Suprasellar pilocytic astrocytoma in an adult with hemorrhage and leptomeningeal dissemination: case report and review of literature

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Abstract: Pilocytic astrocytoma (PA) is a low-grade tumor. It has an excellent prognosis after total resection. Leptomeningeal dissemination and hemorrhage are very rare to be associated with PA and lead to unfavorable prognosis. A 35-year-old man was diagnosed with a hemorrhagic suprasellar PA in 2006. Subsequent examination in 2007 revealed another large subdural hemorrhagic lesion in the sacral region, which proved to be PA by histopathologic assessment. Other leptomeningeal foci were discovered mainly at the craniocervical junction. The patient underwent subtotal resection and received chemotherapy with disease control for 7 years. Progression of the disseminated disease has recently occurred; however, the patient is still alive with stable disease after radiotherapy. The radiological features, management, and relevant literature are also presented. Our report heightens the awareness of PA in the adult population and the importance of close surveillance for the leptomeningeal spread, especially for sellar region tumors.

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Case Report

Suprasellar pilocytic astrocytoma in an adult with hemorrhage and leptomeningeal dissemination: case report and review of literature

Radwa K. Soliman MD[a,*], *Caterina Budai PGDiR*[a], *Pravin Mundada FRCR, DMRE*[a], *Bakar Aljohani EDiR*[a], *Elisabeth J. Rushing MD*[b], *Spyros S. Kollias MD*[a]

[a] *Institute of Neuro-Radiology, University of Zürich, University Hospital Zürich, FrauenKlinkstrasse 10 CH-8091, Zürich, Switzerland*
[b] *Institute of Neuro-Pathology, University of Zürich, University Hospital Zürich, Schmelzbergstrasse 12-8091 Zürich, Switzerland*

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ABSTRACT

Pilocytic astrocytoma (PA) is a low-grade tumor. It has an excellent prognosis after total resection. Leptomeningeal dissemination and hemorrhage are very rare to be associated with PA and lead to unfavorable prognosis. A 35-year-old man was diagnosed with a hemorrhagic suprasellar PA in 2006. Subsequent examination in 2007 revealed another large subdural hemorrhagic lesion in the sacral region, which proved to be PA by histopathologic assessment. Other leptomeningeal foci were discovered mainly at the craniocervical junction. The patient underwent subtotal resection and received chemotherapy with disease control for 7 years. Progression of the disseminated disease has recently occurred; however, the patient is still alive with stable disease after radiotherapy. The radiological features, management, and relevant literature are also presented. Our report heightens the awareness of PA in the adult population and the importance of close surveillance for the leptomeningeal spread, especially for sellar region tumors.

Introduction

Pilocytic astrocytoma (PA) is a low-grade tumor, classified according to the WHO as grade I [1]. PA occurs most commonly in children and young adults before the age of 20 years. About 17% occur in patients older than 30 years old [2,3]. It is associated with an excellent prognosis with 10 years survival rate reaching 95% after complete resection [4,5]. Imaging of PA often reveals a cystic lesion with an intensely enhanced mural nodule occasionally accompanied by enhancement of the wall of the cyst [6]. Less common, PA appears as a solid lesion, either homogenous or heterogeneous, particularly when localized in the hypothalamic region. Intratumoral hemorrhage and leptomeningeal dissemination (LD) are atypical features of PA [6,7]. Intratumoral hemorrhage in PA is very rare with only 32 cases being reported from 1977 to 2008 [2,8].

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* *Corresponding author.*
E-mail address: radwa.soliman@yahoo.co.uk (R.K. Soliman).

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Although LD is more often associated with high-grade tumors such as medulloblastoma, ependymoma, and glioblastoma, a few case studies have investigated tumor dissemination in PA. The first case of PA with LD was reported in 1976 [9], and by 2013, there were 60 cases [10]. We present an additional case of PA in an adult patient with intratumoral hemorrhage and LD.

