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Case Report

Mixed germ cell tumor of the pineal gland in a pediatric patient☆,☆☆

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ABSTRACT

Tumors of the pineal region are a rare clinical entity, comprising approximately 3%-8% of pediatric tumors. Based on their histopathological features, they are typically classified as pineal parenchymal tumors and germ cell tumors, with the latter being more prevalent. Clinical presentation is heterogeneous, with symptoms arising either due to tumor invasion or compression of adjacent neurovascular structures and increased intracranial pressure. Imaging studies are paramount in evaluating pineal region lesions and establishing an accurate diagnosis, with MRI representing the gold standard. Herein, we present the case of a 16-year-old boy presented with recurrent headaches. A head MRI revealed a pineal gland lesion. Histopathological examination confirmed the diagnosis, and the patient underwent a successful gross total resection (GTR) of the tumor. This case report seeks to draw attention to the elusive clinical presentation and management of this infrequently encountered

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tumor, as well as emphasize the importance of considering pineal gland tumors in the differential diagnosis of recurrent, chronic headaches in pediatric patients.

Introduction

Pineal tumors are uncommon, accounting for less than 1% of all intracranial tumors [1]. Pineocytomas, pineoblastomas, pineal parenchymal tumors of intermediate differentiation, papillary tumors of the pineal region, and germ cell tumors (GCTs) are the differential diagnosis for neoplastic masses in the pineal region. GCTs account for half of all tumors detected in the pineal area, with pure germinomas accounting for the majority [2]. Primary germ cell tumors constitute 0.4% of all CNS tumors and are most commonly detected in children aged 10-14 [3]. With a male predominance incidence of primary CNS GCT is 0.10-0.17 per 100,000 population. Germinoma is the most prevalent histological subtype, with 50%-60% of cases arising in the pineal recess. The most common sites where Yolk sac tumor and Germinoma are Suprasellar (30%), bifocal suprasellar and pineal (10%-15%), basal ganglia (5%), and multifocal suprasellar and pineal (10%-15%) [3]. Patients with pineal region tumors commonly present with symptoms related to raised intracranial pressure and/or hydrocephalus, such as headache, vomiting, nausea, lethargy, somnolence and papilledema [2]. Patients with pineal GCTs may present as Parinaud syndrome, which is characterized by upward gaze palsy, as well as loss of convergence, accommodation, and pupillary light reflex [2]. Because of the significant disparities in treatment options compared to other subgroups, establishing a precise diagnosis of a germinoma is critical. Germinomas typically demonstrate hyperintense T1- and T2-weighted MRI with avid contrast enhancement with possible cystic and necrotic changes in larger lesions [4]. On CT, germinomas usually have greater attenuation in comparison to gray matter and a draped structure in relation to the posterior third ventricle. Moreover, lumbar puncture and MRI of the entire spine are recommended to evaluate for CSF dissemination and drop metastases [2]. Radiation therapy has been shown to be very effective in the treatment of germinomas. Diverse opinions exist on the appropriate radiation dose and volume for disease control and recurrence prevention while balancing adverse effects on cognitive and endocrine function [5]. However, maximal resection has the potential to increase diagnostic accuracy as well as the outcome [3].

