

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/radcr

Case Report

Rare case of symptomatic empty sella syndrome in a patient treated with intrathecal chemotherapy for acute myeloid leukemia [☆]

Rahul Khamar, MBBS, BSc*, Raees Lunat, MBBS, BSc, Jonathon Kyriakides, MBBS, BSc, Ruhaid Khurram, MBBS, BMedSci

Department of Radiology, Barnet Hospital, Royal Free London NHS Foundation Trust, Wellhouse Lane, London EN5 3DJ, UK

ARTICLE INFO

Article history:

Received 2 July 2020

Revised 18 August 2020

Accepted 19 August 2020

Keywords:

Empty sella syndrome

Sella turcica

Hypophyseal fossa

Computed tomography

Magnetic resonance imaging

ABSTRACT

The sella turcica is the normal neuroanatomical location of the pituitary gland. Empty sella syndrome (ESS) is a rare condition in which the sella turcica is partially or completely filled with cerebrospinal fluid. It is a radiological diagnosis that is often made incidentally following imaging for another reason (eg, to exclude intracranial hemorrhage following head injury) or as part of the work-up when investigating a patient's neurological symptoms. ESS can be classified as primary or secondary, depending on the identification of underlying etiologies. We report the highly unusual case of a 74-year-old patient who presented with progressive neurological disturbance many years after receiving intrathecal chemotherapy. Clinical assessment (including cross-sectional imaging) led to a diagnosis of secondary ESS.

© 2020 The Authors. Published by Elsevier Inc. on behalf of University of Washington.

This is an open access article under the CC BY-NC-ND license

(<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Introduction

The sella turcica is the bony depression in the body of the sphenoid bone containing the pituitary gland. Empty sella syndrome (ESS) describes the condition in which the sella turcica is filled with cerebrospinal fluid (CSF). ESS can be partial or complete, depending on whether the sella turcica is filled with CSF to a level of less than or more than 50%, respectively [1]. The prevalence of ESS has been estimated to be between 8% and 35% [2].

In primary ESS, the exact etiology underlying replacement of the pituitary gland with CSF is not completely clear. Secondary ESS is more common and occurs as result of another clinical sequelae, such as raised intracranial pressure or pituitary gland damage or removal.

Diagnosis of ESS is achieved following computed tomography (CT) or magnetic resonance imaging (MRI) of the brain. MRI is often favored over CT imaging as T2-weighted images (which are fluid attenuated) highlight CSF within the sella turcica. Further, contrast-enhanced T1-weighted images can

[☆] Competing Interests: The authors have declared that no competing interests exist.

* Corresponding author.

E-mail address: rahul.khamar@nhs.net (R. Khamar).

<https://doi.org/10.1016/j.radcr.2020.08.042>

1930-0433/© 2020 The Authors. Published by Elsevier Inc. on behalf of University of Washington. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

reveal distortion or scarring of the residual pituitary in secondary ESS [3].

We present a unique case, wherein a radiological diagnosis of ESS was made in a symptomatic 74-year-old patient who received intrathecal chemotherapy for acute myeloid leukemia eighteen-years prior to the onset of symptoms.

Case Report

A 74-year-old female patient presented to her local optician in March 2020 with a 2-month history of worsening visual acuity. She reported progressive difficulty in reading small print and was most perturbed when she failed to recognize the faces of relatives when looking at photos. The optician noted a dramatic deterioration in visual acuity over a 3-year period from 6/7.5 to 6/10. Optical Coherence Tomography revealed damage to her retinal nerve fiber layers bilaterally. On assessment, color vision and visual fields were intact and there was no evidence of a relative afferent pupillary defect. Note was made of bilateral cataracts and bilateral papilledema, triggering an urgent referral to Moorfields Eye Hospital.

An ophthalmologist confirmed the presence of bilateral papilledema with normal ocular pressures. They advised urgent next-day local follow-up and specialist review.

Alongside the progressive visual disturbance, she reported a several month history of intermittent headaches. There were no obvious triggers to these headaches, and simple analgesics did not provide symptomatic relief. There were no other pathognomonic features in the history to suggest the presence of migraine, raised intracranial pressure, giant-cell arteritis or meningism.

Her past medical history included acute myeloid leukemia 18 years prior, for which she received a 6-month course of intrathecal chemotherapy. She developed features of raised intracranial pressure (including headaches and papilledema) as a result of intrathecal chemotherapy, for which she required multiple therapeutic lumbar punctures. Following completion of chemotherapy, she was due to be seen in the ophthalmology outpatient department, but was lost to follow-up. She was, however, symptom free and without evidence of disease recurrence at oncology follow-up in January 2020.

On initial assessment, her observations were all within normal range. Neurological examination of the upper and lower limbs was unremarkable. Her visual fields were full and the rest of her cranial nerve examination was normal. Fundoscopy was difficult due to cataracts but once again, revealed bilateral disc swelling.