Case presentation

In January 2006, a 35-year-old man presented with symptoms of increased intracranial pressure and the suspicion of ventriculoperitoneal (VP) shunt obstruction. A VP shunt had been placed in 2000 to control hydrocephalus caused by meningitis. Computed tomography examination was performed and revealed a hemorrhagic suprasellar lesion extending to the right cerebellopontine angle cistern (Fig. 1). Magnetic resonance imaging (MRI) revealed, in addition, prominent leptomeningeal enhancing nodule at the craniocervical (C.C) junction (Fig. 2). Subtotal resection of the suprasellar lesion was performed, and histopathologic evaluation was consistent with PA (WHO grade I). No further treatment was given at that time, but regular follow-up MRI of the brain and spine were recommended for the early detection of further dissemination. In 2007, the residual suprasellar lesion was shown in the MRI, and there was no evidence of further LD in the brain. Whereas, in the spine, MRI examination revealed a large nonhomogenous lesion in the subdural space, at the sacral region with some hemorrhagic components (Fig. 3). Two months later, partial resection of the sacral lesion through L5 laminectomy was performed. Pathologic examination again revealed histologic features typical for PA (Fig. 4). The histologic specimen was submitted for a second opinion at a Tumor Reference Center, and the diagnosis was reconfirmed. Postoperatively, local irradiation was delivered to the sacral mass. The patient then underwent one year of chemotherapy with temozolomide. Follow-up MRI examinations, between 2008 and 2013, revealed a minimal increase in the size of the residual suprasellar lesion with a slight progression of the LD, whereas the residual sacral lesion remained stationary. In 2014, however, there was an evident increase in the size of both the residual suprasellar and sacral lesions with diffuse intracranial leptomeningeal spread (Figs. 5 and 6) accompanied by progressive clinical deterioration. The patient then treated with craniospinal irradiation. He did well after therapy. Follow-up MRI examinations, in 2015, revealed good regression of the suprasellar and the leptomeningeal disease (Fig. 7) with slow regression of the sacral mass.

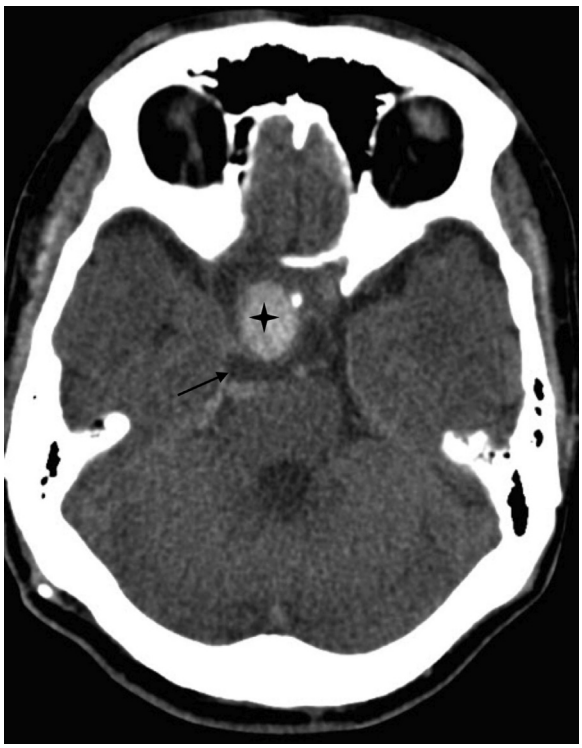

Fig. 1 – Noncontrast computed tomography: hyperdense lesion in the suprasellar region (black star) with cystic component, extending to the right prepontine space (black arrow).

Discussion and review of literature

The present case of PA is notable for the age of the patient, a 35-year-old adult and the multifocal spread of the tumor. The aim of this review was to increase awareness of PA in the adult population and to draw attention to the potential for leptomeningeal spread.

In our case, the primary lesion was located in the suprasellar region, similar to most previously reported cases. In fact, LD in the setting of PA usually occurs when the primary tumor is found in the vicinity of cerebrospinal fluid (CSF) spaces, such as, in the subarachnoid spaces or adjacent to ventricular surfaces. Tumors in the hypothalamic and/or chiasmatic region demonstrate the highest rate of dissemination, about 23-fold higher than PA in other areas [9,11,12]. Tumor cells in these locations may breach the leptomeningeal or ependymal surfaces, and then spread along CSF flow pathways [13–15]. As in the case of other tumors with a predilection for CSF dissemination, secondary deposits are primarily found caudally in the spinal canal due to the effects of gravity, and at the C.C junction, due to slower CSF flow in the cisterna magna [16,17]. In accordance with the above, the largest drop metastasis in our case was found in the subarachnoid space in the sacral region, whereas the other LD foci were in the region of the C.C junction. Other reports have shown that dissemination occurs against gravity, in a cranial rather than caudal direction. This usually occurs when the primary PA is found in the spinal cord [16,18,19]. Tumor cells in from a primary located caudally in the spinal cord may spread cranially during the recumbent position. Intraparenchymal PAs rarely show CSF dissemination. In these rare cases, the mechanism advanced for explaining the dissemination is tumor cells spread through adjacent perivascular spaces [14,20].

