Case Report

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Extra-axial desmoplastic/nodular medulloblastoma in adult mimicking cerebellar metastasis: reappraisal of this rare presentation with literature review

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Introduction and importance: Medulloblastomas are the most common malignant intra-axial brain tumour in paediatric patients and represent 35–40% of posterior fossa tumour types in children between 3 and 9 years of age. Medulloblastomas may also be found in adulthood. These tumours are classified into two groups according to its molecular characteristics and histological type. The desmoplastic/nodular subtype is the second common subtype after the classic one. Only three cases of desmoplastic/nodular extra-axial medelloblastoma have been previously reported in the literature originating from to the cerebellopontine angle.

Case presentation: The authors report a new case of an extra-axial desmoplastic/nodular cerebellar medulloblastoma originating outside the cerebellopontine angle and mimicking a solitary cerebellar metastasis in a 49-year-old female patient who presented for a raised intracranial pressure and cerebellar syndrome.

Clinical discussion: Medulloblastoma is a malignant embryonal intra-axial tumour of the cerebellum or posterior brain stem that occurs mainly in children. Medulloblastomas may also be found in adulthood. Desmoplastic/nodular medulloblastoma is the second most common type of all medulloblastomas. The intra-axial form is always predominant. Only three cases of extra-axial desmoplastic/nodular medulloblastoma have been reported in the literature. The authors will go through the literature to dissect this rare entity.

Conclusion: Although considered a common paediatric intra-axial tumour, there are increasing numbers of solitary cases reporting an extra-axial presentation in different locations of the posterior cerebral fossa even in adulthood. These rare and unusual presentations and locations may mislead the correct diagnosis and delay treatment.

Keyswords: desmoplastic/nodular, extra-axial, medulloblastoma, MRI, surgery

Introduction and importance

Medulloblastomas are the most common malignant intra-axial brain tumour in paediatric patients[1] and represent 35% to 40% of posterior fossa tumour types in children between 3 and 9 years of age[2], although cases have also been reported since birth[3]. Medulloblastomas may also be found in adulthood. At this stage they only represent between 0.4 and 3% of primary tumours of the central nervous system (CNS)[4]. These lesions are of neuroectodermal origin and are considered by the WHO to be malignant and invasive embryonal tumours of the cerebellum, with a high histological grade 1 , with rapid dissemination through the cerebrospinal fluid (CSF) and, unlike low-grade tumours, have a high heterogeneous component[2].

Medulloblastomas are classified into two groups. The first according to its molecular characteristics[5]: medulloblastoma with WNT activation, medulloblastoma with SHH activation, Group 3 (no WNT alteration/no SHH alteration), and Group 4 (no WNT alteration/no SHH alteration). The second according to its histological type[6,7]: classic medulloblastoma, desmoplastic/nodular medulloblastoma, medulloblastoma with extensive nodularity, large cell medulloblastoma, and finally anaplastic medulloblastoma.

Today, the cause of medulloblastoma is still not known for sure. Various clinical trials have tried to identify a viral cause; however, neither cause has been considerably accepted. Other studies speak of alterations in some hereditary genes in children, but in adults the reason is still unknown[8].

Here, the authors report a new case of an extra-axial desmoplastic/nodular cerebellar medulloblastoma originating outside the cerebellopontine angle and mimicking a solitary cerebellar metastasis in a 49-year-old female patient who presented for a raised intracranial pressure and cerebellar syndrome.

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This case report has been reported in line with the SCARE Criteria[9].

Case presentation

A 49-year-old female patient, household chores, known to have a benign ovarian cyst under clinical and radiological follow-up was referred to our department of neurosurgery for progressive onset of holocranial headaches of approximately one month with occipital origin resistant to non-opioid analgesics without vomiting or epileptic seizures. These headaches were associated with occasional dizziness, blurred vision, walking disorders and left upper limb clumsiness altering her daily life. There was no evidence of prior head trauma of fever.

