Int J Clin Exp Pathol 2017;10(1):39-49
www.ijcep.com /ISSN:1936-2625/IJCEP0034785

Original Article

Intramedullary spinal cord metastasis from parotid gland carcinoma expleomorphic adenoma: a case report

Jing Zhang[1], Weiya Wang[2], Lihong Wang[3], Lei Liu[4]

[1]State Key Laboratory of Biotherapy and Cancer Center, West China Hospital, West China Medical School, Sichuan University, Chengdu 610041, Sichuan, People's Republic of China; [2]Department of Pathology, West China Hospital, Sichuan University, Chengdu 610041, Sichuan, People's Republic of China; [3]West China Medical School, West China Hospital, Sichuan University, Chengdu 610041, Sichuan, People's Republic of China; [4]The Department of Medical Oncology, Cancer Center, State Key Laboratory of Biotherapy, West China Hospital, West China Medical School, Sichuan University, Chengdu 610041, Sichuan, People's Republic of China

Received June 30, 2016; Accepted October 9, 2016; Epub January 1, 2017; Published January 15, 2017

Abstract: Intramedullary spinal cord metastasis (ISCM) is an infrequent lesion of systemic malignant tumors, and the most common primary sources of ISCM are lung and breast cancers, as well as melanoma and lymphoma. Patients with ISCM usually accompany with rapidly progressive neurological compromise and the prognosis of ISCM is poor. We present a case of a 40-year-old male with a history of parotid gland carcinoma ex pleomorphic adenoma (CXPA) who had undergone surgical excision and chemotherapy presented with progressive paralysis and hypotonia of the bilateral upper and lower extremities. Magnetic resonance imaging (MRI) revealed two intramedullary metastases at the C5 and T6 level, respectively. The patient underwent surgical resection after intramedullary spinal cord metastasis was diagnosed and survived 8 months without any systemic progression and with partially neurological improvement following surgery. The aim of this study was to present the clinical features, diagnosis, and treatment of a patient with ISCM resulting from parotid gland CXPA. The present case highlighted the importance of early diagnosis and surgery when ISCM is suspected. Clinicians should choose the optimum management considering the patient's individual condition when ISCM is suspected.

Keywords: Intramedullary spinal cord metastasis, parotid gland carcinoma ex pleomorphic adenoma, surgery

Introduction

Intramedullary spinal cord metastasis (ISCM) is an extremely rare lesion of systemic malignant tumors, comprising less than 1% of all spinal tumors. The most common primary sources of ISCM are lung and breast cancers, as well as melanoma and lymphoma [1, 2].

Carcinoma ex pleomorphic adenoma (CXPA) is an uncommon tumor that arises in or from pleomorphic adenoma (PA). Parotid gland CXPA accounts for about 3.6% of all salivary gland neoplasms and 11.6% of all salivary gland malignancies, which is typically associated with frequent metastasis and significant mortality [3-5].

A retrospective review suggestsd that ISCM had an adverse prognosis, and many patients with ISCM were along with rapidly progressive neurological compromise. Once the first symptom appeared, the mortality rate within 3-4 months was 80% [6, 7]. With the development of imaging, early diagnosis is possible via gadolinium-enhanced magnetic resonance imaging (MRI), and surgical resection can partially improve the prognosis and neurological deficits of patients with ISCM. In fact, the overall median survival can increase up to 6 months for patients treated with surgery [8]. For patients treated with radiotherapy, there was no significant survival benefit and only about 50% showed improvement of neurological deficits reported in the literature, emphasizing the importance of early

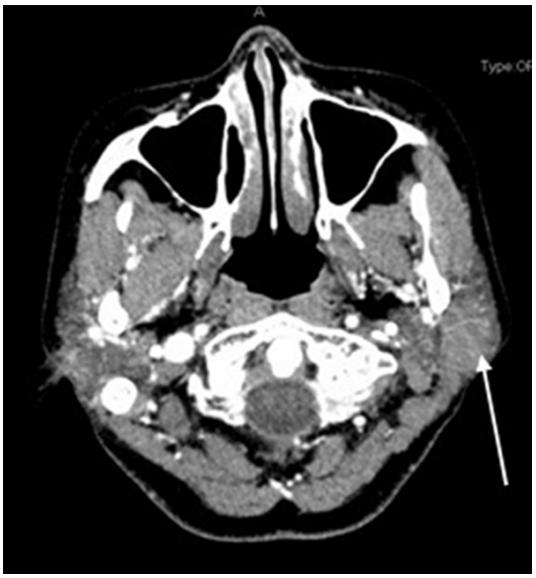

Figure 1. Primary tumor of parotid gland. Enhanced computed tomography (CT) of the neck demonstrates a 2.0 cm*2.0 cm mass (arrow), thought to be a mixed tumor of left parotid gland.

diagnosis and surgery when ISCM is suspected [1, 9, 10].

In this case, we present a patient with ISCM resulting from parotid gland CXPA, which was detected by gadolinium-enhanced MRI and definitively diagnosed by biopsy through spinal cord tumor resection. The patient survived for 8 months without any systemic progression and with partially neurological improvement following surgery. It was extremely rare for a patient with ISCM arising from parotid gland CXPA could survive as long as 8 months.

Case presentation

A 40-year-old male was diagnosed with secondary epithelial malignant neoplasm with a left post-auricular swelling by fine-needle aspiration cytology (FNAC) at a community hospital in 2011. The patient was admitted to the West China Hospital of Stomatology and computed tomography (CT) was prescribed, which revealed a lesion in his left parotid region (**Figure 1**). He subsequently underwent the left parotidectomys, plus the ipsilateral deep and superficial lobes' excision, and facial nerve dissection. Histopathological examination of the surgical specimen confirmed the diagnosis of parotid gland CXPA (**Figures 2**, **3**). The Ki-67 index was 50%. He declined subsequent adjuvant chemotherapy and radiotherapy.