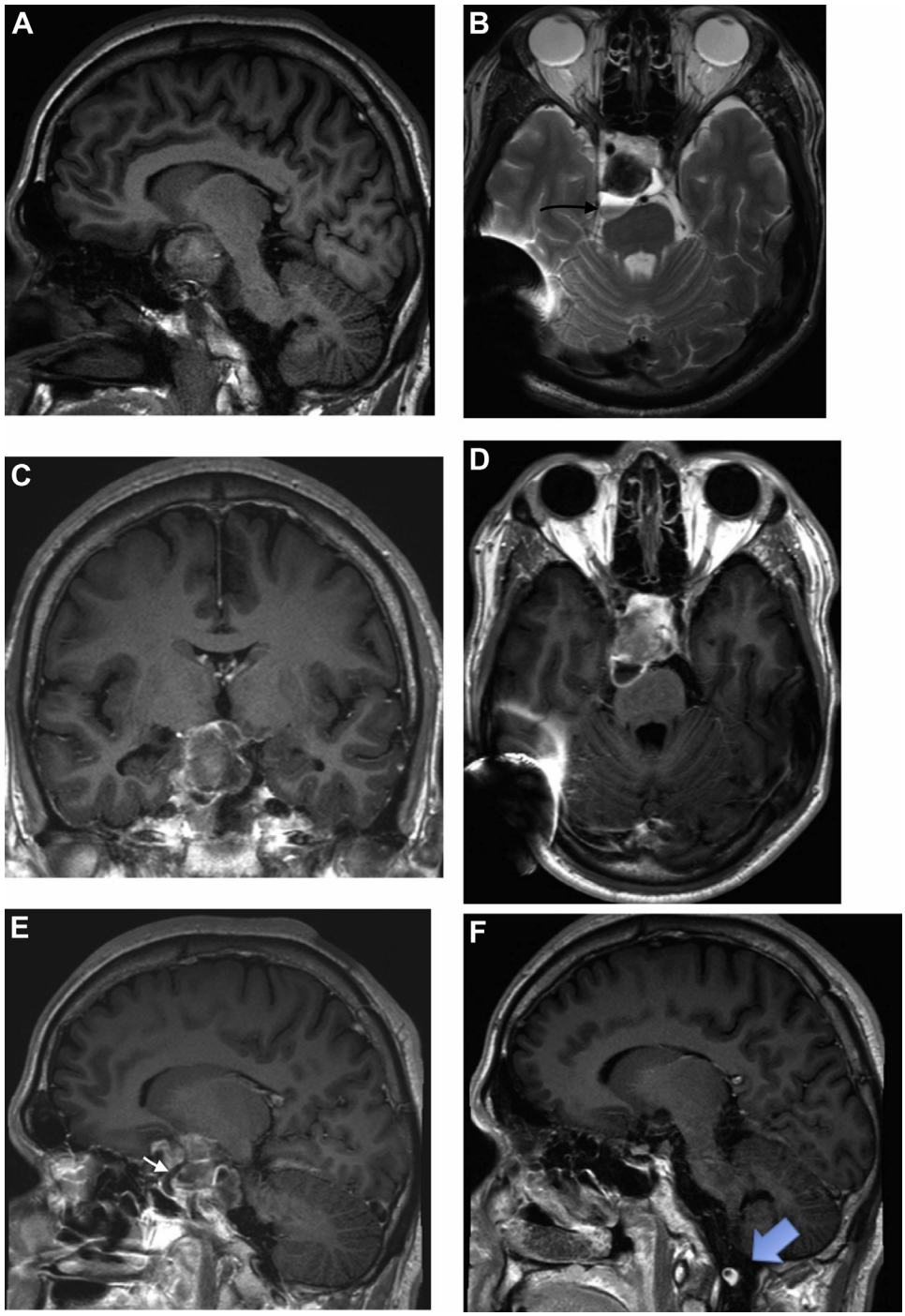

Fig. 2 – Noncontrast images: (A) sagittal T1WI, (B) axial T2WI. Postcontrast images: (C) coronal, (D) axial, and (E and F) sagittal. They showed a mixed solid and cystic lesion located mainly in the suprasellar region with a rightward retroclival extension. The lesion elicits isointense signal intensity (SI), to the brain parenchyma, on T1WI and hypointense SI on T2WI, the cystic component showed a fluid—fluid level (black arrow) with SI indicative of a hemorrhagic content. Associated partial encasement of the right cavernous sinus (white small