Upon neurological examination, the patient was conscious and alert. She had a significant ataxic gait with left cerebellar syndrome made of intention tremor that increases in amplitude as her finger approaches the target at finger–nose test, dysdiadochokinesis, and upper left limb hypotonia at Stewart-Holmes test. There was no gaze-evoked nystagmus or saccadic eye movements and her speech was coherent without any signs of cerebellar 'staccato' speech during the whole interview. Her fundoscopic examination was normal. The rest of her general condition examination revealed no abnormalities. Both frontal chest radiograph and laboratory tests were all in normal range.

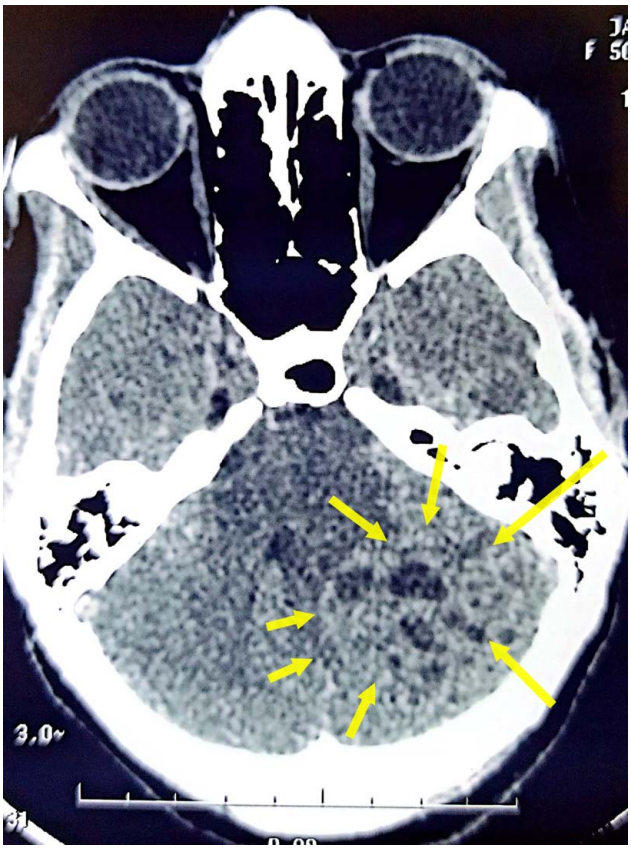

Figure 1. Axial non-enhanced brain computed tomography scan in parenchymal window showing a solitary heterogeneous left cerebellar tumour measuring 32 × 54 × 40 mm in diameter with a multicystic spongiform architecture (yellow arrows) causing a mass effect on the 4th ventricle.

HIGHLIGHTS

- Medulloblastoma is a malignant and invasive embryonal intra-axial tumour of the cerebellum or posterior brain stem that occurs mainly in children, with a tendency to metastasize via the cerebrospinal pathway.
- Desmoplastic/nodular medulloblastoma is the second most common type of all medulloblastomas after the classic form.
- The intra-axial form is always predominant and only three cases of extra-axial desmoplastic/nodular medulloblastoma have been reported in the literature.
- Patients with medulloblastoma typically present with symptoms that evolve over a period of weeks to months. Frequently, a combination of signs and symptoms of cerebellar dysfunction and increased intracranial pressure are found.
- Medulloblastoma appears, in computed tomography scan or MRI, as a rounded or ovoid tumour, with circumscribed margins.
- Radiological differential diagnosis is based on ependymomas, meningiomas, rare malignant gliomas, pilocytic astrocytomas, metastases, hemangioblastomas or Lhermitte-Duclos disease.
- The treatment of medulloblastoma includes the triad of surgery, radiotherapy and chemotherapy.
- The prognosis of medulloblastoma depends on several factors. Patients under 3 years of age, the presence of metastasis, partial tumour resection, male sex, and anaplastic and large cell medulloblastomas have a poor prognosis.

