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Primary intramedullary spinal cord pilocytic astrocytoma with anaplasia in an adult: illustrative case

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BACKGROUND Primary intramedullary spinal cord (IMSC) pilocytic astrocytoma (PA) with anaplasia is extremely rare.

OBSERVATIONS A 50-year-old man presented to our hospital with numbness of the left posterior rib region, back, and bilateral lower limbs. Contrast-enhanced T1-weighted magnetic resonance imaging (MRI) revealed an intramedullary lesion at T2–T3 with no contrast enhancement. The patient opted for conservative treatment. Eighteen months after the first consultation, the patient presented with slowly progressive numbness of the bilateral upper limbs, paraparesis, and dysuria, with rapid deterioration over the following 3 months. T1- and T2-weighted MRI revealed expansion of the intramedullary lesion, which extended from C7 to T5, and syringomyelia at C5–C6. Contrast-enhanced T1-weighted MRI revealed an enhancing intramedullary lesion at C7–T5. Open biopsy and C5–T5 laminectomy were performed for diagnosis and decompression. PA with anaplasia was diagnosed based on pathological and immunohistochemical findings. The patient received postoperative radiotherapy and chemotherapy.

LESSONS Rapidly progressive IMSC PA with a change in contrast enhancement is extremely rare in adults. PA may undergo a spontaneous malignant transformation during its natural clinical course. In this case, the change in contrast enhancement may have been associated with the malignant transformation of the PA.

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KEYWORDS anaplasia; astrocytoma; intramedullary tumor; malignant transformation; primary tumor; spinal cord tumor

Intramedullary spinal cord (IMSC) tumors are rare central nervous system neoplasms that account for 2%–4% of all central nervous system tumors.[1] They most commonly occur at the cervical level (33%), followed by the thoracic (26%) and lumbar (24%) levels.[2] Intramedullary astrocytomas account for approximately 60% of all spinal cord tumors in children and adolescents.[3] Pilocytic astrocytomas (PAs) rarely occur in adults, have been classified as World Health Organization grade I astrocytic tumors, and are associated with favorable outcomes.[4,5] However, tumor recurrence and malignant transformation frequently occur in adults with PA, resulting in poor outcomes.[6,7] We report the first adult case of primary IMSC PA with anaplasia that changed from noncontrast-enhancing to contrast-enhancing on magnetic resonance imaging (MRI) during its clinical course.

Illustrative Case

A 50-year-old man with no significant past or medical history presented to our hospital with left posterior axilla and bilateral lower limb numbness. T1- and T2-weighted thoracic spinal cord imaging revealed a homogenous lesion with marked isointensity and hyperintensity in the intramedullary region at T2–T3. Contrast-enhanced T1-weighted imaging revealed an intramedullary lesion with no contrast enhancement in the thoracic spinal cord (Fig. 1). Although the patient was advised to receive intramedullary tumor biopsy, he opted for conservative treatment until symptom exacerbation. MRI was performed every 6 months for follow-up.

Eighteen months later, he presented with slowly progressive numbness of the bilateral upper limbs and paraparesis, with rapid

ABBREVIATIONS ATRX = alpha thalassemia/mental retardation syndrome X-linked; IMSC = intramedullary spinal cord; MRI = magnetic resonance imaging; PA = pilocytic astrocytoma; TMZ = temozolomide.

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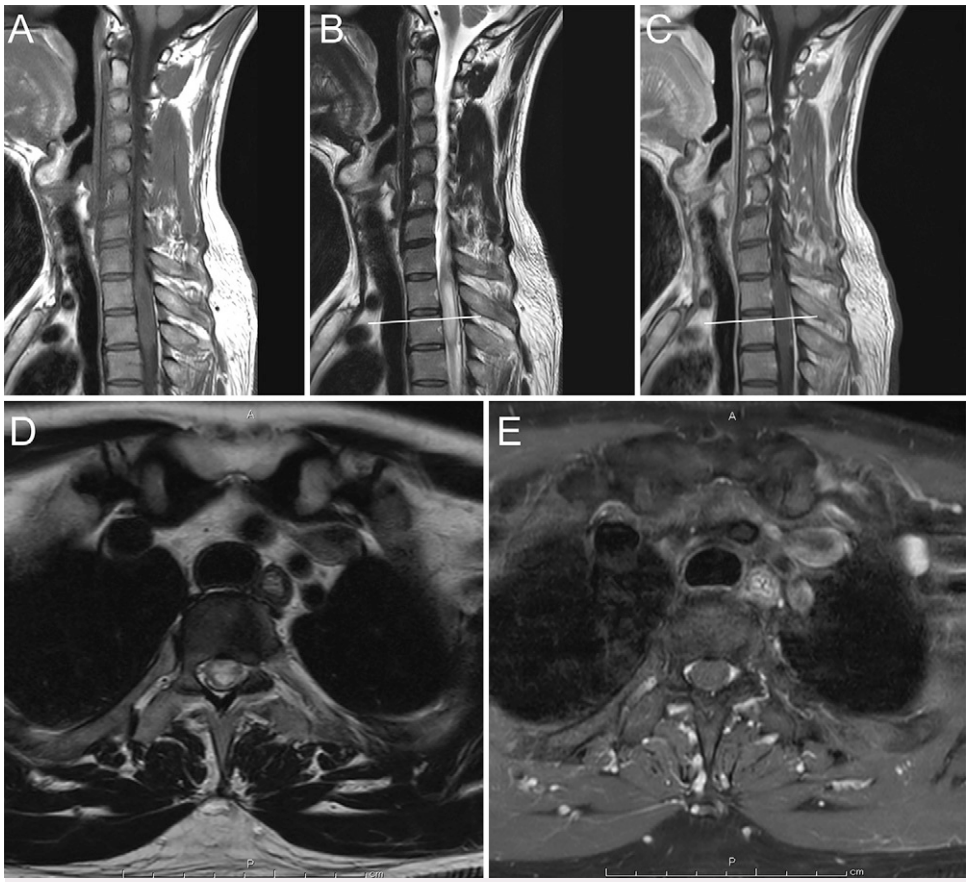