The patient palpated a soft lump in his left neck region in 2012, and he subsequently underwent an ipsilateral neck lymph node biopsy in West China Hospital, which indicated neck lymph node metastasis (**Figure 4**). F-fluorodeoxyglucose (FDG) positron emission tomography-computed tomography (PET-CT) was prescribed, and the results confirmed recurrence of parotid gland carcinoma, and showed numerous metastases including the left neck lymph nodes, lungs, and the left adrenal gland (**Figure 5**). Subsequent therapy including four cycles of chemotherapy was administrated. At the follow-up examination, PET-CT confirmed shrinkage of the metastatic lesions mentioned above. Clinical response evaluation was partial response (PR) according to the RECIST 1.1 criteria, and the patient completed two more cycles of chemotherapy. Then he had no follow-up re-examination.

The patient was admitted to the neurosurgery department of West China Hospital with progressive paralysis and hypotonia of the bilateral upper and lower extremities in 2015. Magnetic resonance imaging (MRI) was performed in view of his neurological signs, and the results showed two new suspicious intramedullary spinal cord lesions at the C5 and T6 level, respectively, along with the central canal expansion; intramedullary spinal cord metastasis was also considered (**Figure 6**). He subsequently underwent C4-5/T5-6 laminectomy for tumor debulking and then tumor resection was undertaken. Intraoperative findings revealed the intramedullary lesion located at the C5 level was growing on the dorsal aspect of the spinal cord, while the lesion at the T6 level was growing on the ventral aspect. There was not a clear plane of separation between the tumors and the spinal cord, and both tumors had an abundant blood supply. Postoperative pathology findings and immunohistochemistry (IHC) revealed neoplastic cells positivity for PCK, CK7 and EMA (**Figure 7**), negative for TTF-1, CK20, P63, CDX2, TG, PSA, ALK-V and ROS-1 (**Figure 8**), indicating intramedullary spinal cord metastatic carcinoma derived from a salivary gland tumor in context with the clinical history. The Ki-67 proliferative index was more than

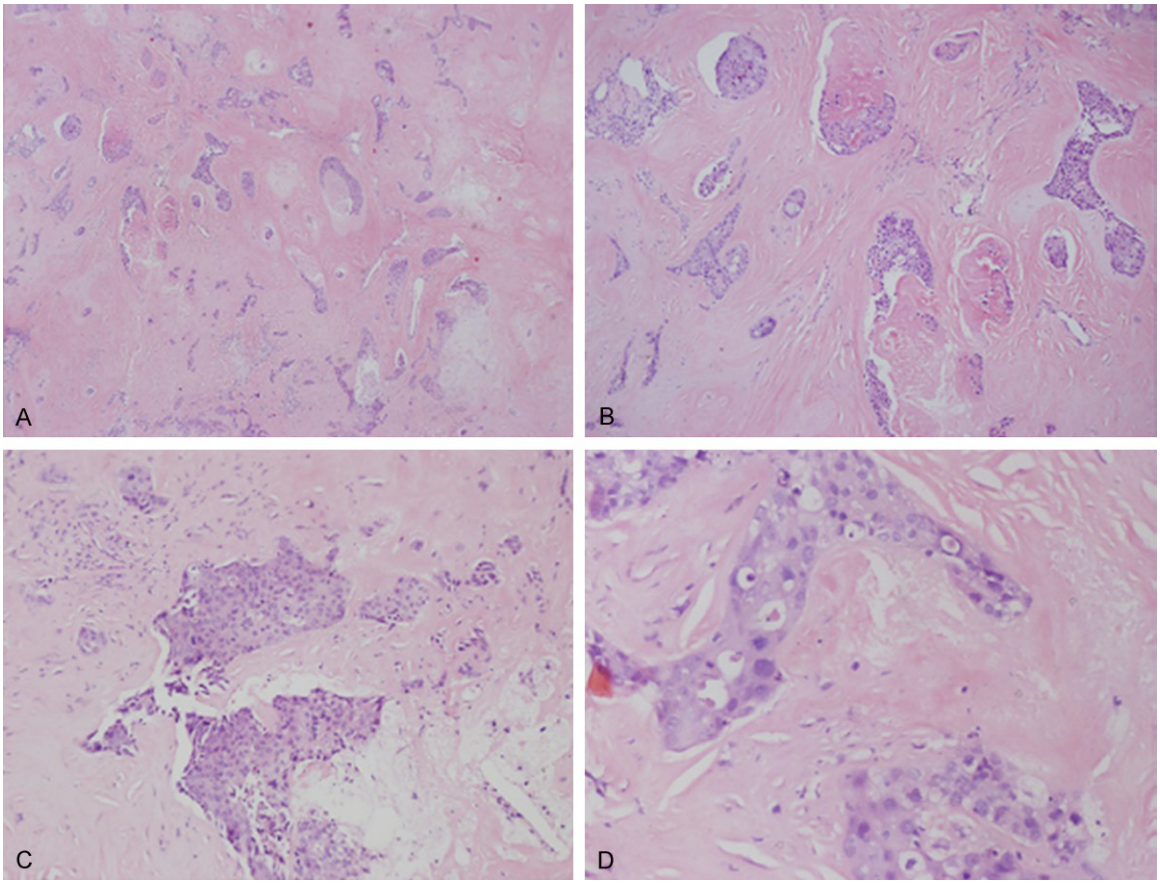

Figure 2. The pathology results of primary tumor. Photomicrograph of left parotid region biopsy specimen displays parotid gland carcinoma ex pleomorphic adenoma. A. H&E stain; original magnification 30×. B. H&E stain; original magnification 75×. C. H&E stain; original magnification 150×. D. H&E stain; original magnification 300×.

75% (**Figure 9**). The patient was transferred to the rehabilitation department after surgery, and his muscle force of all the four limbs had improved obviously after rehabilitation training. He survived for 8 months without any systemic progression.

Discussion

Malignancies of the salivary glands comprise approximately 5% of all head and neck cancers, and consist of considerable pathologic diagnoses, such as mucoepidermoid carcinoma, adenoid cystic carcinoma, and adenocarcinoma, representing >75% of the salivary gland malignancies. CXPA is one of the histologic subtypes of parotid gland adenocarcinoma and only accounts for between 4.5% and 15% of all salivary gland cancers [11-14]. It has been reported that five-year overall and disease-free survival rates were 43% and 37%, respectively. The negative prognostic factors of CXPA include symptoms of a fixed mass, rapid growth, and positive surgical margins [12]. In our case, the patient was initially diagnosed with parotid gland CXPA, which the Ki-67 index was 50%, and he did not undergo ipsilateral neck dissection or adjuvant treatments. As the first operation was not complete, the tumor recurred locoregionally and invaded the neck lymph nodes. The undetected residual tumor could have increased the probability of the subsequent distant metastases.