A non-enhanced brain computed tomography (CT) scan (Fig. 1) was quickly performed and revealed a solitary heterogeneous left cerebellar lesion measuring 32 × 54 × 40 mm in diameter with a multicystic spongiform architecture causing a mass effect on the fourth ventricle and a triventricular hydrocephalus. More contrast-enhanced brain MRI (Fig. 2) was performed showing the left cerebellar spongiform tumour with dual solid and cystic components having extensive contact with the tentorium cerebellum. The fleshy component was in isosignal on T2-weighted sequence whereas the cystic part was in hypersignal on the same sequence. There was a visible thin rim of CSF between the tumour and the healthy cerebellar parenchyma defining the CSF cleft sign and reflecting the extra-axial nature of the lesion. This lesion enhances heterogeneously and moderately after Gadolinium chelate injection with a minor oedematous reaction all around on the T2 Fluid attenuated inversion recovery (Flair) sequence. The diffusion-weighted sequence showed a discrete hypersignal with an intermediate apparent diffusion coefficient (ADC). The perfusion analysis revealed a relative cerebral blood volume (rCBV) varying between 3 and 4. There was no bleeding on the gradient echo sequence and the magnetic resonance spectroscopic study showed a significant drop in N-acetylaspartate (NAA) with choline peak and reversal of the creatine choline ratio. The spinal MRI did not reveal any leptomeningeal dissemination.

Given the patient's age, her clinical history of an ovarian cyst, even benign, and the infratentorial location of the lesion and its radiological features, a cerebellar metastasis was first mentioned. Our aetiological investigation was completed by carrying out a

