



Case Report

A rare case of brain metastasis from poorly differentiated small bowel adenocarcinoma

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ABSTRACT

Background: Small bowel adenocarcinoma (SBA) accounts for <2% of all gastrointestinal malignancies. The most common organs of SBA metastases are the abdominal lymph node, liver, and peritoneum. There have been almost no reports of brain metastases of SBA. Dabaja *et al.* reported 1 case of brain metastasis out of 217 SBA cases, but details of the clinical course of the case were unclear. Our case might be the first report covering the full clinical course, pathological findings, and genetic data. Here, we report a very rare case of brain metastasis from poorly differentiated SBA.

Case Description: A 54-year-old man who suffered from abdominal pain and melena visited a nearby hospital. This patient had no risk factors for SBA. He underwent partial resection of the jejunum with regional lymphadenectomy and combined resection of the transverse colon. Pathological diagnosis was poorly differentiated adenocarcinoma, pT4N2M0 Stage IIIB (UICC-TNM: 8th edition). One month after curative surgery, liver metastasis was detected by a computed tomography (CT) scan, and then, palliative chemotherapy was started. During the third-line chemotherapy, a brain tumor on the left cerebellum was detected by the CT scan. Tumor resection was performed, and the histopathological features coincided with the primary jejunum tumor. Based on surgical, radiological, pathological, and genetic findings, this brain tumor was comprehensively diagnosed as a metastasis from poorly differentiated SBA.

Conclusion: Here, we experienced a very rare case of brain metastasis from poorly differentiated SBA.

Keywords: Brain metastases, Jejunum, Metastatic brain tumor, Small bowel, Small intestine

INTRODUCTION

Small bowel adenocarcinoma (SBA) is an extremely rare tumor, accounting for <2% of all gastrointestinal tumors. Its annual incidence rate is 1.2–6.5/1 million people.^[3] SBA occurs on the duodenum in 57% of cases, jejunum in 29%, and the ileum in 10%.^[3] Inflammatory bowel diseases, such as Crohn's disease, and polyposis, such as familial adenomatous polyposis, are risk factors for SBA.^[10] We report a very rare case of brain metastasis from poorly differentiated SBA.

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CASE REPORT

A 54-year-old man who suffered from abdominal pain and melena visited a nearby hospital. He had a medical history of hyperlipidemia and diabetes but had no risk factors for SBA. After clinical evaluation, a jejunum tumor was suspected. In July 2017, he underwent partial resection of the jejunum with regional lymphadenectomy and combined resection of the transverse colon. The transverse colon was attached to the jejunum tumor and they could not be separated. The jejunum tumor was approximately 10 cm caudal to Treitz ligament. Pathological diagnosis was poorly differentiated adenocarcinoma, pT4N2M0 Stage IIIB [UICC-TNM: 8th edition; Figure 1 a,b,c,d].

In August 2017, he was referred to our hospital for the purpose of adjuvant treatment. However, due to a liver metastasis detected by a computed tomography (CT) scan at the time of admittance, palliative chemotherapy using capecitabine and oxaliplatin (CAPOX) was selected. However, the efficacy of CAPOX and second-line FOLFIRI (5-fluoropyrimidine/leucovorin/irinotecan) chemotherapy was limited.

In April 2018, during the course of the third-line chemotherapy using nab-paclitaxel, he presented with dizziness, followed by headache, nausea, and ataxia symptoms which were remarkable. Magnetic resonance imaging (MRI) revealed a cystic lesion with a major axis of 38 mm attached to the tent in the left cerebellum. The lesion had weak contrast effect and was accompanied by edema. Tumor resection was performed for symptom control. The contents of the cyst were old brownish hematoma-like liquid with nodular lesions.

The pathological diagnosis revealed brain metastasis of poorly differentiated SBA [Figures 1e, f and 2a, b].

Pathological findings of the primary jejunum tumor were reviewed. The jejunum tumor was poorly differentiated adenocarcinoma resembling cerebellum tumor. Squamous differentiation was limited, observed in part of the tumor. Immunohistochemically, the jejunum tumor cells were positive for cytokeratin (CK) 7, CK8, hepatocyte nuclear factor 4 α (HNF4 α), vimentin, and p40 (partially positive on cancer cells with squamous differentiation). They were negative for CK20, thyroid transcription factor 1, and caudal-type homeobox protein 2 (CDX2). Next-generation DNA sequencing (NGS) of primary lesions showed a KRAS codon 12 mutation, which is the most frequent genetic alteration of SBA. Based on surgical, radiological, pathological, and genetic findings, this brain tumor was comprehensively diagnosed as a metastasis from poorly differentiated SBA.

