest: None

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