Case presentation

A 16-year-old male presented to the emergency department with complaints of severe, frontal headaches that had progressively worsened in the span of a few months. He had initially received treatment for sinusitis, to a mild improvement at first. Nevertheless, the headaches persisted. In the last 5 days prior to admission, he reported an increase in the frequency and severity of headaches, as well as concurring nausea and vomiting in the morning. Visual disturbances including blurry vision, deviation of the right eye and difficulty moving the eyes up and down were observed. Neurological examination showed signs of increased intracranial pressure including fixed, dilated pupils bilaterally, with loss of the light reflex and grade I, papillary edema. Furthermore, it revealed the presence of Parinaud syndrome. Static and dynamic ataxia were noted, as well. No associated motor or sensory deficits were evident. Tendon reflexes were normal in all extremities, with no evidence of muscular wasting or pathological reflexes. Routine laboratory studies were within normal limits. The rest of the physical examination, including examination of the cardiovascular, respiratory and musculoskeletal system was unremarkable. His personal and family medical history were not significant for any neurological, hereditary conditions, or illicit drug use. Considering the patient's age and long history of complaints, a head MRI was ordered. MRI images of the brain were obtained using TSE/T1W (Fig. 1) sequence in axial plane, TSE/T2W sequence in axial plane, FLAIR/T2W and DWI/T2W sequences in axial plane, as well as Post Gadolinium-T1W sequences in axial, coronal and sagittal planes. It revealed a massive, expansive mass located in the posterior segment of the cerebral aqueduct and extending to the distal segment of the third ventricle. The lesion was presented as "hypointense" in T1-weighted images and as "hyperintense" with cystic components in FLAIR and T2-weighted sequences (Figs. 1 A, and B). Heterogeneous post- contrast enhancement was visible, following gadolinium administration (Figs. 1 C, and D) Involvement of the midbrain, corpus callosum and potentially the left lateral ventricle was evident, along with early signs of obstructive hydrocephalus and periventricular edema. Aside from a concomitant, chronic bilateral maxillary sinusitis, the MRI showed no other abnormalities. No pathological findings were present in the orbital cavities, basal cisterns or the posterior cranial fossa. Imaging findings were suggestive of a pineocytoma. The patient underwent a gross total resection (GTR) of the tumor, through a suboccipital craniotomy, infratentorial supracerebellar approach. Histopathological examination revealed the tumor consisted of 2 distinct components. The larger component showed glandular, honeycomb-like structures consisting of tumor cells with vacuolated cytoplasm and a smaller component containing large, pleomorphic tumor cells with prominent nucleoli, organized in sheets with numerous mitotic figures and some apoptotic bodies (Figs. 3 A-C). Immunohistochemistry in the larger component showed tumor cells positive for AE1/AE3, PLAP and AFP, meanwhile the smaller component showed tumor cells positive for PLAP, OCT3/4, CD17 and negative for AFP and CD30. These features were consistent with yolk sac tumor and germinoma. Subsequently, the patient underwent multiple chemotherapy cycles (Figs. 2 and 3).