Although parotid gland carcinoma has a favorable prognosis, locoregional recurrence can frequently occur after operation, and treatment most frequently fails due to distant metastases to the lung, liver, or bone [15, 16]. This case showed complications of parotid gland carci-

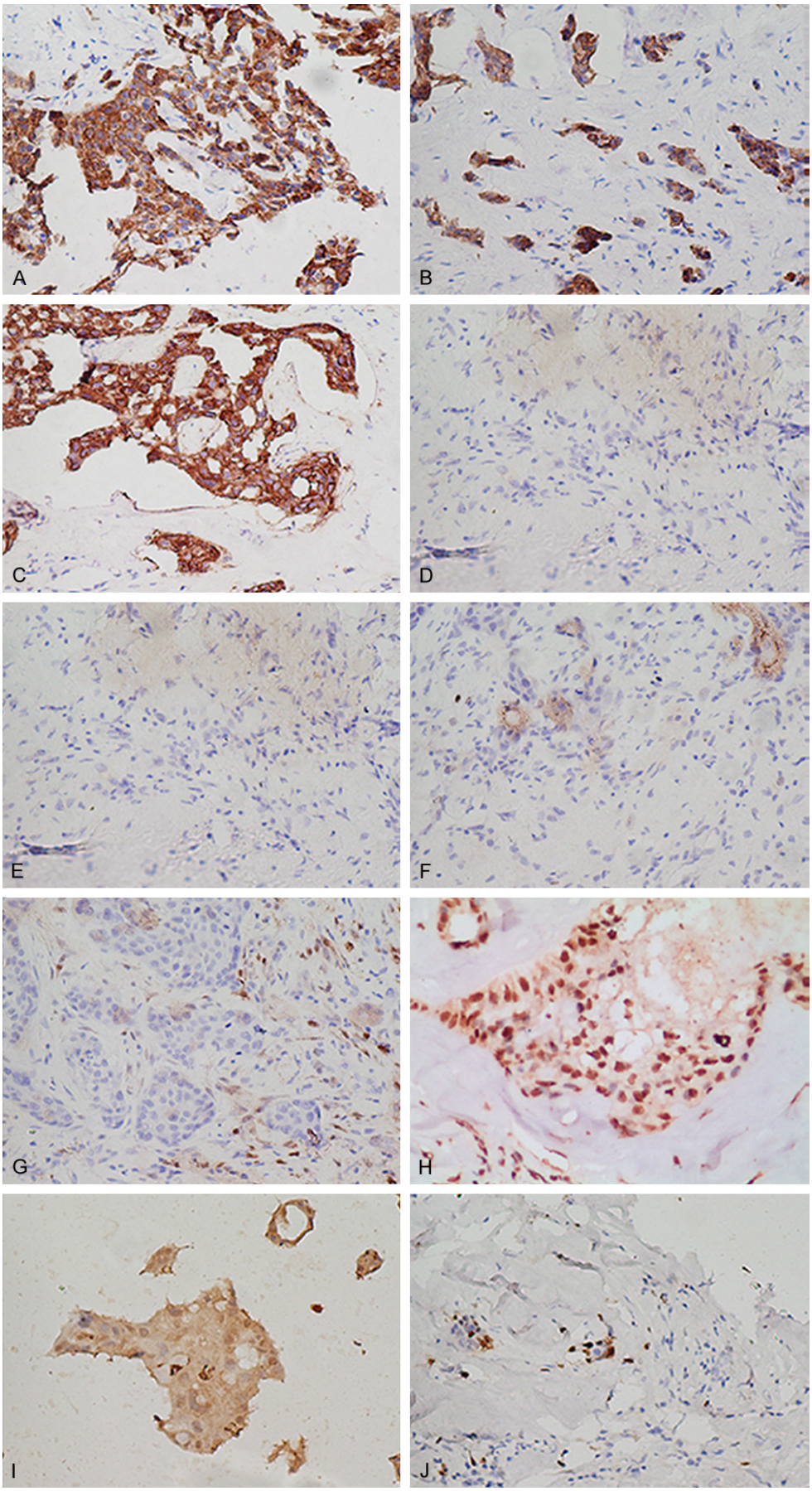
A
B
C
D
E
F
G
H
I
J

Figure 3. Immunohistochemistry results of primary tumor revealed neoplastic cells positivity for CK-H, CK-L, CK-P, EMA, HMB-45, P63, S-100, SMA, VIM. A. CK-H IHC stain; original magnification 200×. B. CK-L IHC stain; original magnification 200×. C. CK-P IHC stain; original magnification 200×. D. EMA IHC stain; original magnification 200×. E. HMB-45 IHC stain; original magnification 200×. F. P63 IHC stain; original magnification 200×. G. S-100 IHC stain; original magnification 200×. H. SMA IHC stain; original magnification 200×. I. VIM IHC stain; original magnification 200×. J. KI-67 IHC stain; original magnification 200×.