FIG. 1. Initial spinal cord magnetic resonance images. Sagittal T1-weighted (**A**) and T2-weighted (**B**) images show an intramedullary lesion. A contrast-enhanced T1-weighted image (**C**) shows a noncontrast-enhancing lesion. Axial (level of the *white line* in the sagittal images in panels B and C) T2-weighted (**D**) and contrast-enhanced T1-weighted (**E**) images show an intramedullary lesion.

bladder and bowel function deterioration over the following 3 months. The bilateral triceps, patellar, and Achilles tendon reflexes were exaggerated. T1- and T2-weighted imaging revealed expansion of the intramedullary lesion, which now extended from C7 to T5, and syringomyelia at C5–C6. Contrast-enhanced T1-weighted imaging revealed a contrast-enhancing intramedullary lesion at C7–T5 (Fig. 2). Intracranial MRI revealed no significant abnormalities. Laminectomy from C4 to T5 and open biopsy at the level of T1–T3 were performed for decompression and diagnosis. After the dura matter was opened between T1 and T3, a swollen spinal cord was revealed. A biopsy of the lesion was taken through the posterior median sulcus of the spinal cord and submitted for histopathological examination. The biopsied specimens were confirmed to be tumor tissue in the intraoperative rapid pathological examination, and the additional specimens were biopsied from the same lesion to complete the procedure.

Histopathological and Immunohistochemical Examination

Histopathological examination revealed cells with long bipolar piloid processes, eosinophilic granular bodies, and Rosenthal fibers. Additionally, four mitotic figures per 10 high-power fields were found. Immunohistochemical analysis revealed strong glial fibrillary acidic protein immunoreactivity, S-100 protein and oligodendrocyte transcription factor 2 positivity, and a high MIB-1 labeling index (34.3%) (Fig. 3). The tumor exhibited negative immunoreactivity to the IDH1-R132H, p53, and H3K27M antibodies. The nuclear expression of alpha thalassemia/mental retardation syndrome X-linked (ATRX) was lost. Based on these findings, PA with anaplasia was diagnosed.

Radiotherapy and Chemotherapy

No symptom improvement occurred despite adjuvant therapy consisting of focal radiotherapy (50.4 Gy in 28 fractions) and chemotherapy with temozolomide (TMZ; 75 mg/m^2 per day for 6 weeks). No change in tumor size was noted on comparing posttherapy and postoperative MRI. Although the patient received maintenance therapy with TMZ, symptoms progressed, and MRI showed tumor extension. After two TMZ cycles for maintenance therapy, the patient was discharged home with a Modified Ranking Scale score of 4 and received home therapy.

Discussion

Observations

Here, histological findings were not available to prove that the IMSC tumor that showed no contrast enhancement on the first T1-weighted MRI was a PA. However, circumstantial findings strongly