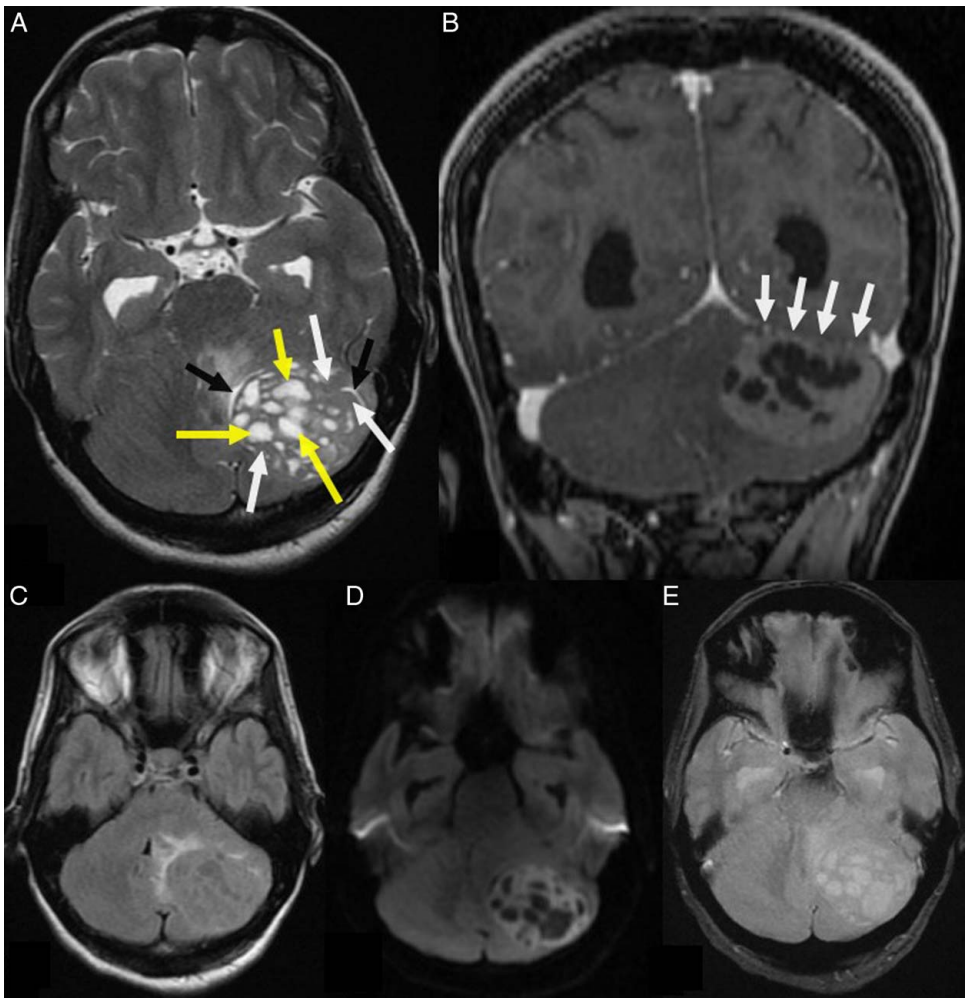

Figure 2. Axial and coronal brain MRI showing the left cerebellar spongiform tumour with dual solid and cystic components having significant tentorial attachment. The fleshy component is in isosignal on T2-weighted sequence (A; white arrows) whereas the multicystic part in a significant hypersignal (A; yellow arrows). There is a visible thin rim of cerebrospinal fluid (CSF) between the tumour and healthy cerebellar parenchyma defining the CSF cleft sign and reflecting the extra-axial origin (A; black arrows). Note the heterogeneous and moderate enhancement after Gadolinium chelate injection (B) and the extensive contact with the tentorium cerebellum (B; white arrows) with minor oedema on T2-FLAIR sequence (C). Diffusion-weighted image showed a discrete hypersignal (D). No bleeding on the gradient echo sequence (E).

thoraco-abdominopelvic CT scan which revealed multiple well-marginated border osteolytic lesions without peripheral osteosclerosis of the pelvic girdle of the lumbar spine type IB according to Lodwick classification. The pelvis MRI discovered a benign cervico-isthmic sessile subserosal uterine fibroid of 64 mm of diameter without signs of atopy or degeneration. Breast ultrasound scan revealed a solitary fibroadenolipoma of the upper outer quadrant of her left breast.

Routine laboratory tests such as complete blood cell count, complete metabolic panel, and coagulation studies were performed and revealed no abnormalities. Blood typing and crossmatching assessing the patient's general health were also performed.

After advancing the diagnosis to our patient and having obtained her informed consent for surgery, she underwent a total en-bloc tumour excision via a midline suboccipital craniectomy in classic prone position with her head maintained in the MAYFIELD Skull Clamps. Intraoperatively, the tumour-cerebellum interface was well-defined testifying to its extra-axial nature. The lesion had a soft friable consistency of heterogeneous yellow and pink colour traversed by small blood vessels on its surface (Fig. 3) containing multicysts upon dissection.

The patient was gradually weaned and extubated few hours postoperatively. The postoperative course was uneventful with a significant regression of both left cerebellar dysfunction and headaches. The postoperative CT scan (Fig. 4) performed 24 h later did not reveal any residual tumour except a minor bleeding and pneumocephalus.

The histopathological study of her surgical specimen revealed a sheet of tumour proliferation made of undifferentiated cells of the embryonic type with small hyperchromatic and pleomorphic ovoid nuclei with the presence of some mitoses and apoptic corns and without evidence of anaplastic cells. This proliferation includes paler nodules (lower cell density) corresponding to a network of neutrophils. Reticulin staining showed a dense intranodular reticulin network (Fig. 5). In immunohistochemistry, tumour cells were positive for neuron specific enolaseand NeuN antibodies (Fig. 5), irregularly positive for beta-cathenin and Ki 67 (15% positivity limited to internodular territories);