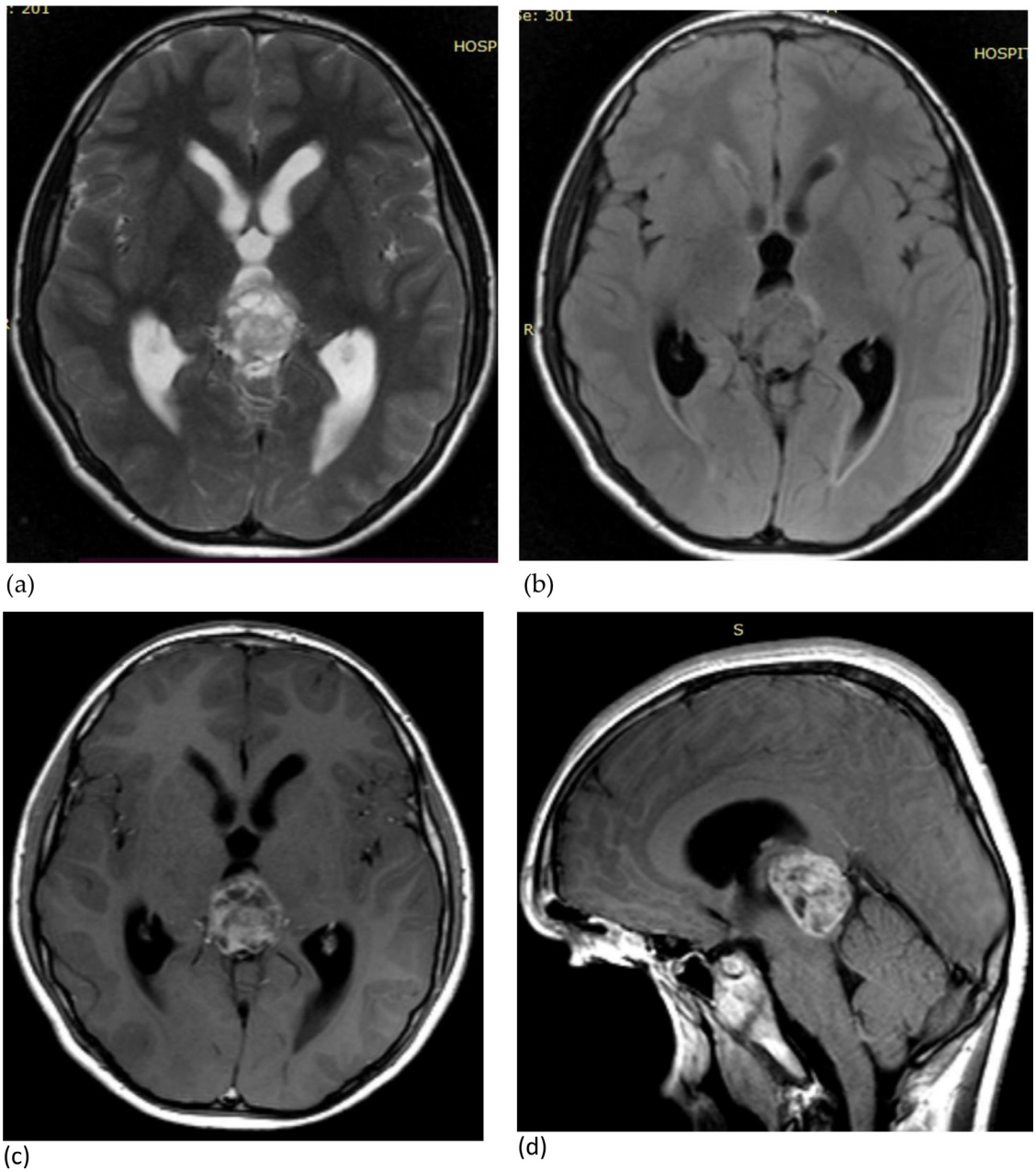

Fig. 1 – Brain MRI shows expansive process with localization in the pineal region and originating in the pineal region. The lesion is heterogeneous, with cystic components that presents hypersignal T2-weighted image (A, red arrow), solid vital mass with contrast reinforcement intensively (C and D, yellow arrow), infiltration of the thalamus left with light perifocal edema. Cerebrospinal fluid circulation obstruction at the level of Aqueductus Sylvi (D, white arrow) and triventricular hydrocephalus with periventricular edema best presented in T2-weighted image and FLAIR (A and B, green arrowheads).

Discussion

Pineal gland is a neuroendocrine gland located between cerebral hemispheres in the epithalamus. It is attached to the posterior wall of the third ventricle by a stalk, projecting posteroinferiorly into the quadrigeminal cistern. The gland comprises 2 cell types: (1) pinealocytes, which produce primarily the hormone melatonin; and (2) neuroglial cells, which resemble astrocytes and serve as supporting cells. Hence, both types of cells can become neoplastic as well as any residual germ cells or cells of surrounding tissue can form neoplasm [6]. Pineal tumors are rare in adults, accounting for 0.5% of all intracranial tumors compared to 1% in adults aged 20-34 years and 2.7% in children 1-12 years [7]. Additionally, the obstruction of cerebral aqueduct leads to a noncommunicating hydrocephalus. This may be managed clinically through an external ventriculostomy, endoscopic third ventriculostomy, ventriculoperitoneal/ ventriculoatrial shunts, or direct removal [8]. In children, tumors in this region result in invasion and