arrow). Also, noted enhancing leptomeningeal nodular thickening at the C.C junction (thick blue arrow). Nota Bene: artifact seen on axial images is due to the previously placed VP shunt.

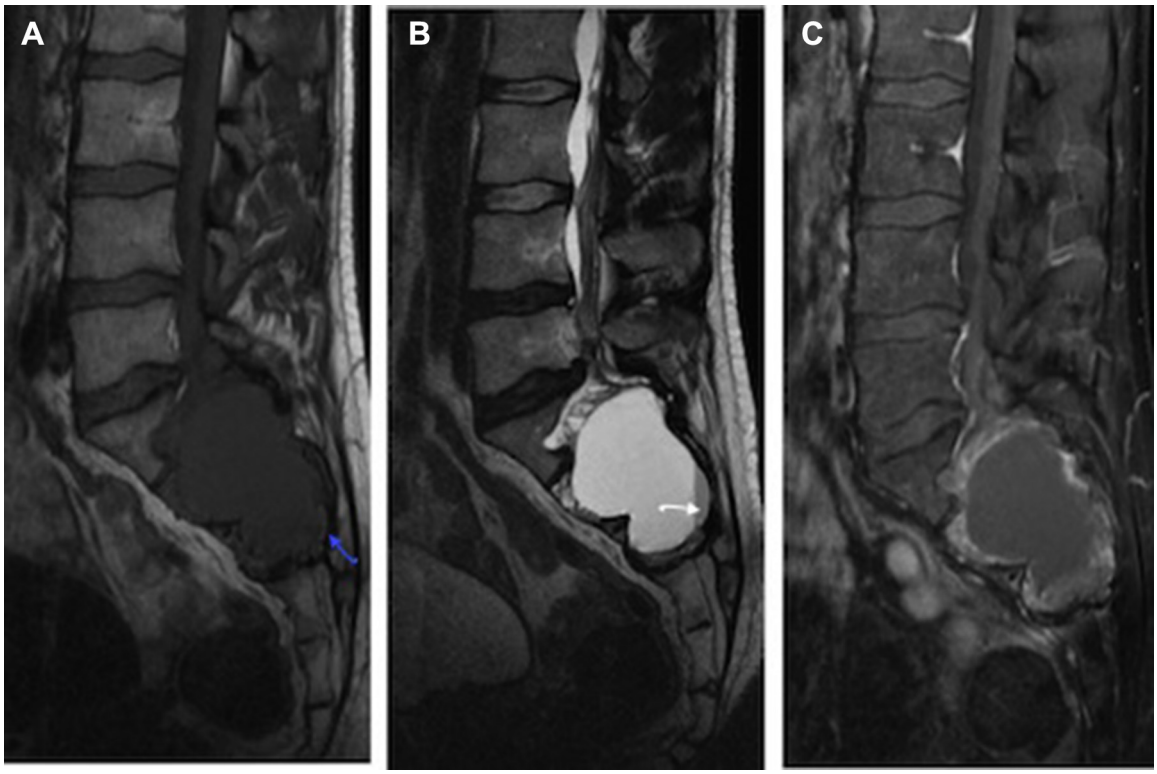

Fig. 3 – MRI of the lumbar spine: (A) sagittal T1WI, (B) sagittal T2WI, and (C) sagittal postcontrast images. Figure shows large subdural mixed solid and multilobulated cystic components. There is fluid–fluid level (white arrow) with faint hyperintense on T1WI signal posteriorly (blue arrow), indicative of a hemorrhagic content. It shows thick irregular peripheral enhancement.