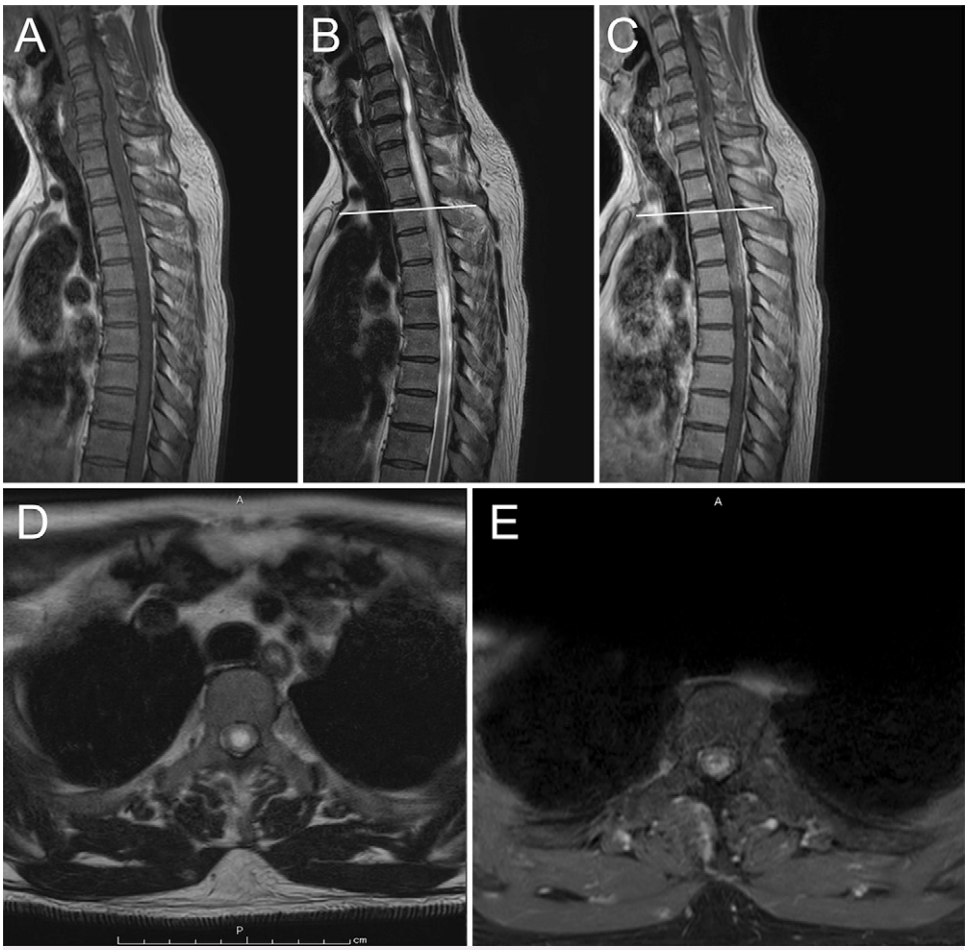

FIG. 2. Subsequent MRI. Sagittal T1-weighted (**A**) and T2-weighted (**B**) images show expansion of intramedullary lesion. A contrast-enhanced T1-weighted image (**C**) shows an intramedullary lesion with contrast enhancement. Axial (level of the *white line* in the sagittal images in panels B and C) T2-weighted (**D**) and contrast-enhanced T1-weighted (**E**) images show an intramedullary lesion.

suggest that the original tumor was a PA that subsequently underwent an anaplastic change as part of its natural clinical course. First, typical features of PA, such as cells with long bipolar piloid processes, eosinophilic granular bodies, and Rosenthal fibers, were observed on histological examination. The MIB-1 labeling index was $>$25%. Second, contrast-enhanced T1-weighted MRI revealed a noncontrast-enhancing intramedullary tumor at T2–T3. However, subsequent MRI indicated progression due to rapid tumor growth and a change from predominantly nonenhancing to predominantly enhancing, leading to a preoperative diagnosis of malignant glioma. In the histopathological examinations, diffuse astrocytoma, anaplastic astrocytoma, and glioblastoma can be considered as the differential diagnosis; however, based on the high MIB-1 labeling index, typical features of PA, clinical progress, and contrast change in MRI, we believe our patient had a PA with malignant transformation rather than a de novo high-grade glioma. Although the mechanism underlying the malignant transformation of PA remains unknown, anaplastic change in PA after radiotherapy has been reported,[8] and radiotherapy is considered an important cause of malignant transformation of PA. However, our patient's PA progressed to high-grade glioma during its natural clinical course, representing spontaneous malignant transformation. Similar cases of spontaneous progression of PA have been reported previously.[9,10]

MRI is important for predicting malignancy based on the degree of contrast enhancement in gliomas, and the absence of contrast enhancement may be suggestive of low-grade gliomas. Frazier et al. reported that nonenhancing low-grade astrocytomas tranformed into high-grade astrocytomas, which is indicated by contrast enhancement on MRI.[11] In this case, the change in contrast enhancement may reflect the malignant transformation of PA.