Initial blood tests were unremarkable with full blood count, renal function and bone profile all within normal limits. Notably, the erythrocyte sedimentation rate (ESR) and HbA1c (both of which are indicators of key differentials) were normal at 26 mm/h and 38 mmol/mol, respectively.

An unenhanced CT examination of the brain by a 64-slice CT scanner was performed. The protocol included a non-contrast CT scan with 1mm slice thickness. As demonstrated in Fig. 1 below, this revealed an enlarged, fluid-filled pituitary fossa, in-keeping with ESS.



Fig. 1 – Coronal section of an unenhanced CT head scan illustrating the enlarged, fluid-filled pituitary fossa, consistent with ESS. CT, computed tomography.

The patient was reviewed by a neurologist who arranged an urgent MRI brain scan to exclude venous sinus thrombosis as a possible etiology. The MRI scan confirmed ESS and excluded any other clinically significant intracranial pathology (Fig. 2). In the first instance, the patient was managed supportively with analgesics, a headache diary and a robust follow-up plan that included referral to a neuro-ophthalmologist for further evaluation and surveillance. At follow-up in July 2020 a lumbar puncture was performed to ensure the current clinical presentation wasn't an acute manifestation of raised intracranial pressure. This revealed an opening pressure of 23 cm (normal <20 cm). The patient was kept under specialist review whilst an interim plan for cataract removal was made to ensure these did not further contribute to on-going decline in acuity.

Discussion

Whilst the exact etiology of primary ESS remains unclear, a congenital defect in the diaphragm sellae is likely to play a significant role. A weakness in this fold of dura mater may allow CSF to leak from the suprasellar subarachnoid space into the sella [4]. This exerts pressure within the cavity, resulting in cavity expansion or displacement of the pituitary gland [5]. In contrast, the etiopathogenesis of secondary ESS differs; secondary ESS occurs as a consequence of an underlying process in which there is damage to the pituitary gland.

Symptoms associated with ESS depend on the underlying cause. The majority of patients with primary and secondary ESS are asymptomatic, although symptoms in secondary ESS occur more frequently. The most common symptom associ-

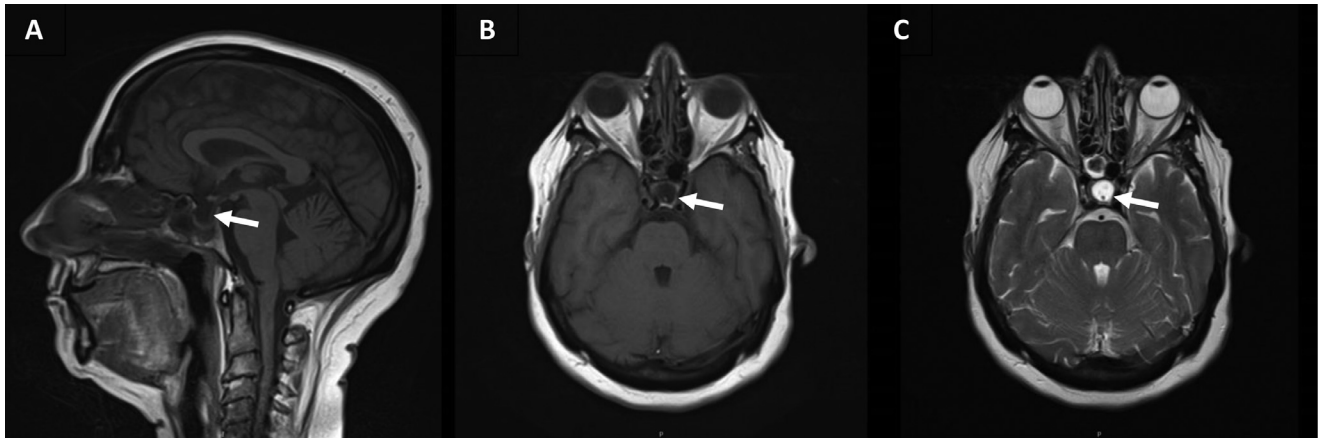


Fig. 2 – MRI brain scans confirming the diagnosis of ESS. (A) is a T1-weighted mid-sagittal section that demonstrates a fluid-filled sella turcica with a flattened pituitary that is just visible at the base of the pituitary fossa. (B) is a T1-weighted coronal section that illustrates the enlarged, fluid-filled sella. (C) is a T2-weighted (fluid attenuated) coronal section that illustrates the increased signal intensity of the CSF occupying the sella turcica. CSF, cerebrospinal fluid; ESS, empty sella syndrome; MRI, magnetic resonance imaging.

ated with ESS is chronic headaches, however this may be a coincidental association [6]. Visual abnormalities and symptoms associated with decreased pituitary function can also occur in ESS [1,7].

ESS is often an incidental diagnosis following neuroimaging. Although CT can be diagnostic for ESS, MRI more accurately images the sella turcica and its contents. As such, MRI can reveal CSF within the sella, as well as identifying displacement of the pituitary stalk and pituitary gland [3].