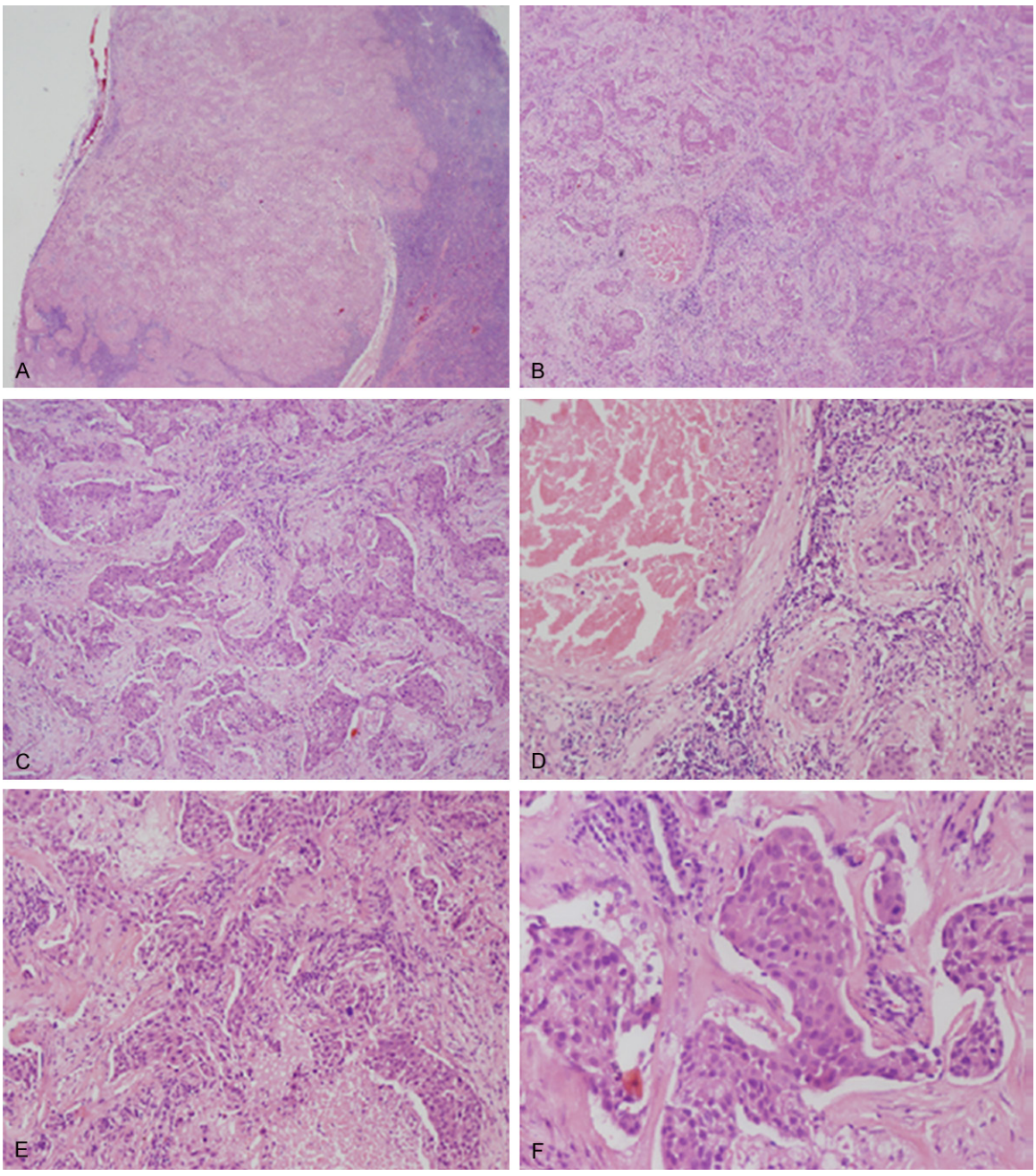

Figure 4. The pathology results of neck lymph node metastasis. Photomicrograph of left neck lymph node biopsy specimen indicates the neck lymph node metastatic carcinoma. A. H&E stain; original magnification 15×. B. H&E stain; original magnification 30×. C. H&E stain; original magnification 75×. D. H&E stain; original magnification 150×. E. H&E stain; original magnification 150×. F. H&E stain; original magnification 300×.

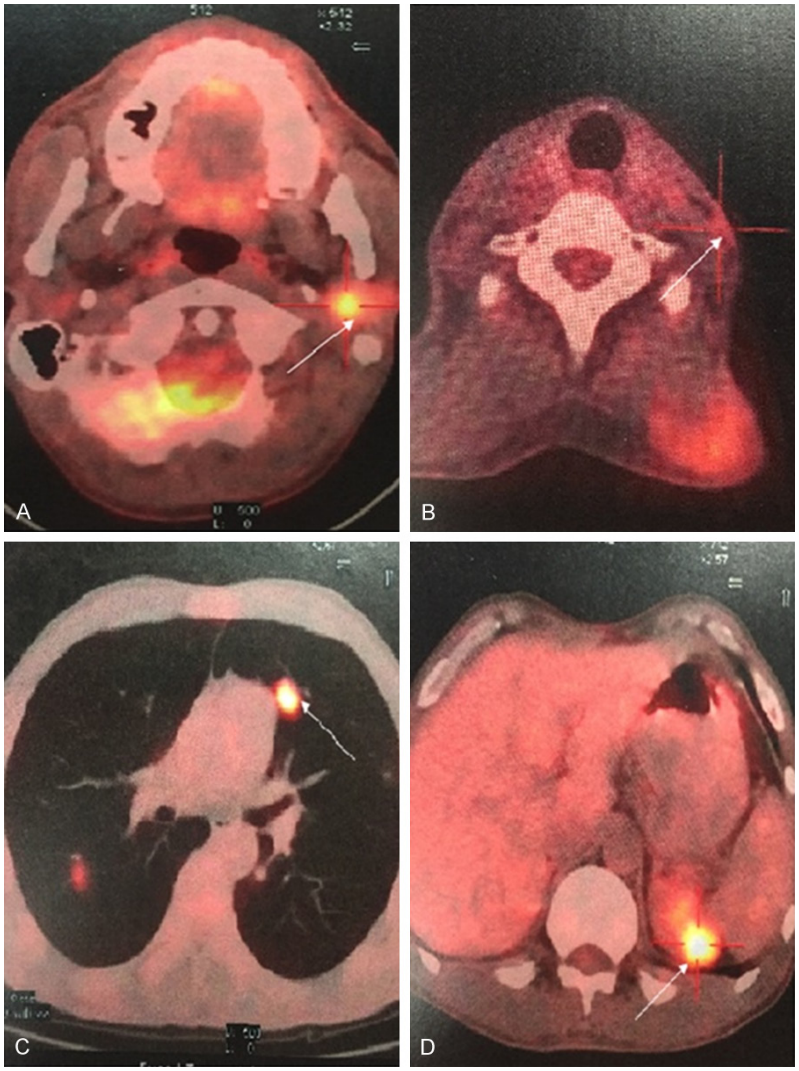

Figure 5. The results of PET/CT. F18 fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT) shows recurrence of parotid gland carcinoma and metastases of left neck lymph node, lung, and adrenal gland. A. Metabolic activity (standardized uptake values of 5.4 g/ml) was observed in the left parotid gland region (arrow); B. Metabolic activity (standardized uptake values of 1.9 g/ml) was observed in the left neck lymph node region (arrow); C. Metabolic activity (standardized uptake values of 9.2 g/ml) was observed in the lung (arrow); D. Metabolic activity (standardized uptake values of 6.7 g/ml) was observed in the left adrenal (arrow).

noma including neck lymph node recurrence, lung and adrenal metastases, and manifested an extremely rare secondary lesion in the form of ISCM, which the Ki-67 index was more than 75%. And this case showed increase of malignant degree with the occurrence of tumor metastasis.