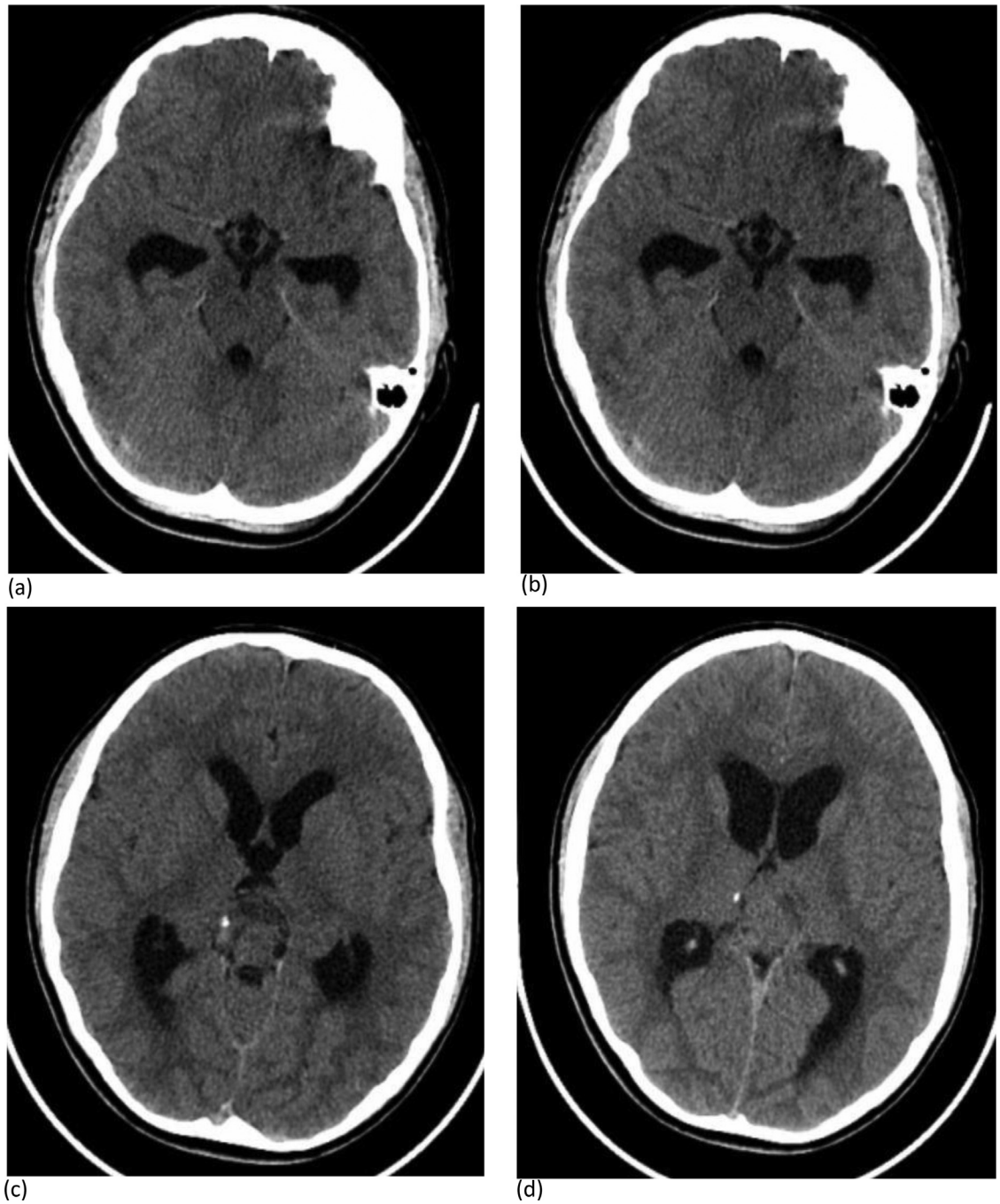

Fig. 2 – Native computed tomography presents an heterogeneous expansional mass in the pineal region (green arrows, B-D), cystic components (red, B), marginal calcification (yellow arrow B-D) and triventricular obstructive hydrocephalus (blue arrows A-D) with increased intraventricular suppression and periventricular edema (white arrowheads, A-D).

