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CASE REPORT

Attention deficit hyperactivity disorder: diagnosis and treatment masking the ophthalmic clinical presentation of a pineal gland tumour in a teenager

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Abstract A 17-year-old male was found to have a fourth cranial nerve palsy and chronic papilloedema following his presentation to our institution with a 6-week history of blurred vision in both eyes and vertical binocular diplopia. A diagnosis of pineal germinoma was made following imaging studies and endoscopic neurosurgical biopsy of the tumour. He was diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) 3 years earlier and treated with amphetamines. Since this diagnosis, he continued to suffer from hyperactive behaviour, poor concentration, worsening headaches and insomnia. Pineal pathology has a known association with sleep disturbance through the disturbance of melatonin synthesis and/or metabolism. This case report serves to highlight how the presence of organic brain disease presenting to an eye department can be masked by a diagnosis of ADHD.

Keywords Attention Deficit Hyperactivity Disorder (ADHD) · Pineal germinoma · Papilloedema

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Introduction

Behavioural and functional disorders clouding the presentation of organic brain disease is not unknown in medicine [1, 2]. We present a patient whose diagnosis and treatment of Attention Deficit Hyperactivity Disorder (ADHD) obscured and possibly delayed the diagnosis of a pineal germinoma.

Germinomas are rare tumours constituting approximately 0.1–3.4% of all intracranial tumours [3–6]. ADHD, however, is common and is known to affect between 4 and 12% children [7]. Pineal mass lesions can present in a variety of ways [8, 9], but this is the first case reported to our knowledge of ADHD and its treatment obscuring the clinical presentation of an underlying pineal germinoma.

Case report

A 17-year-old male presented to the ophthalmic emergency referral service with a 6-week history of binocular vertical diplopia and blurred vision in both eyes, mainly on the left. He had previously suffered from non-specific intermittent headaches with no diurnal variation for 2–3 years. His headaches had increased in both intensity and frequency over the 6 months prior to presentation. He denied any other neurological symptoms. In his past medical history, he was diagnosed with ADHD because of restlessness and poor concentration at school as well as sleep

disturbance at the age of 14 years, and was treated with dextroamphetamines as and when required. His family history was unremarkable.

On examination, the unaided Snellen acuity in the right eye was 6/9, and 6/24 in the left. He had no relative afferent pupillary defect, with no red desaturation and normal colour vision. Cranial nerve examination revealed a left fourth nerve palsy resulting in a left superior oblique palsy, with a normal peripheral neurological assessment. Ocular examination was entirely normal apart from bilateral champagne-cork papilloedema (Figs. 1, 2).

A computed tomography (CT) scan of his head revealed a pineal tumour with evidence of triventricular hydrocephalus and the patient was referred to the neurosurgical service for further management. Upon admission to the neurosurgical unit, the patient had a blood profile carried out to include: full blood count, urea and electrolytes, coagulation screen, liver function tests, human chorionic gonadotrophin, alpha fetoprotein and c-reactive protein. All blood results were normal. A magnetic resonance imaging (MRI) scan of his head and whole spine showed similar cranial findings to the previous CT scan with no evidence of intra-spinal metastases. The patient was commenced on dexamethasome 4 mg daily by mouth.

One week following his presentation to the eye department, he underwent endoscopic third ventriculostomy and biopsy of the pineal tumour under general anaesthesia. Cerebrospinal fluid taken peroperatively for cytological and biochemical analysis revealed no evidence of inflammation or metastases.

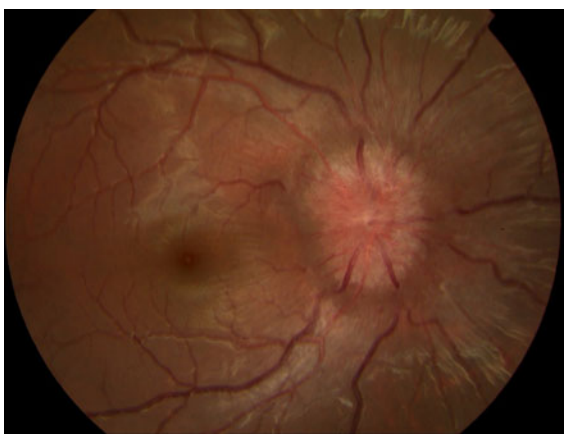

Fig. 1 Fundus photograph of the right eye showing "champagne–cork" papilloedema

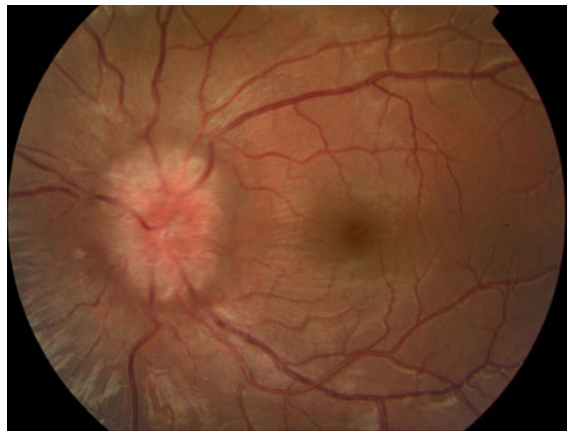

Fig. 2 Fundus photograph of the left eye showing "champagne–cork" papilloedema

Frozen section analysis of the biopsy specimen was consistent with germinoma and confirmed later on formal paraffin histopathological sectioning. No normal pineal parenchyma was identified. He had an uneventful postoperative recovery period and was discharged 1 week following surgical intervention. His headaches had resolved at this stage, but diplopia and blurred vision remained unchanged. Subsequent follow-up was arranged for radiotherapy with the oncology department. Oral dexamethasone was discontinued.