ISCM is an extremely rare complication of cancers, presenting in only 0.1-0.4% of all cancer patients. To date, lung and breast cancers are the most common known primary sources. After onset, ISCM can quickly cause neurological deficits and even death. Currently, the optimum management of ISCM remains controversial [1, 8, 17]. Multiple studies have reported that surgical resection of ISCM in selected patients, especially those with controlled systemic disease and a single neurological metastatic lesion, can lead to optimal outcomes, improving both the quality and length of survival [18, 19]. The crucial aims of surgery are decompression of the spinal cord, neurological function preservation, and histological confirmation [8]. In contrast, aggressive surgery may actually lead to worse functional outcome, due to the infiltrative nature of ISCM, and has no definite survival benefit [20, 21]. Radiation therapy can also be considered, either as an adjuvant treatment when surgical debulking is accomplished or as a primary treatment for patients without operative candidates. The effect of chemotherapy, meanwhile, is still questionable and must depend on the primary tumor [22, 23]. Sheedy et al. reported a study in which a patient with parotid gland CXPA developed brain and ISCMs within nineteen months after completion of therapy, and then died two months after the metastases was diagnosed [24]. In our case, the patient underwent surgical resection successfully, decreasing tension in the spinal cord and reducing the tumor burden. The patient survived for 8 months without any systemic progression. In general, radiotherapy or chemo-

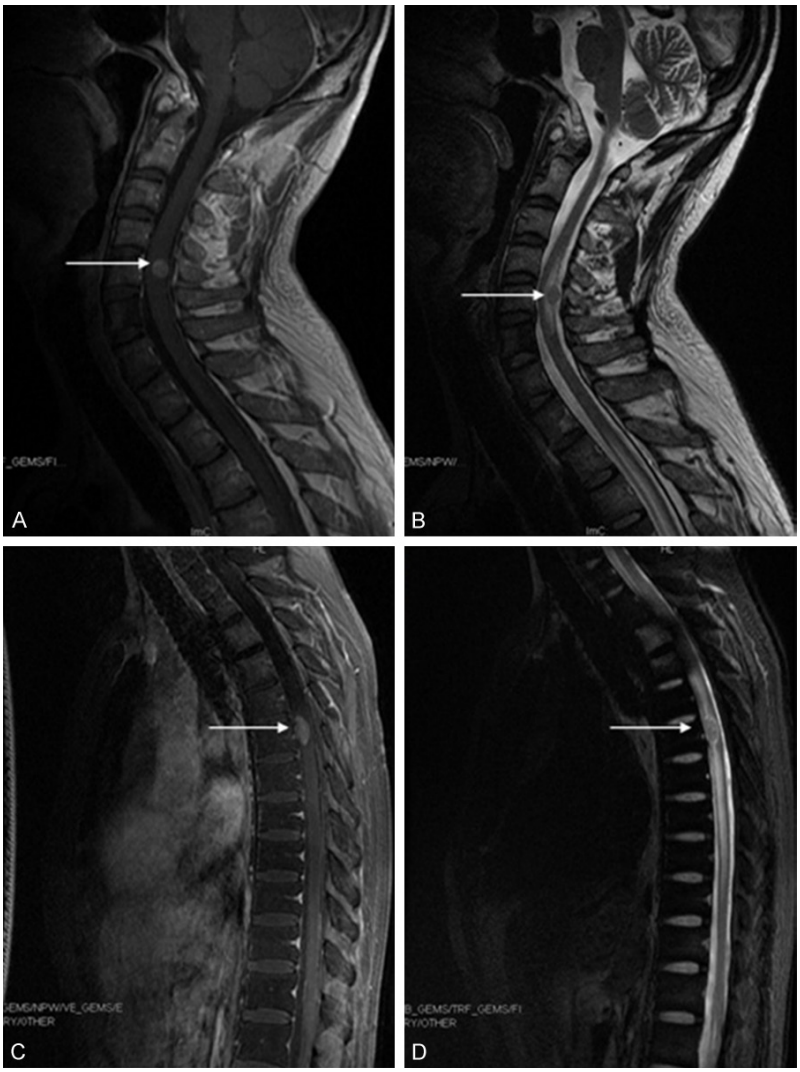

Figure 6. The results of MRI of the cervical and thoracic spine. Magnetic resonance imaging (MRI) of the cervical and thoracic spine demonstrates heterogeneous increased signal intensity in spinal cord and the central canal expansion expansion, consistent with intramedullary spinal cord metastases. A. MRI of the cervical spine with T1-weighted image demonstrates a solitary enhancing intramedullary nodular lesion at C5 level (arrow); B. T2-weighted image shows a solitary intramedullary nodular lesion at the same level as in A with expansion of the upper and lower spinal cord (arrow); C. MRI of the thoracic spine with T1-weighted image demonstrates a solitary enhancing intramedullary nodular lesion at T6 level (arrow); D. T2-weighted image demonstrates a size of 2.0 cm×0.9 cm solitary enhancing intramedullary nodular lesion at the same level as in C (arrow).

therapy after operating can be considered, but must be tailored to the patient's individual condition.

ISCM caused by parotid gland CXPA is rare, and appearance of ISCM generally indicates an unfavorable prognosis. This case highlights the significance of early diagnosis and surgical treatment for selected patients with ISCM. Surgical resection of ISCM is prudent, not only relieving symptoms and controling spinal cord damage. While there are multiple options of postoperative treaments for patients, to date, early diagnosis, surgical resection, and adjuvant therapy may result in a satisfactory outcome and prolonged survival for patients with ISCM.