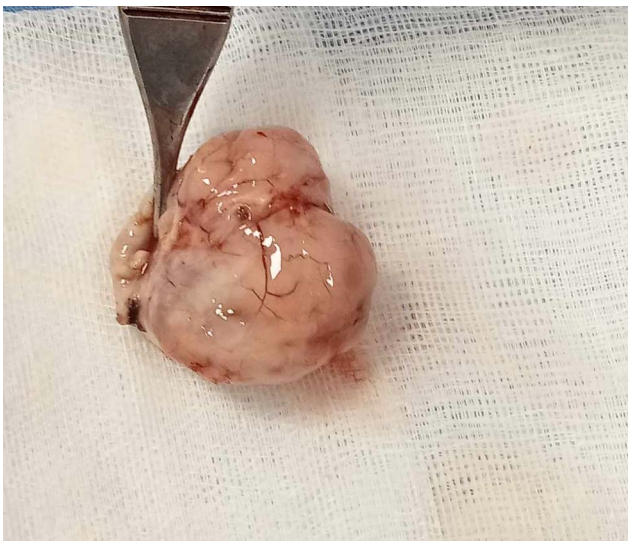

Figure 3. Immediate postoperative photograph of the whole specimen with soft friable consistency of heterogeneous yellow and pink colour traversed by small blood vessels on its surface.

Immunolabeling was inconclusive for synaptophysin. Molecular study is currently not available in our country. All these features were in favour of a cerebellar desmoplastic/nodular medulloblastoma.

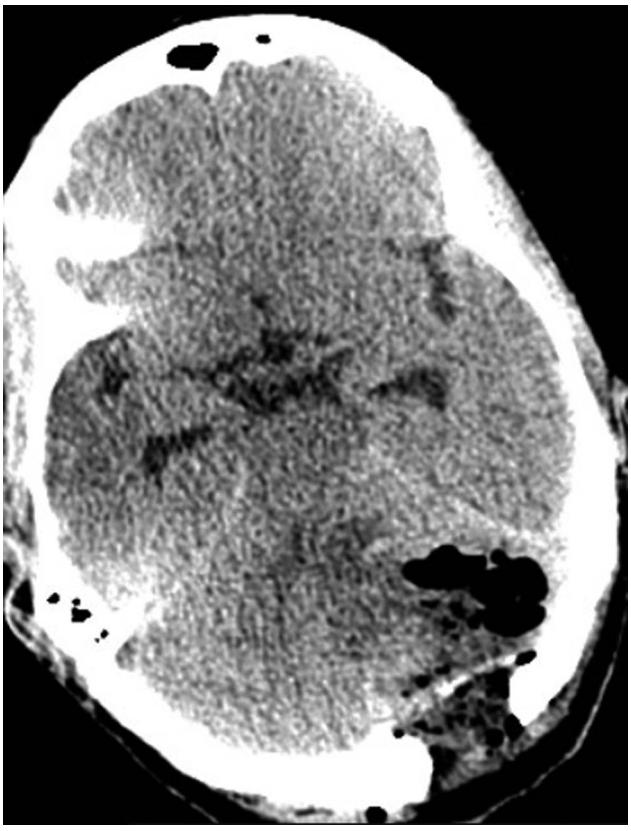

Figure 4. Axial computed tomography scan in parenchymal window performed 24 h postoperatively revealing no residual tumour.

The patient was discharged at day 4 postoperatively under degressive systemic corticosteroids and was referred to the radiotherapy department for further treatment.

Clinical discussion

Medulloblastoma is a malignant and invasive embryonal intra-axial tumour of the cerebellum or posterior brain stem that occurs mainly in children, with predominantly neuronal differentiation and a tendency to metastasize via the cerebrospinal pathway[2,6]. Medulloblastomas may also be found in adulthood and represent between 0.4 and 3% of primary tumours of the CNS[4]. Despite finding a higher incidence in men in the literature[10], 81.8% of the patients were women, without finding a clear justification for this finding

Furthermore, it is more common in white people and people of Hispanic origin[5]. This lesion is known to be localized intra-axially at the hemispheric level. Extra-axial location is rarely reported, difficult to diagnose radiologically and even clinically. According to Ali *et al.*[11]. there are only 12 cases of extra-axial medulloblastoma in the literature in adults. In 2021, Ali and colleagues added a 13th case of extra-axial medulloblastoma of the cerebellopontine angle in a 27-year-old patient. Our case is then the 14th case of such extra-axial tumour in adult population.