The multiplicity of PA is hypothesized to result from the presence of concomitant multicentric disease, with no evidence of spread from the primary tumor, rather than secondary multifocal spread. Although tumor manifestations were present in both suprasellar and C.C regions at the time of diagnosis, tumor progression at later stages was characterized by diffuse dissemination along the CSF pathways.

Surgical manipulation, whether subtotal resection or VP shunt placement, is another important risk factor for tumor dissemination in patients with PA. Surgical intervention may facilitate the seeding of tumor cells in different locations or open a pathway for tumor cell migration to the CSF spaces [12,21]. Several cases of PA dissemination have been reported after surgical intervention [17,22]. This is less likely the case in our patient, since LD was already visible on the initial MRI examination, before any surgical manipulation of the tumor. The placed VP shunt could, however, be responsible for this dissemination, though unlikely, as it had been placed 6 years earlier to control hydrocephalus caused by meningitis. This is in accordance with other previously reported cases, in which LD was evident before any intervention [9,12].

In addition to the close proximity of tumor to CSF spaces and spread secondary to iatrogenic manipulation, other inherent biological properties, such as tumor consistency, pattern of adhesiveness, and protease secretion, may facilitate the invasion of ependymal surfaces and tumor fragmentation with subsequent free flow and dissemination of the tumor cells within the CSF [12,15,23].

Hemorrhagic components were evident in our case. Hemorrhage associated with PA is very rare with only 32 documented cases from 1997 to 2008 [2,8]. Hemorrhage in a PA may be considered as an additional risk factor for LD, as it may potentiate adhesion of the tumor to the leptomeninges and subsequent invasion.

It is well accepted that LD is more common with malignant neoplasms.

Malignant transformation of PA has been reported in the literature, through several case studies [24–26]. It is thought to be mostly radiation-induced in most instances [3,27]. Only rare examples of PA show spontaneous malignant transformation [26]. LD can be associated with a potential malignant transformation of PA. This is supported by some reports that documented higher histologic grades in the metastatic leptomeningeal foci [28,29]. However, this is not the case in our patient, in which histologic evaluation of all specimens failed to reveal evidence of anaplasia. Of note, LD had been already observed at the time of the initial diagnosis, before treatment. Most previously reported PAs with LD lacked evidence of malignant transformation [13,14,17].

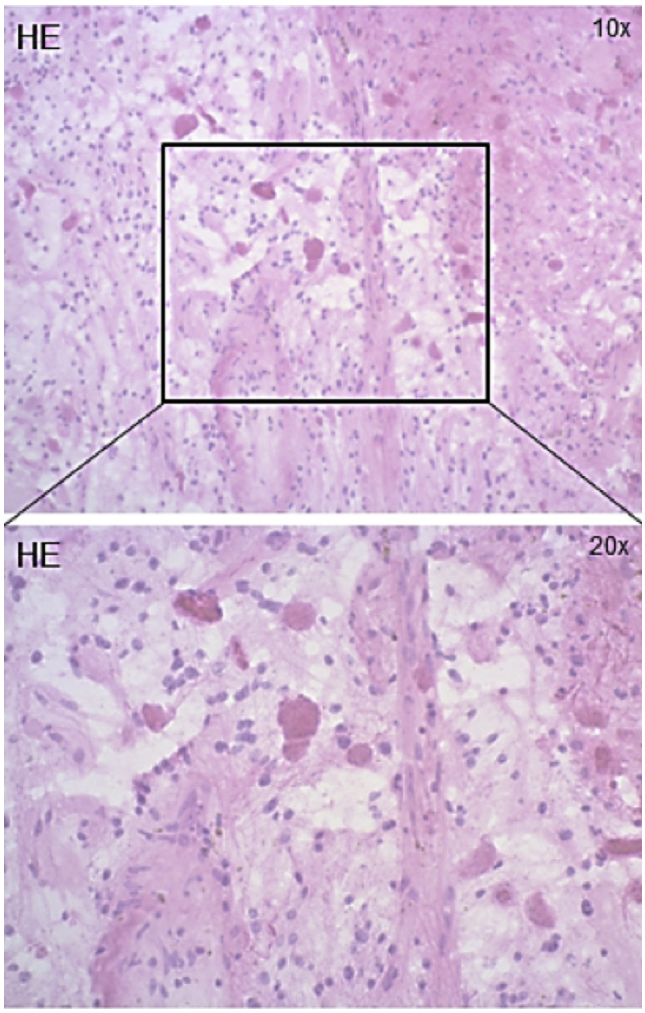

Fig. 4 – Low-grade astrocytic neoplasm composed of small, uniform clear cells embedded in a fibrillary matrix. Higher magnification reveals aggregates of protein droplets and eosinophilic granular bodies commonly found in PA.