Three weeks later he was admitted by the oncology department for commencement of cranio-spinal axis radiotherapy to deliver 25 Grays in 15 fractions followed by a CT planned boost to the pineal germinoma site of a further 15 Grays in 9 fractions over a period of 1 month. Apart from nausea and vomiting, no further short-term radiotherapy-related complication was observed. Ophthalmic and orthoptic assessment carried out during radiotherapy sessions revealed no change in the ocular examination. Visual field analysis at this time revealed bilateral enlarged blind spots with a generalised reduction in sensitivity of the test.

Further follow-up of this patient was not possible in the UK as he emigrated following his course of radiotherapy.

Discussion

Germ cell tumours arise because of neoplastic changes during embryonic development. The germinomas are

pure germ line tumours that represent a less malignant form of germ cell tumour. The incidence of germinoma varies widely in different parts of the world. It constitutes approximately 0.1–3.4% of all intracranial tumours, depending on the individual's age [3–6], and 50–60% of all pineal tumours [10–14]. The male to female ratio of distribution of germinoma is reported as 1.88:1 [2].

Pineal mass lesions can present in a variety of ways including symptoms of raised intra-cranial pressure, diplopia, and Parinaud's syndrome [8, 9]. Further presenting symptoms depend on dissemination of the tumour by direct infiltration or spread along the cerebrospinal fluid pathways. Our patient presented with a fourth nerve palsy and headache secondary to raised intracranial pressure, and did not display any endocrine abnormality that suggested extension of the lesion into the suprasellar space.

Radiological imaging can be carried out using CT and/or MRI. Cerebrospinal fluid examination for cytological and marker studies is useful in the evaluation of a patient with a suspected germ cell tumour. Bailey et al. [9] found that if a raised alpha fetoprotein (αFP) or beta human chorionic gonadotrophin (βHCG) in serum was present, it was taken that the tumour was of non-germinomatous mixed germ cell type and treated according to the Charing Cross regimen [15]. If the markers are negative then a biopsy was undertaken. Historically, open biopsy or resection of tumour were fraught with danger, especially prior to the advent of endoscopic techniques. Stereotactic surgery with 0–0.5% morbidity provides a safer method of sampling deep intracranial tissues [16]. The extreme radio sensitivity of germinomas has led some to initiate radiation therapy of suspected lesions without a tissue diagnosis. Biopsy, therefore, may increase survival by increasing diagnostic accuracy and as a result allow for the institution of appropriate therapy [17]. Radiation regimes for germinoma therapy vary widely [17–19]. As diagnostic and therapeutic methods have improved, the current survival rate for patients with germinoma ranges from 66 to 86% after a median follow-up of 5 years or longer [20].

The pineal gland, through its hormone melatonin, is involved in the regulation of essential endocrine processes. Melatonin secreted mainly during the dark phase of the day–night cycle is implicated in the regulation of the sleep–wake cycle. Etzioni et al., in 1996, reported a case of a child with germ cell tumour involving the pineal region who had marked suppression of melatonin secretion associated with severe insomnia [21]. Low melatonin levels are associated with pineal destruction and high levels with presence of a melatonin-secreting neoplasm. Melatonin levels were not, however, assayed in our patient but no normal parenchymal tissue was in evidence on histological examination of biopsy specimens. This might well explain the sleep disturbance associated with this patient's presentation.

ADHD is known to affect approximately 4–12% children [7] and continues into adulthood for approximately in 50% of those diagnosed in childhood [22]. ADHD in children is more common in males, but the prevalence of adult ADHD is almost equally divided between men and women. Descriptions of hyperactivity disorder in children exist as far back as 1902. A number of other psychiatric, medical and neurological disorders such as traumatic brain injury, epilepsy and depression can lead to disturbances in attention and/or activity level [23]. Therefore, the diagnosis of "primary" ADHD is made when there is no evidence from the history, physical examination or laboratory findings of any other condition producing a similar clinical picture. Some features of our patient's history did not strictly fit the current classification [7], in particular that of headache and sleep disturbance. These symptoms, admittedly mild on initial presentation, worsened with the passage of time since diagnosis of ADHD in this young man. Amphetamine, since its introduction to treat the disorder in the mid-1900s, has well-documented side effects which include insomnia and headache [24, 25]. This patient, therefore, may well have had worsening symptoms attributed to the side effects of dextroamphetamine sulphate after his initial diagnosis of ADHD. His headache subsequently ceased following neurosurgical intervention for pineal gland mass.

This case demonstrates how the features of attention deficit hyperactivity disorder, coupled with its drug treatment, may mask evolving organic brain disease.

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