Until now, there is no well-defined aetiology for the different types of medulloblastoma. Although some previously published research has highlighted a link between maternal diet and blood/immune disorders during pregnancy[12], other authors report an association with viral infections such as John Cunningham (JC) virus or human cytomegalovirus (CMV) infections during childhood[13]. Indeed, the tumour growth of medulloblastomas begins in the fourth ventricle and can develop until occupying it. It is generally accepted that this growth may arise from the precursors of the granule cells of the outer germinal layer (EGL) of the developing cerebellum[14].

Desmoplastic/nodular medulloblastoma is the second most common type of all medulloblastomas after the classic form[5]. The intra-axial form is always predominant. Only 3 cases of extra-axial desmoplastic/nodular medulloblastoma have been reported in the literature[15,16,11]. All these lesions were located in the cerebellopontine angle. Our case is from now on the 4th case of such subtype of this tumour in its rare location and the first case that does not belong to the cerebellopontine angle.

Patients with medulloblastoma typically present with symptoms that evolve over a period of weeks to months. Frequently, a combination of signs and symptoms of cerebellar dysfunction and increased intracranial pressure are found. Hydrocephalus may arise due to obstruction of the flow of CSF in the fourth ventricle. The most common symptoms include irritability, lethargy, nausea and/or vomiting, morning headaches, anorexia, and behavioural changes. In addition, ataxia may be found with gait disorders and inability to make rapid movements[7,8]. It may also affect vision, causing diplopia, nystagmus or papilledema[7,8]. In cases where there is dissemination of the disease, symptoms related to the location of the metastatic involvement can also be observed[7]. Our patient had a significant ataxic gait with left cerebellar syndrome made of intention tremor that increases in amplitude as her finger approaches the target at finger–nose test, dysdiadochokinesis, and upper left limb hypotonia at Stewart-Holmes test. Another important symptom may be