Pilomyxoid astrocytoma (PMA), first reported in 1999 [30], PMA can be distinguished from PA by the presence of a prominent myxoid stroma, the angiocentric arrangement of the neoplastic cells forming rosette-like structures, and the absence of Rosenthal fibers and eosinophilic granules. PMA is considered as a variant of PA, most often found in the hypothalamus or optic pathways [3,6]. PMA is more aggressive than the classic PA and classified as WHO grade II [1]. Previous reports have shown a strong association between PMA and LD [22,30,31]. In addition, other reports indicate an association between PMA and intratumoral hemorrhage [7,32], (25%) in PMA compared with PA (8%) [33,34]. In our case, pilomyxoid features were not present.

Molecular genetics studies showed that overexpression of the epidermal growth factor receptor (EGFR), found on the short arm of chromosome 7, is positively correlated with aggressive tumor behavior [35,36]. In addition, it has been reported that overexpression of EGFR is higher in low-grade glioma associated with LD [16,37].

PA is more common in pediatric than in adult patients and typically occurs between the age of 5 and 14 years old [4]. In adults, PA tends to exhibit a less favorable prognosis [38] as witnessed in our patient. Previous studies ascribe the poor prognosis in older patients to the high rate of recurrence, tumor progression, and frank malignant transformation [24,39]. Interestingly, only 20% of previously reported 60 cases of PA associated with LD were more than 15 years old. LD in PA does not appear to correlate with an older age of the patients.

The prognosis of PA, even with LD is more favorable than for diffuse astrocytomas (WHO grades II-IV) [40], particularly when there is no evidence of anaplasia. Mazloom et al., in a retrospective review of 58 patients with PA with LD, reported that the 5-year survival rate approached 55%. Few cases, however, have shown longer survival [17,22], that may reach 20 years [22]. Several factors including the extent of the surgical resection, adjuvant radiotherapy, and chemotherapy, the age of the patient and location of the primary tumor play a significant role in patient outcome. Therefore, early diagnosis and effective management are critical for long-term survival. Optimal therapy for patients with PA accompanied by LD remains controversial. Initial total resection of the tumor remains the goal to reduce the risk of LD [15,41]. Close long-term follow-up with regular MRI should facilitate early detection of dissemination. The value of adjuvant chemotherapy and/or radiotherapy is variable in the previous reports. To avoid long-term toxicity, radiotherapy is usually not favored in young patients [40,42]. In this context, Bain et al., in 2013, introduced proton therapy in the treatment of dissemination in an attempt to eliminate the exit dose, with radiation focused only to the craniospinal axis. In cases with EGFR overexpression, EGFR inhibitors would represent useful adjuvant therapy [16,43].

The treatment regimen in our case consisted of subtotal resection, local irradiation to the sacral mass, and chemotherapy, with relatively effective disease control for 7 years. However, the patient has recently developed progressive dissemination, which has required additional radiotherapy. The overall survival time is 9 years, and the patient remains on follow-up.

Conclusions

The diagnosis of PA in adults is rarely made preoperatively; therefore, enhanced awareness is crucial to facilitate correct diagnosis and management. The possibility of LD in cases of PA should be considered when tumors are in close proximity to CSF spaces, especially in the sellar region, and after subtotal resection or VP shunt placement. The risk of LD is also increased in cases of PMA or when features of anaplasia are present. In addition, molecular genetic studies for overexpression of EGFR may be predictive of an aggressive course. Finally, spinal MRI is recommended whenever PA is found to be associated with the above risk factors.