destruction of the pineal gland leading to early onset of puberty. Therefore, it is imperative to utilize advanced imaging methods, together with the help of both clinical and laboratory data to be able to distinguish between the pineal neoplasms and thus realize accurate primary diagnoses and correct treatment and management plans [8]. Al-Hussaini et al. [1] used the SEER database to find that GCTs and PPTs are predominantly found in children whereas gliomas are more commonly seen in adults. Of all the subtypes of pineal tumors, GCTs showed better survival, highlighting that histology of the tumor was an important indicator in outcome. PPTs were associated with poor outcomes.

Disclafani et al. [9] reported 6 cases of pineocytomas, 3 of whom died. D'Andrea et al. [10] reported similar results, 4 of 6 cases of treated pineocytomas had recurrence. This may be due to pineocytomas' high propensity for leptomeningeal dissemination. The pineal gland is located in a complex area intracranially, hence, the tumors occurring in the vicinity make

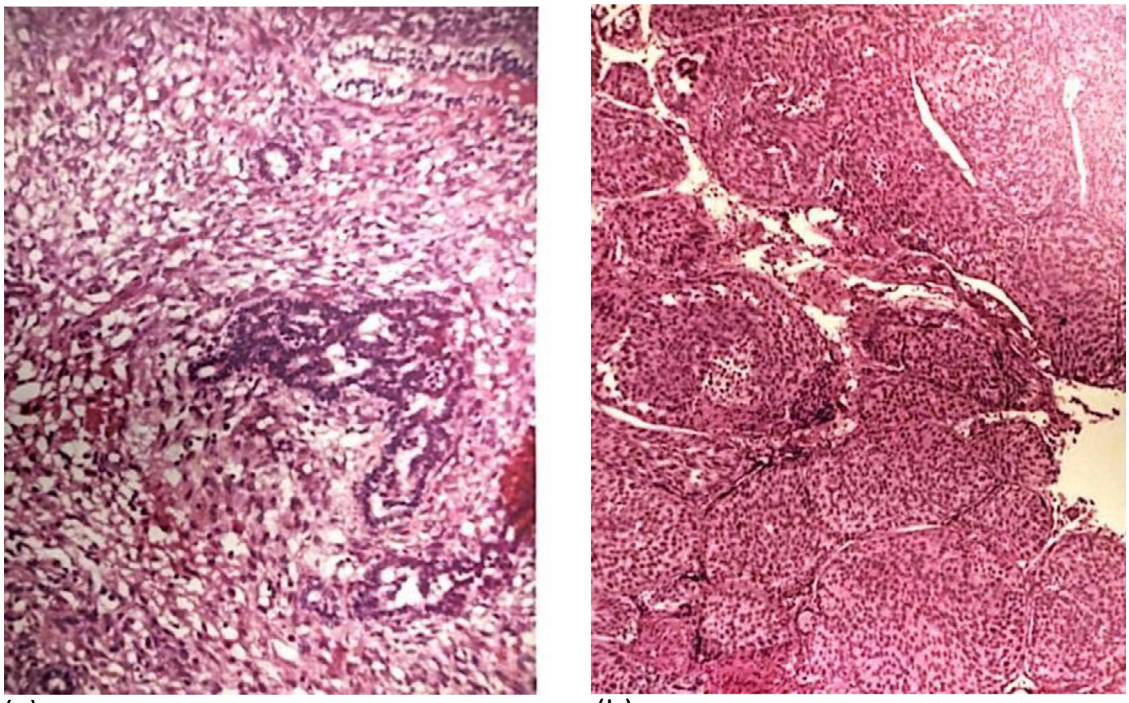

Fig. 3 – Microscopic examination in H&E stained sections (A) showed large glandular, honeycomb-like structures consisting of tumor cells with vacuolated cytoplasm and a smaller component (B) containing large, pleomorphic tumor cells organized in sheets, with prominent nucleoli, numerous mitotic figures and some apoptotic bodies.