As in patients with intracranial high-grade gliomas, TMZ-based chemotherapy and radiotherapy are recommended in patients with high-grade spinal cord gliomas.[12] Our patient received postoperative chemotherapy with TMZ and radiotherapy. In patients with progressive or recurrent spinal cord gliomas, despite administration of TMZ-based chemoradiotherapy, salvage therapy with bevacizumab may be considered.[13] In recent times, analysis of the genetic characteristics of gliomas has provided valuable information on their diagnosis. *BRAF*, 1p19q codeletion, p53, p16/*CDKN2A*, and *PTEN*, which are predictive biomarkers of PA, have been analyzed.[14] The most commonly identified marker, *KIAA15491-BRAF* fusion, is important for the molecular diagnosis of PA. *IDH1*-R132H, *BRAF*, and *H3K27M* mutations and

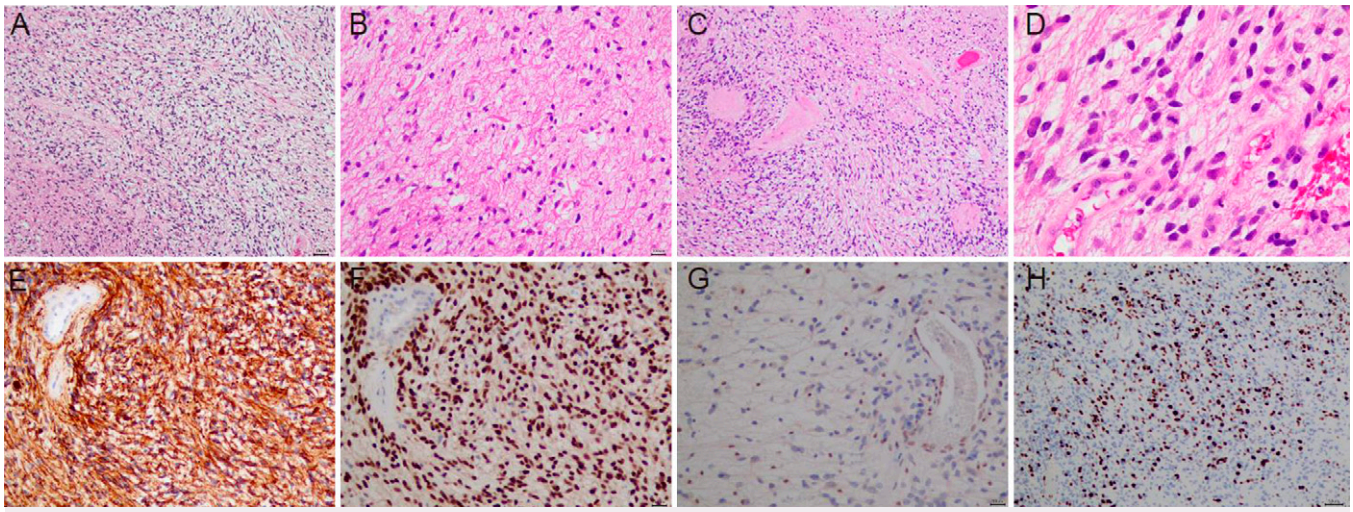

FIG. 3. Histopathological and immunohistochemical features of pilocytic astrocytoma with anaplasia. **A:** Relatively highly cellular neoplasm (hematoxylin and eosin). Original magnification ×100. **B:** Neoplastic cells showing a piloid morphology with long bipolar processes and Rosenthal fibers (hematoxylin and eosin). Original magnification ×200. **C:** Neoplasm with scattered hyalinized vessels (hematoxylin and eosin). Original magnification ×100. **D:** Mitotic figures of neoplastic cells (hematoxylin and eosin). Original magnification ×400. Neoplastic cells stained by glial fibrillary acidic protein (**E**, GFAP stain, original magnification ×200) and oligodendrocyte transcription factor 2 (**F**, Olig2 stain, original magnification ×200). **G:** Loss of nuclear expression of alpha thalassemia/mental retardation syndrome X-linked protein. ATRX stain, original magnification ×200. **H:** The MIB-1 labeling index is 34.3%. Ki67 stain, original magnification ×100.

KIAA1549-BRAF fusion were not observed in our patient although the loss of ATRX expression was detected. ATRX loss is one of the features associated with a worse prognosis in PA with anaplasia.[15] In the future, molecular-targeted chemotherapy might be available for treating patients with PA with incomplete tumor resection, malignant transformation, or potent growth potential.

Lessons

Rapid progression of intramedullary PA with a change in contrast enhancement in an adult patient is extremely rare. In adults, PA may undergo a spontaneous malignant transformation during its natural clinical course.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Kawasaki. Acquisition of data: Kawasaki, Maki, Shirahata, Adachi. Analysis and interpretation of data: Kawasaki.

Drafting the article: Kawasaki, Adachi. Critically revising the article: Kobayashi, Maki. Reviewed submitted version of manuscript: Adachi, Ioroi. Approved the final version of the manuscript on behalf of all authors: Kawasaki. Study supervision: Takayama. Pathological analysis: Homma.

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