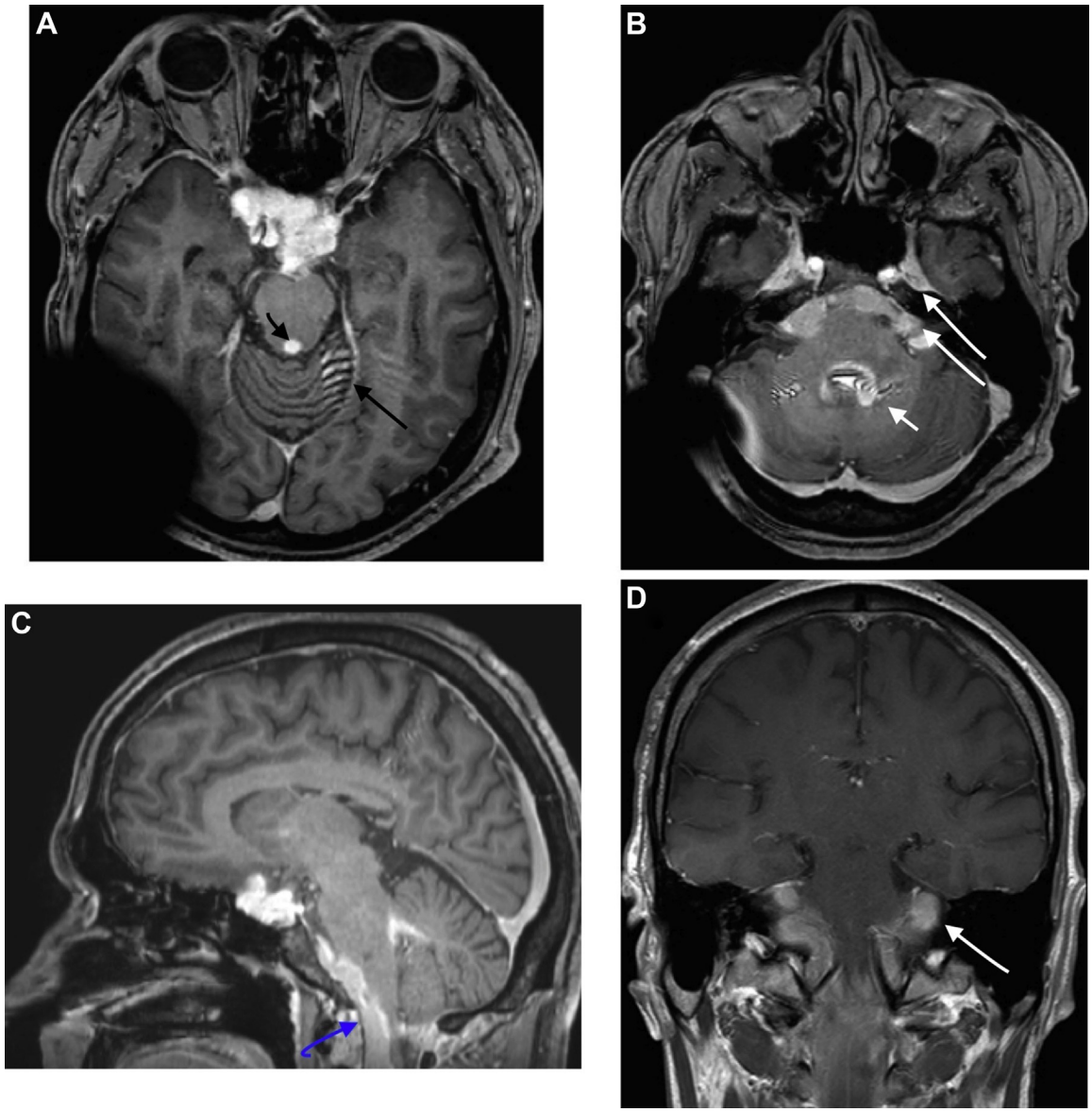

Fig. 5 – MRI of the brain (A, B) axial postcontrast T1WI. (C) Sagittal postcontrast T1WI, (D) coronal postcontrast T1WI. Progressive course evident by increase the size of the suprasellar lesion, diffuse LD appears in Meckel's caves, cerebellopontine angles (white long arrows), anterior to the upper cervical cord (blue arrow), in the ependymal surface of the fourth ventricle (white short arrow), and in the aqueduct of sylvius (short black arrow) as well as along the vermis (long black arrow).