Postoperative MRI revealed total removal of the tumor; thus, according to the results of the JCOG 0504 trial, we chose close observation without additional radiotherapy [Figures 2c-f and 3a].^[4] After the surgery, his general condition was improved, and he was discharged from our hospital without any neurological deficits.

The next day, he was urgently admitted due to bowel obstruction and melena. A CT scan showed the progression of multiple peritoneal metastases. A month later, periodical MRI revealed obstructive hydrocephalus accompanying the recurrence of brain tumor [Figure 3b]. Ventricular drainage was scheduled in case the symptoms worsened, but he suddenly died the next day due to cerebral hernia caused by intratumoral hemorrhage [Figure 3 c,d].

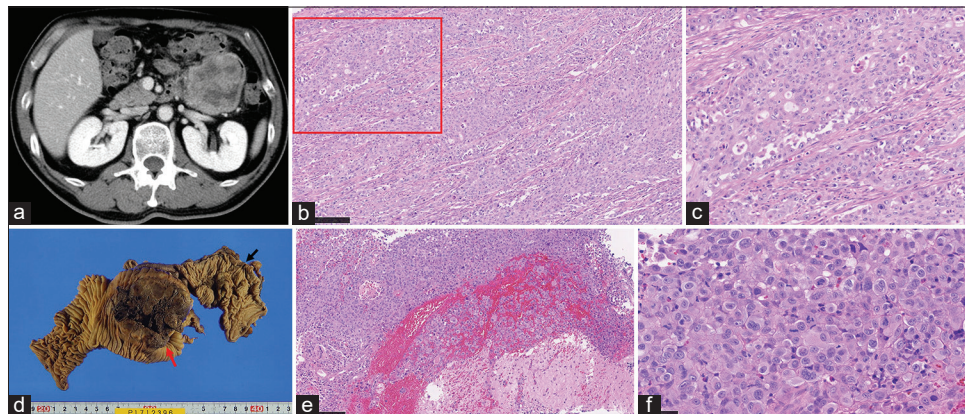


Figure 1: (a) Contrast computed tomography preoperative imaging of jejunum. (b) Pathology of the primary jejunum lesion, hematoxylin-eosin (HE) staining, low magnification. Poorly differentiated small bowel adenocarcinoma is proliferating solidly. The scale bar is 250 μm . (c) Pathology of the primary jejunum lesion, HE staining, high magnification. There was nuclear atypia, pleomorphism, and prominent nucleoli. The scale bar is 250 μm . (d) Jejunum tumor (red arrow), invading transverse colon (black arrow). (e) Pathology of the cerebellum lesion, HE staining, low magnification. Cerebellum histopathology is seen in the lower right of the screen; there is poorly differentiated adenocarcinoma metastasis. The scale bar is 250 μm . (f) Pathology of the cerebellum lesion, HE staining, high magnification. The histopathological feature of the left cerebellum lesion coincided with that of the primary jejunum lesion. There were nuclear atypia, pleomorphism, and prominent nucleoli. The pathological diagnosis was poorly differentiated small bowel adenocarcinoma metastasis. The scale bar is 50 μm .