Conclusions

ISCM is a rare complication of several types of cancers. The prognosis of ISCM is poor with an overall survival of 6 months in surgically treated patients, and optimum management remains controversial. In the present study, the case described a patient with ISCM from parotid gland CXPA, who underwent surgical resection successfully and survived for 8 months. In the authors' opinion, it is extremely rare that a patient with ISCM from parotid gland CXPA can survive as long as 8 months, indicating that early diagnosis and surgical resection are vitally important when ISCM is suspected.

Acknowledgements

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editor of this journal.

Disclosure of conflict of interest

None.

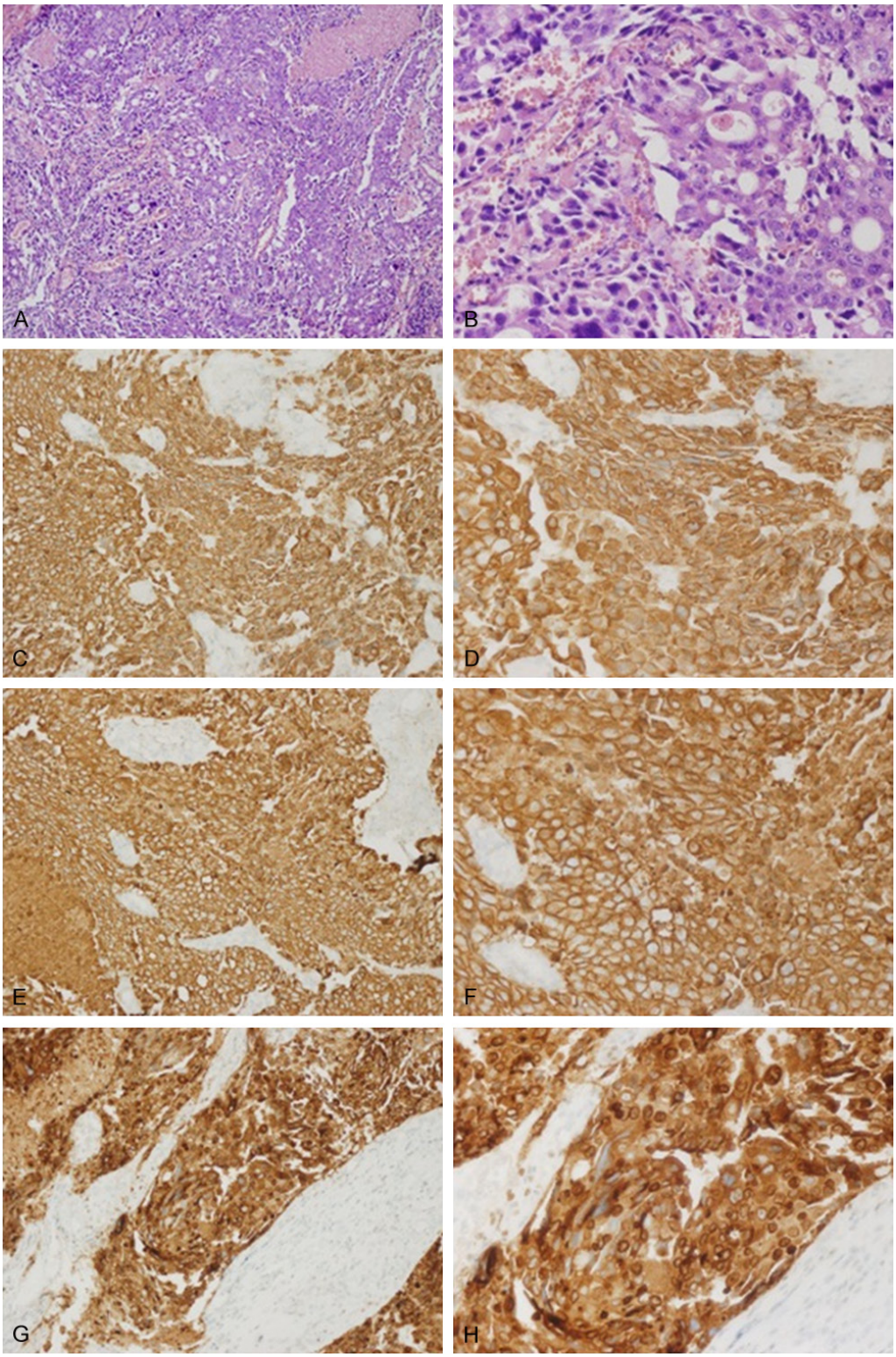

Figure 7. The pathology results of ISCM. Photomicrograph of spinal cord biopsy specimen displays the metastatic carcinoma, which arises from original parotid gland carcinoma, and invades normal spinal cord parenchyma. A. H&E stain; original magnification 75×. B. H&E stain; original magnification 300×. C. PCK immunohistochemistry (IHC); original magnification 150×. D. PCK IHC stain; original magnification 300×. E. CK7 IHC stain; original magnification 150×. F. CK7 IHC stain; original magnification 300×. G. EMA IHC stain; original magnification 150×. H. EMA IHC stain; original magnification 300×. H&E, Hematoxylin and eosin; PCK, protein kinase C; CK7,cytokeratins 7; EMA, Epithelial membrane antigen.