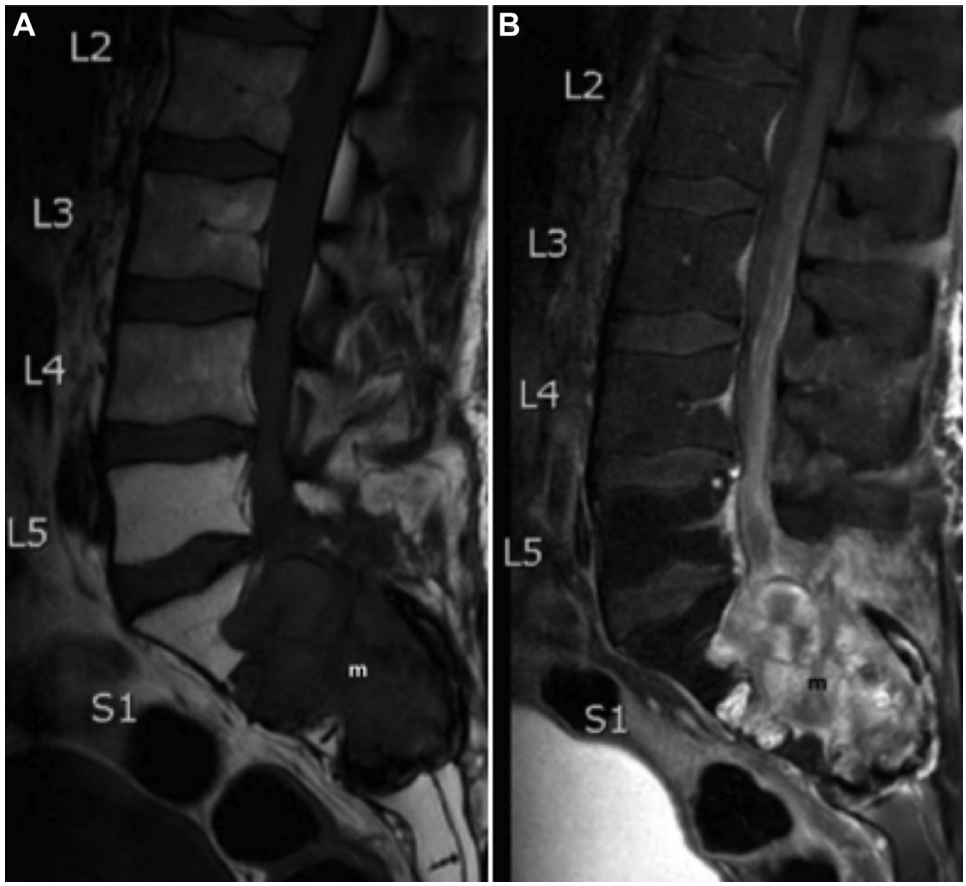

Fig. 6 – MRI of the spine: (A) sagittal T1WI, (B) sagittal postcontrast image. Figure shows a progressive course evident by an increase in the size of the, partially resected, subdural lesion (m) at the sacral region. The lesion appears more solid compared to the preoperative images shown in Figure 3.

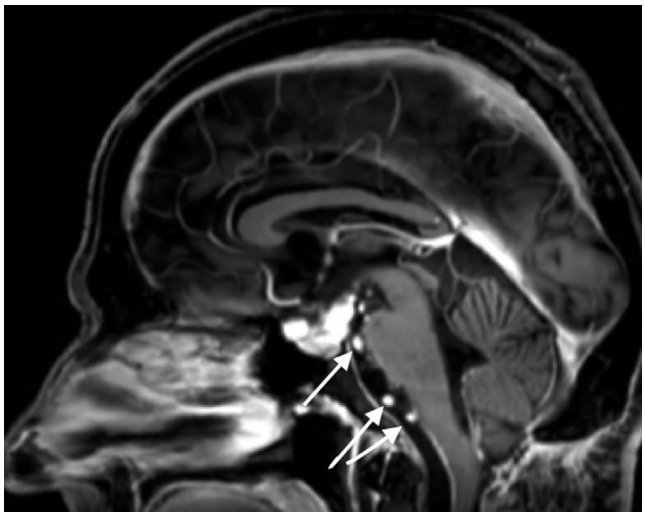

Fig. 7 – MRI of the brain: sagittal postcontrast T1WI. Figure shows reduction in the size of the suprasellar lesion and marked resolution of the diffuse LD previously shown in Figure 6 with only noted small focal enhancing nodules in the prepontine cistern and anterior to the spinal cord (white arrow heads).

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