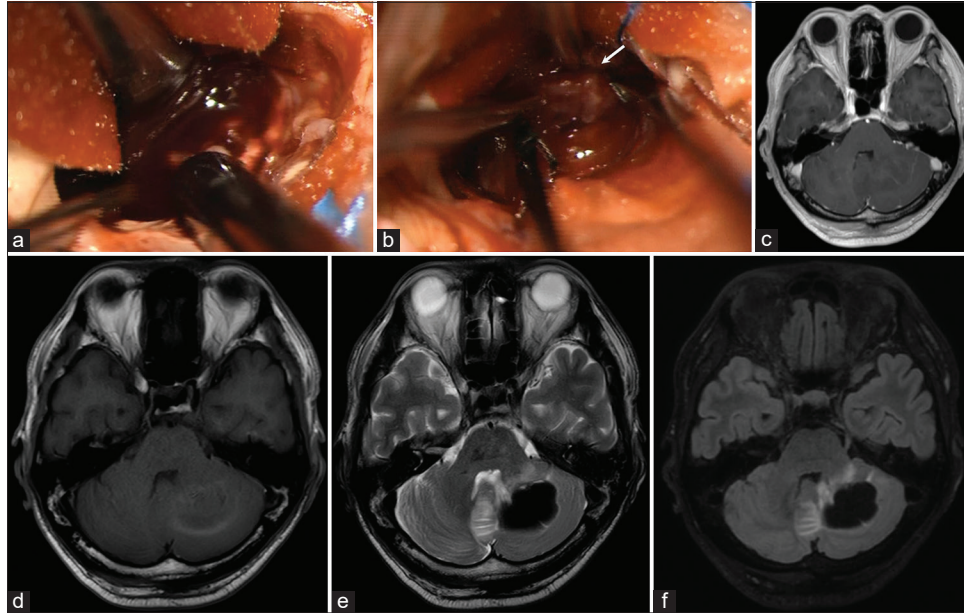


Figure 2: The contents of the cerebellum cyst were old brownish hematoma-like liquid (a), and partially nodular lesions were inside the cyst (b; arrow). Preoperative magnetic resonance imaging (MRI) of cerebellar metastasis lesion (c: T1WI MRI with contrast, d: T1WI, e: T2WI, f: Fluid-attenuated inversion recovery).

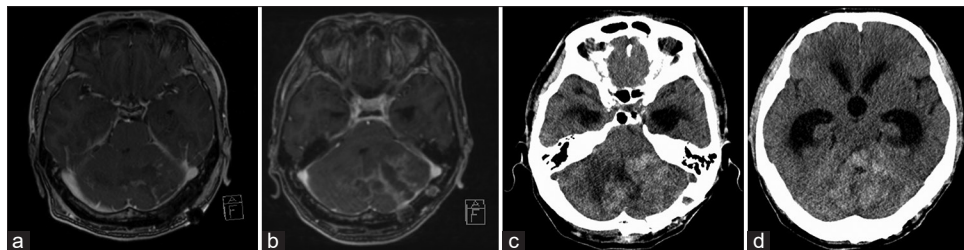


Figure 3: T1WI magnetic resonance imaging with contrast (a: 1 postoperative day, b: 1 month after operation). Computed tomography, hemorrhage from the cerebellar metastasis recurrent lesion (c, left and d, right).

DISCUSSION

The breakdown of small bowel malignancies in the United States is 37.4% neuroendocrine tumor, 36.9% adenocarcinomas, 8.4% stromal tumors, and 17.3% lymphomas.^[1] The most common organs of SBA metastases are the abdominal lymph node, liver, and peritoneum; there have been almost no reports on brain metastases of SBA.^[2,3,5,9] Dabaja *et al.* reported 1 case of brain metastasis out of 217 SBA cases, but details of the clinical course of the case were unclear.^[2] Salvati *et al.* reported 10 cases of cerebral metastases from small intestine carcinoma, though no information about the clinical features of small intestine carcinoma was reported.^[9] Our case might be the first report covering the full clinical course, pathological findings, and genetic data. In this case, the jejunum tumor was diagnosed as a primary lesion of brain tumor by surgical, radiological, pathological, and genetic findings. Although brain metastases typically show strong contrast enhancement, our SBA

metastatic lesion was characteristic in its weak contrast effect. Postgadolinium MRI of SBA is reported to demonstrate heterogeneous and moderate enhancement.^[7] Our case was poorly differentiated adenocarcinoma and this might be one of the MRI findings of SBA.

Immunohistochemically, the jejunum tumor was HNF4 α positive and CDX2 negative. HNF4 α is consistent with poorly differentiated adenocarcinoma of the gastrointestinal tract. CDX2 is usually positive in differentiated SBA, but in undifferentiated types, the positive rate drops to 58%. Thus, this finding might not be contradictory to the standard immunohistochemistry of poorly differentiated SBA.^[8] CK8 expression is characteristic of adenocarcinoma. In typical SBA, CK7 is negative and CK20 is positive. This case was CK7 positive and CK20 negative, corresponding to 13% of SBA cases.^[8] Vimentin expression suggests poor differentiation. P40 was partially positive, which indicates partial differentiation to squamous carcinoma.

In NGS of the primary lesion, a KRAS codon 12 mutation was detected. It was reported that the mutation of the KRAS gene was frequently observed in SBA, occurring in 43–53% of cases.^[6,11]

This patient died of intratumoral bleeding from a recurrent tumor, which grew rapidly 1 month after surgery. Considering the initial brain metastasis had intratumoral bleeding, postoperative adjuvant radiotherapy might have avoided it.

CONCLUSION

Here, we experienced a very rare case of brain metastasis from poorly differentiated SBA.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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