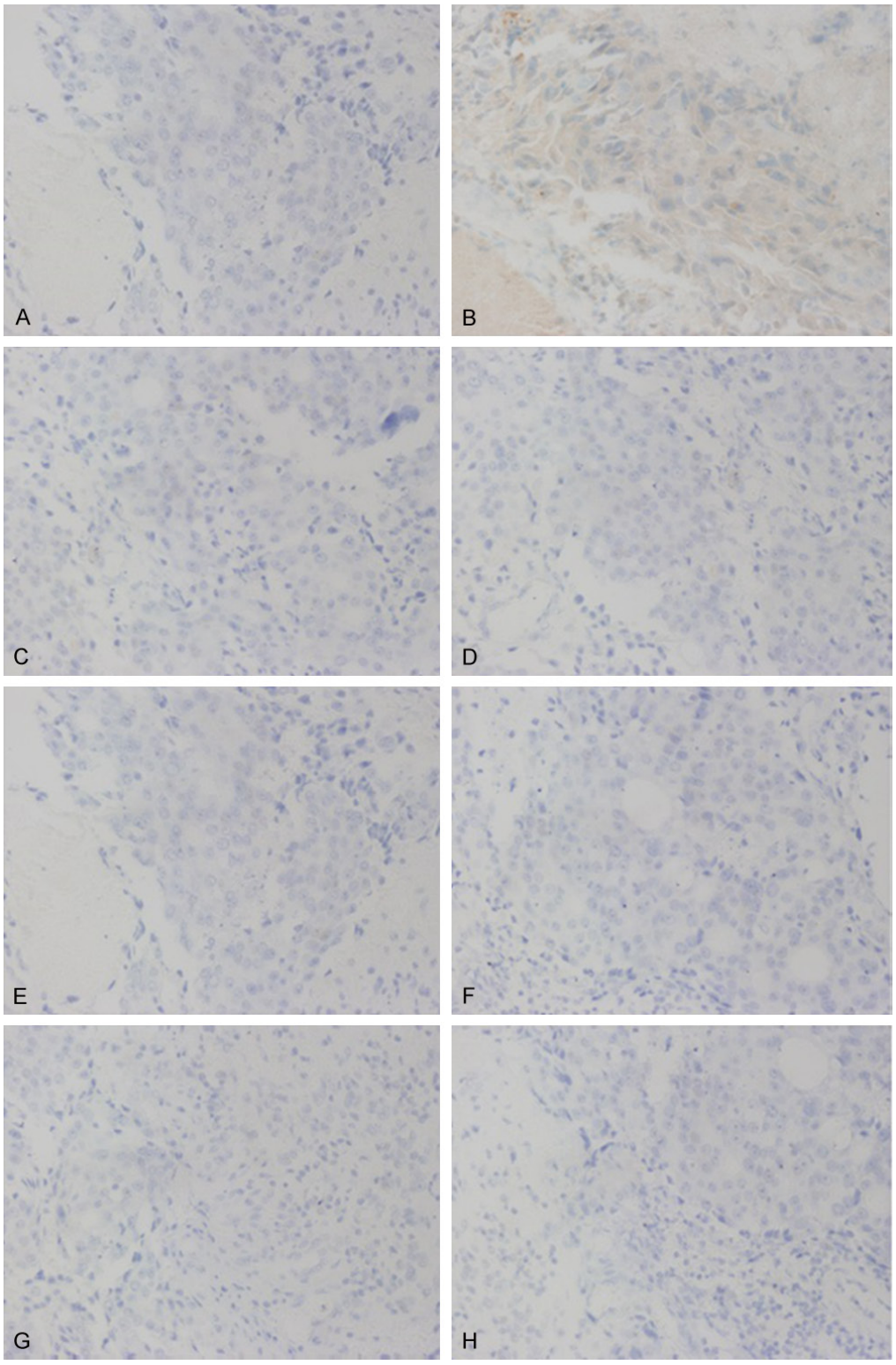

Figure 8. The pathology results of ISCM. A. TTF-1 IHC stain; original magnification 300×. B. CK20 IHC stain; original magnification 300×. C. P63 IHC stain; original magnification 300×. D. CDX2 IHC stain; original magnification 300×. E. TG IHC stain; original magnification 300×. F. PSA IHC stain; original magnification 300×. G. ALK-V IHC stain; original magnification 300×. H. ROS-1 IHC stain; original magnification 300×. TTF-1, Thyroid transcription factor 1; CK20, cytokeratins 20; CDX2, caudal type homeobox 2; TG, thyroglobulin; PSA, prostate-specific antigen; ALK-V, anaplastic lymphoma kinase; ROS-1, c-ros oncogene 1 receptor tyrosine kinase.

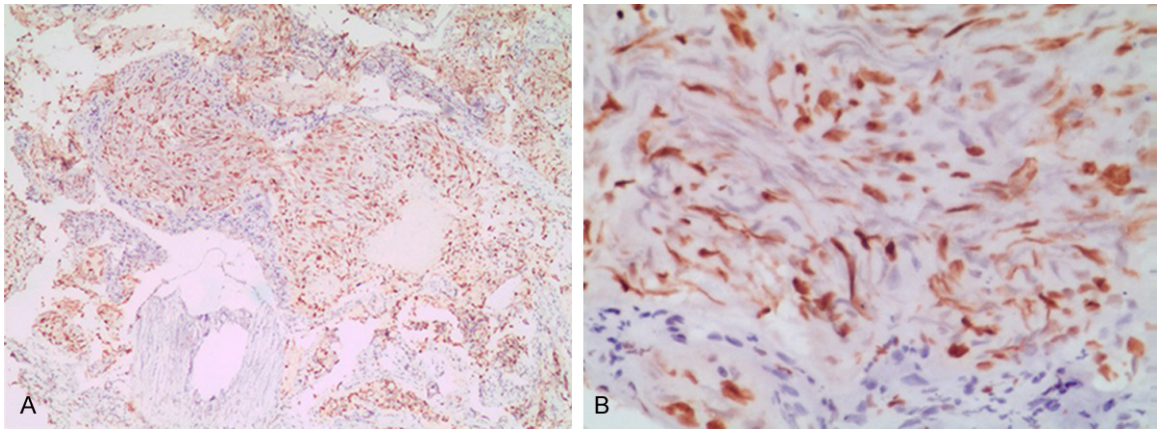

Figure 9. The Ki-67 proliferative index of ISCM. A. Ki-67 IHC stain; original magnification 40×. B. Ki-67 IHC stain; original magnification 200×.

Authors' contribution

All authors fulfill the authorship criteria because of their substantial contributions to the conception, design, analysis, and interpretation of the data. LL and JZ conceived the study, analyzed the data, and drafted the manuscript. LL, JZ, WYW and LHW participated in its data acquisition. All authors read and approved the final manuscript.

Abbreviations

ISCM, Intramedullary spinal cord metastasis; CXPA, carcinoma ex pleomorphic adenoma; FNAC, fine-needle aspiration cytology; PA, pleomorphic adenoma; CT, Computed tomograph; MRI, Magnetic resonance imaging; FDG PET-CT, F-fluorodeoxyglucose positron emission tomography-computed tomography; PR, partial response; IHC, immunohistochemistry.