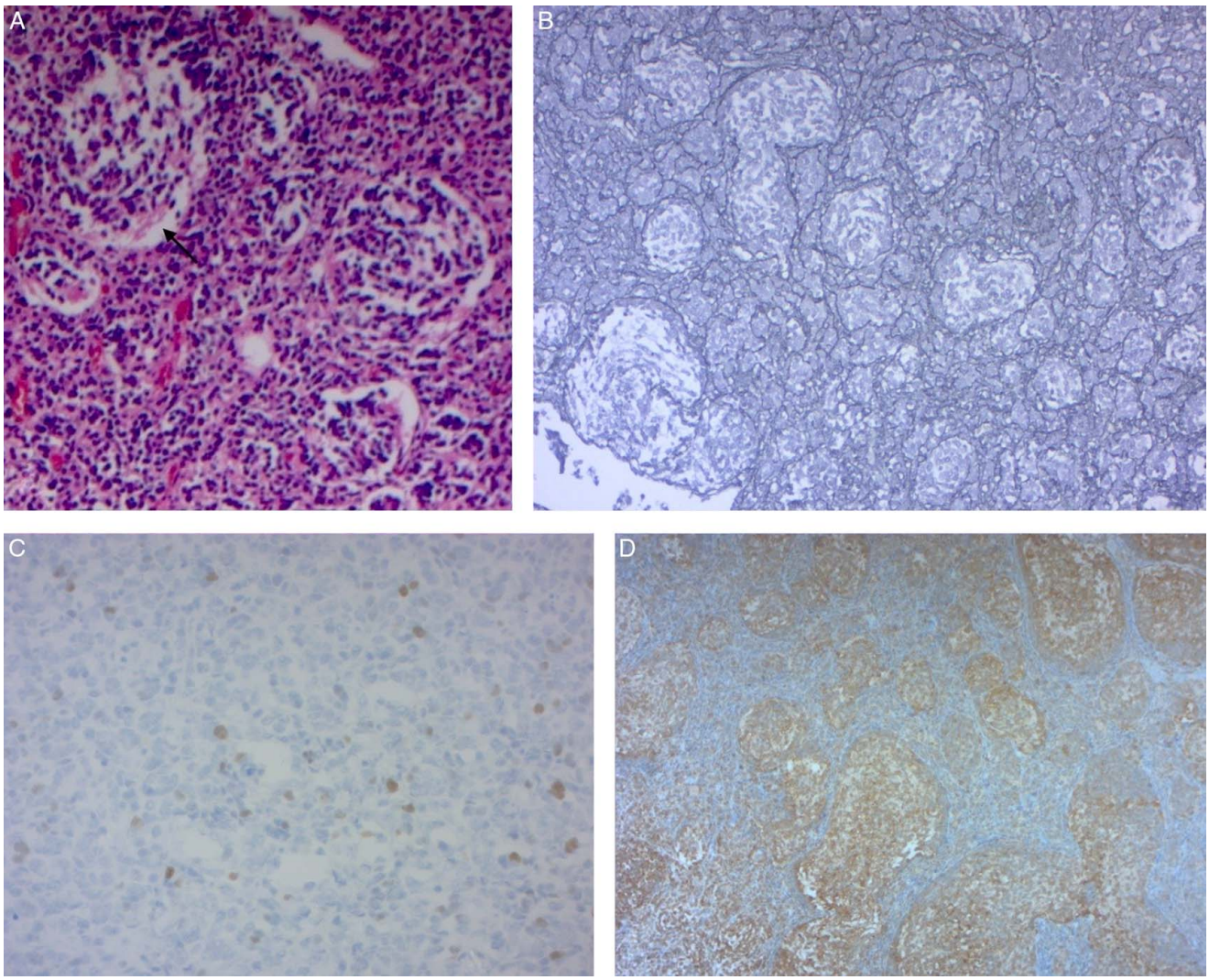

Figure 5. Microscopic photograph of the surgical sample showing a nodular architecture: pale nodules (A, black arrow) made up of undifferentiated embryonic-type cells [hematoxylin and eosin (HE) ×100] integrated into a fibrillar matrix of the neuropil type (HE ×40). Note the Silver impregnation of the internodular reticulin network (reticulin ×200) (B). At nuclear immunostaining, few tumour cells from the internodular territory were positive (< 15%) (×200) (C); cytoplasmic immunostaining was positive for the NeuN antibody (×200) (D).

leptomeningeal dissemination, which can cause seizures and cranial nerve paralysis something our patient did not have. Sometimes, neurological symptoms can also be due to haemorrhage derived from the tumour which was also absent in our patient[7].

Medulloblastoma appears, in CT scan or MRI, as a rounded or ovoid tumour, with circumscribed margins. Its most frequent location in adults is the cerebellar hemisphere (in children it most frequently affects the cerebellar vermis)[4]. Both characteristics were identified in the case of our patient. It has been previously reported that findings in imaging studies are more variable in adult cases than those observed in children[17]. CT allows an initial evaluation by establishing the presence of the lesion in 95% of cases[18]; however, given that the posterior fossa generates a lot of "noise" due to the beam hardening artifact, in some cases its use is limited[19]. As found in our clinical case, medulloblastoma on CT presents as a hyperdense and heterogeneous lesion in relation to the adjacent grey matter, which is related to its histological composition, which is characterized by having densely grouped round cells. Medulloblastoma presents enhancement, although to a lesser extent in the case of adults, compared to children. This has been related to the high amounts of reticulin fibres in the tumour stroma, especially in the desmoplastic subtype, which occurs more frequently in adults. The presence of peritumoral oedema can also be evaluated. In a high percentage of cases, the lesions present areas of low density, related to intratumoral cysts or necrosis, as observed in our case[1,17]. On MRI, medulloblastoma has been found to have a variable appearance[17]. In T1-weighted and T2-weighted images we may find variable contrast intensity and enhancement (usually hypointense on T1 and iso- or hyperintense on T2). Cystic or necrotic areas are easily detected on T2 sequences due to their hyperintensity[17]. Areas of haemorrhage or calcification and leptomeningeal infiltration may be found[1]. They restrict diffusion in MRI studies (which differentiates medulloblastomas