surgical excision an extremely challenging task associated with high risk. At present, microsurgical excision is the primary mode of management for the tumors occurring in the pineal region. However, germ cell tumors are an exception. This is due in fact that germinomas may be treated with chemotherapy and radiotherapy without the surgical excision. A biopsy may or may not be performed [11]. The most effective initial management strategy is an endoscopic tumor biopsy with a concurrent endoscopic third ventriculostomy (ETV). This minimally invasive technique allows for tissue diagnosis and simultaneously solves the occurrence of hydrocephalus which may often be associated with these patients [12–14]. Surgical management of tumors of the pineal region consists of multiple microsurgical and endoscopic techniques. The single most important step in surgical management of pineal region tumors is the preoperative planning for an individualized approach [15]. Oppenheim and Krause are reported to have been the first to successfully remove a pineal tumor via an infratentorial supracerebellar approach in 1913 [PMID: Oppenheim, H. (1913). Operative Erfolgebei Geschwulsten der Sehhugel-and Vierhugel- gegend. *Berl Klin Wchschr,* 50, 2316-2322]. Over the years, various approaches have been modified and tried to access the tumors occurring in the pineal gland region. These include: infratentorial supracerebellar, occipital transtentorial, combined supra- infratentorial transsinus, posterior transcallosal interhemispheric, and transcortical transventricular approaches [15]. The most frequently used passages are the infratentorial supracerebellar corridor and the occipital transtentorial corridor to surgically excise pineal region tumors [11]. In this case, we used the infratentorial supracerebellar approach which allows a direct view of the tumor in the midline allowing for dissection without intersecting the Galenic system situated above the tumor. This approach allows for convenient removal of veins adhering to the surface of the tumor, as well as reduced pooling of blood and cerebrospinal fluid (CSF) in the field of view during surgery. This technique allows easier orientation; however, the operative field may be restricted due to narrow angle laterally and caudally [12,13]. Ellenbogen and Moores were the first to describe a simultaneous ETV and biopsy for tumors in the pineal region [14]. It has thus far become the most likely approach in pineal region tumors as many patients at diagnosis present with noncommunicating hydrocephalus [15]. This method not only treats the hydrocephalus but allows collection of CSF samples for cytology and presence of any tumor markers. Tissue obtained via endoscopic biopsy also allows for direct view of inspecting the structures surrounding the tumor and identify any malignant seeding that may otherwise was not visible on the preoperative MRI [16].

Conclusions

Pineal gland tumors are rare, more commonly arising in the pediatric population. Through this case report we aim to highlight the significance of considering pineal gland tumors in the

differential diagnosis of recurrent, chronic headaches in pediatric patients.

Patient consent

Written informed consent has been obtained from the parent of the patient to publish this paper,

Data availability

Not applicable.

CRediT authorship contribution statement

Serbeze Kabashi: Conceptualization, Writing – original draft, Investigation, Project administration. **Ilir Ahmetgjekaj:** Conceptualization, Writing – original draft, Investigation, Supervision, Project administration. **Edlira Harizi:** Conceptualization, Investigation. **Fjolla Hyseni:** Investigation, Resources, Writing – review & editing, Visualization. **Erisa Kola:** Writing – review & editing. **Valon Vokshi:** Resources. **Guri Hyseni:** Resources. **Ina Kola:** Writing – review & editing. **Humza Haroon:** Writing – original draft. **Masum Rahman:** Writing – review & editing. **Kledisa Shemsi:** Writing – original draft. **Arlind Decka:** Supervision. **Livia Capi:** Supervision. **Kaltrina Goçaj:** Software, Project administration. **Juna Musa:** Writing – original draft.

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