Address correspondence to: Lei Liu, The Department of Medical Oncology, Cancer Center, State Key Laboratory of Biotherapy, West China Hospital, West China Medical School, Sichuan University, Chengdu 610041, Sichuan, People's Republic of China. Tel: 18980606231; Fax: 028-85422432; E-mail: liuleihx@gmail.com

References

[1] Kalaycı M, Çağavi F, Gül S, Yenidünya S, Açıkgöz B. Intramedullary spinal cord metastases: diagnosis and treatment - an illustrated review. Acta Neurochir (Wien) 2004; 146: 1347-54.

[2] Mut M, Schiff D, Shaffrey ME. Metastasis to nervous system: spinal epidural and intramedullary metastases. J Neurooncol 2005; 75: 43-56.

[3] Sedassari BT, da Silva Lascane NA, Tobouti PL, Pigatti FM, Franco MI, de Sousa SC. Carcinoma ex pleomorphic adenoma of the palate composed of invasive micropapillary salivary duct carcinoma and adenoid cystic carcinoma components. Medicine 2014; 93: e146.

[4] Magaki SD, Bhuta S, Abemayor E, Nabili V, Sepahdari AR, Lai CK. Carcinoma ex-pleomorphic adenoma of the parotid gland consisting of high-grade salivary duct carcinoma and keratinizing squamous cell carcinoma. Oral Surg Oral Med Oral Pathol Oral Radiol 2015; 120: e169-73.

[5] Antony J, Gopalan V, Smith RA, Lam AK. Carcinoma ex pleomorphic adenoma: a comprehensive review of clinical, pathological and molecular data. Head Neck Pathol 2012; 6: 1-9.

[6] Schijns OE, Kurt E, Wessels P, Luijckx GJ, Beuls EA. Intramedullary spinal cord metastasis as a first manifestation of a renal cell carcinoma: report of a case and review of the literature. Clin Neurol Neurosurg 2000; 102: 249-54.

[7] Schiff D, O'Neill BP. Intramedullary spinal cord metastases: clinical features and treatment outcome. Neurology 1996; 47: 906-12.

[8] Ding D, Fullard M, Jarrell HS, Jones DE. Intramedullary spinal cord metastasis from salivary ductal carcinoma of the parotid gland mimicking transverse myelitis in a patient with radiologically isolated syndrome. J Neurol Sci 2014; 336: 265-8.

[9] Hashii H, Mizumoto M, Kanemoto A, Harada H, Asakura H, Hashimoto T, Furutani K, Katagiri H, Nakasu Y, Nishimura T. Radiotherapy for patients with symptomatic intramedullary spinal cord metastasis. J Radiat Res 2011; 52: 641-5.

[10] Lee EQ. Nervous system metastases from systemic cancer. Continuum (Minneap Minn) 2015; 21: 415-28.
[11] Adelstein DJ, Koyfman SA, El-Naggar AK, Hanna EY. Biology and management of salivary gland cancers. Semin Radiat Oncol 2012; 22: 245-53.
[12] Huang AT, Tang C, Bell D, Yener M, Izquierdo L, Frank SJ, El-Naggar AK, Hanna EY, Weber RS, Kupferman ME. Prognostic factors in adenocarcinoma of the salivary glands. Oral Oncol 2015; 51: 610-5.
[13] Altemani A, Martins MT, Freitas L, Soares F, Araújo NS, Araújo VC. Carcinoma ex pleomorphic adenoma (CXPA): immunoprofile of the cells involved in carcinomatous progression. Histopathology 2005; 46: 635-41.
[14] Foss RD, Ellis GL, Auclair PL. Salivary gland cystadenocarcinomas. A clinicopathologic study of 57 cases. Am J Surg Pathol 1996; 20: 1440-7.
[15] Chang JW, Hong HJ, Ban MJ, Shin YS, Kim WS, Koh YW, Choi EC. Prognostic factors and treatment outcomes of parotid gland cancer: a 10-year single-center experience. Otolaryngol Head Neck Surg 2015; 153: 981-9.
[16] Sessa S, Ziranu A, Di Giacomo G, Giovanni A, Maccauro G. A rare case of iliac crest metastasis from acinic cell carcinoma of parotid gland. World J Surg Oncol 2014; 12: 48.
[17] Connolly ES Jr, Winfree CJ, McCormick PC, Cruz M, Stein BM. Intramedullary spinal cord metastasis: report of three cases and review of the literature. Surg Neurol 1996; 46: 329-37.
[18] Constantini S, Miller DC, Allen JC, Rorke LB, Freed D, Epstein FJ. Radical excision of intramedullary spinal cord tumors: surgical morbidity and long-term follow-up evaluation in 164 children and young adults. J Neurosurg 2000; 93: 183-93.
[19] Sandalcioglu IE, Gasser T, Asgari S, Lazorisak A, Engelhorn T, Egelhof T, Stolke D, Wiedemayer H. Functional outcome after surgical treatment of intramedullary spinal cord tumors: experience with 78 patients. Spinal Cord 2005; 43: 34-41.
[20] Gasser TG, Pospiech J, Stolke D, Schwechheimer K. Spinal intramedullary metastases. Report of two cases and review of the literature. Neurosurg Rev 2001; 24: 88-92.
[21] Gasser T, Sandalcioglu IE, El Hamalawi B, van de Nes JA, Stolke D, Wiedemayer H. Surgical treatment of intramedullary spinal cord metastases of systemic cancer: functional outcome and prognosis. J Neurooncol 2005; 73: 163-8.
[22] Kumar R, Banerjee S. Management and functional outcome of intramedullary spinal cord tumors: a prospective clinical study. Asian J Neurosurg 2014; 9: 177-81.
[23] Vassiliou V, Papamichael D, Polyviou P, Koukouma A, Andreopoulos D. Intramedullary spinal cord metastasis in a patient with colon cancer: a case report. J Gastrointest Cancer 2012; 43: 370-2.
[24] Sheedy SP, Welker KM, DeLone DR, Gilbertson JR. CNS metastases of carcinoma ex pleomorphic adenoma of the parotid gland. AJNR Am J Neuroradiol 2006; 27: 1483-5.