from other posterior fossa tumours)[1,2]. In our patient, the tumour was multicystic with heterogeneous and moderate enhancement after Gadolinium chelate injection and a discrete hypersignal on diffusion-weighted imaging.

Attempts have been made to use different sequences to differentiate between low- and high-grade tumours. Perfusion studies have shown good sensitivity but low specificity. The ADC map has been studied to try to differentiate posterior fossa tumours, classifying tumours into 3 classes according to the ADC value: high, medium and low[20]. High-grade tumours, such as medulloblastoma, have abundant heterogeneous tissue, which does not allow adequate evaluation with the ADC sequence, but it has been reported that they have a low ADC[21]. Our patient had an intermediate ADC. Spectroscopy has excessive disturbance of magnetic susceptibility and low spatial resolution, which is why it has not been effective[20]. On spectroscopy, medulloblastoma generally behaves like other neuroectodermal tumours, showing high levels of Choline, decreased NAA and creatine, and occasionally, elevated peaks of lipids and lactic acid[2]. This finding was corroborated in the spectroscopy of our patient.

The radiological differential diagnosis is based on ependymomas, meningiomas, rare malignant gliomas, pilocytic astrocytomas, metastases (adults much more often than children), hemangioblastomas or Lhermitte-Duclos disease[22].

The treatment of medulloblastoma includes the triad of surgery, radiotherapy and chemotherapy[7]. With surgery, patients undergo a safe surgical resection, reducing postoperative neurological damage and restoring normal CSF flow in the case of obstructive hydrocephalus as it was performed in our patient who underwent a safe en-bloc resection of her tumour without any need of CSF shunting[23]. Recently, there is growing interest in the use of proton therapy which may reduce irradiation of non-target tissues and may therefore reduce late toxicities related to photon radiotherapy treatment[24].

The prognosis of medulloblastoma depends on several factors. Patients under 3 years of age, the presence of distant spread (metastasis), partial tumour resection, male sex, and anaplastic and large cell medulloblastomas have a poor prognosis[7]. On the contrary, female sex, a lower residual amount after surgery and desmoplastic medulloblastomas have a better prognosis[7]. Survival in previous reports is around 81% at 5 years and 62% at 10 years[25].

Through our present case, we were able to enrich the literature with the fourth case of extra-axial desmoplastic nodular medulloblastoma in an adult patient. Our report is, therefore, the first case where tumour does not belong to the cerebellopontine angle unlike the three other cases of extra-axial medelloblastoma previously reported in the literature. And from now on, the diagnosis of medulloblastoma, in its desmoplastic/nodular form more precisely, must appear among the differential diagnoses list of extra-axial tumours of the posterior cerebral fossa in adult population.

Conclusion

Cerebellar medulloblastoma, in its several subtypes, has always shown significant heterogeneity in clinical presentation, radiological diagnosis and biological features. Although considered a common paediatric intra-axial tumour, there are increasing numbers of solitary cases reporting an extra-axial presentation in different locations of the posterior cerebral fossa even in adulthood. These rare and unusual presentations and locations may mislead the correct diagnosis and delay treatment.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Patient perspective

During hospitalization and at the discharge, the patient has given the opportunity to share their perspectives on the intervention the boy received and she was satisfied with the care.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

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Author contribution

All authors contribute to write this manuscript

Conflicts of interest disclosure

The authors declared no potential conflicts of interests with respect to research, authorship and/or publication of the article.

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