Management of patients with ESS also varies. Management is directed at the cause in secondary ESS; these patients may require hormone replacement or endoscopic closure surgery if CSF rhinorrhea is present. In the minority of patients with symptomatic primary ESS, the mainstay of management is supportive with analgesia for headaches.

Intracranial hypertension as a direct consequence of intrathecal chemotherapy has been described in the literature, however no causal mechanism has been proposed to date [8]. Furthermore, systemic chemotherapy can result in intracranial hypertension in few cases [9]. Intracranial hypertension is a well described cause of secondary ESS, but has also been hypothesized to occur in patients with primary ESS [10,4]. Furthermore, patients with ESS as a result of intracranial hypertension have been noted to have an empty sella with a larger absolute area [11]. Interestingly, an empty sella can be the only radiological finding in patients with intracranial hypertension [12].

The patient in this case received intrathecal chemotherapy for the treatment of acute myeloid leukaemia 18 years prior to the onset of symptoms. At that time, she developed clinical features of intracranial hypertension (including papilledema), requiring therapeutic lumbar punctures. It was then 18 years later (after being lost to follow-up in the ophthalmology department) that she developed visual symptoms, which led to a diagnosis of ESS. Bilateral papilledema, which is a sign of raised intracranial pressure, was noted in the clinical

work-up prior to the radiological diagnosis of ESS. Due to the lack of neuroimaging in the 18-year period between the patient receiving intrathecal chemotherapy and the diagnosis of ESS, the exact point of the development of ESS remains unclear. We hypothesize, however, that the development of ESS occurred due to persistently elevated intracranial pressure, a consequence of the intrathecal chemotherapy.

In summary, we present an interesting sequence of events where intrathecal chemotherapy resulted in chronic intracranial hypertension and secondary ESS. Intracranial hypertension as a cause for ESS is well-documented, however, there may be a critical point at which visual symptoms occur in the pathogenesis of this condition. Further data including regular interval neuroimaging of patients with ESS and careful objective assessment of vision is necessary to draw more definitive conclusions.

REFERENCES

- [1] De Marinis L, Bonadonna S, Bianchi A, Maira G, Giustina A. Primary empty sella. *J Clin Endocrinol Metab* 2005;90(9 Sep):5471–7.
- [2] Aruna P, Sowjanya B, Reddy PA, Krishnamma M, Naidu JN. Partial empty sella syndrome: a case report and review. *Indian J Clin Biochem* 2014;29(2):253–6.
- [3] Miljic D, Pekic S, Popovic V. Empty sella [Updated 2018 Oct 1]. In: Feingold KR, Anawalt B, Boyce A, et al., editors. *Endotext* [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK532084/> [Access date: 01/07/2020].
- [4] Chiloiro S, Giampietro A, Bianchi A, Tartaglione T, Capobianco A, Anile C, et al. Diagnosis of endocrine disease: primary empty sella: a comprehensive review. *Eur J Endocrinol* 2017;177(6):R275–85.
- [5] Degli Uberti EC, Teodori V, Trasforini G, Tamarozzi R, Margutti A, Bianconi M, et al. The empty sella syndrome.

- Clinical, radiological and endocrinologic analysis in 20 cases. *Minerva Endocrinol* 1989;14(1):1–18.
- [6] Ucciferro P, Anastasopoulou C. Empty sella. StatPearls [Internet], Treasure Island FL: StatPearls Publishing; 2020. [cited 2020 Jun 27]. <http://www.ncbi.nlm.nih.gov/books/NBK541002/> [Access date: 01/07/2020].
- [7] KAuer M, RStieg M, Crispin A, Sievers C, KStalla G, Kopczak A. Primary empty sella syndrome and the prevalence of hormonal dysregulation. *Dtsch Arztebl Int* 2018;115(7):99–105.
- [8] Lunsken S, Lammertijn L, Deeren D, Bergmans B, Maertens J, Vandenberghe R. Intracranial hypertension following intrathecal administration of liposomal cytarabine. *J Neurol* 2011;258(1):162–3.
- [9] Nurgat Z, Alzahrani H, Lawrence M, Mannan A, Ashour M, Rasheed W, et al. Intracranial hypertension secondary to high dose cytosine arabinoside – A case study. *J Infect Chemother* 2017;23(5):319–22.
- [10] Julayanont P, Karukote A, Ruthirago D, Panikkath D, Panikkath R. Idiopathic intracranial hypertension: ongoing clinical challenges and future prospects. *J Pain Res* 2016;9:87–99.
- [11] Ranganathan S, Lee SH, Checkver A, Sklar E, Lam BL, Danton GH, et al. Magnetic resonance imaging finding of empty sella in obesity related idiopathic intracranial hypertension is associated with enlarged sella turcica. *Neuroradiology* 2013;55(8):955–61.
- [12] Saindane AM, Lim PP, Aiken A, Chen Z, Hudgins PA. Factors determining the clinical significance of an ‘empty’ sella turcica. *Am J Roentgenol* 2013;200(5):1125–31.