Metastatic adrenal pheochromocytoma to the thoracic spine

Feocromocitoma adrenal metastático para a coluna torácica

Feocromocitoma adrenal metastásico para la columna torácica

Michael T. Scalfani[1]
Paul M. Arnold[2]
Karen K. Anderson[3]

ABSTRACT

To report on a case of pheochromocytoma metastases to the spine occurring more than 20 years after initial diagnosis. A 34-year-old female with a history of metastatic pheochromocytoma diagnosed at age 12 presented with weakness, heart palpitations, and circumferential back pain of five months duration. The patient had undergone multiple laparatomies for abdominal and hepatic metastases. Work-up revealed a destructive lesion at T9. After two weeks of preoperative phenoxybenzamine to control her hypertension, she underwent decompression, posterior fixation and fusion. Surgical intervention was followed by radiation therapy, zoledronic acid, and only one cycle of chemotherapy due to intolerance of side effects. The patient survived 25 years after original diagnosis, which far exceeds the average survival of less than 15 years. The patient died 26 months postoperatively due to progression of disease. Pheochromocytoma with spine metastases occurring more than 20 years after diagnosis is very uncommon, and should be considered in the differential diagnosis of a patient with a history of pheochromocytoma.

RESUMO

Relato de caso de feocromocitoma adrenal com metástase para a coluna que ocorreu há mais de 20 anos após o diagnóstico inicial. Mulher de 34 anos com história de feocromocitoma metastático diagnosticado na idade de 12 anos, apresentando fraqueza, palpitações do coração e dor nas costas circunferencial há cinco meses. A paciente tinha realizado laparotomia para metástases abdominal e hepática. Durante o procedimento revelou uma lesão destrutiva em T9. Após duas semanas de fenoxibenzamina pré-operatórios para controlar sua hipertensão, submeteu-se a descompressão, fixação e posterior fusão. A intervenção cirúrgica foi seguida por terapia de radiação, ácido zoledrônico e apenas um ciclo de quimioterapia, devido à intolerância e aos efeitos colaterais. A paciente sobreviveu 25 anos após o diagnóstico original, o que excede em muito a sobrevida média de menos de 15 anos. A paciente morreu 26 meses após o pós-operatório, devido à progressão da doença. Feocromocitoma com metástases para coluna ocorrida há mais de 20 anos após o diagnóstico é muito raro, devendo ser considerada no diagnóstico diferencial de um paciente com uma história de feocromocitoma.

RESUMEN

Relato de un caso de feocromocitoma adrenal con metástasis para la columna que ocurrió con más de 20 años de diagnóstico inicial. Mujer de 34 años con historia de feocromocitoma metastásico diagnosticado en la edad de 12 años, con presencia de debilidad, palpitaciones del corazón y dolor en la espalda circunferencial, con evolución de cinco meses. A la paciente se le había realizado diversas laparotomías por causa de metástasis abdominales y hepáticas. Durante la inspección, se mostró una lesión destructiva en T9. Después de dos semanas de fenoxibenzamina preoperatoria para controlar la hipertensión, se sometió a descompresión, fijación y posterior fusión. La intervención quirúrgica fue seguida por radioterapia, ácido zoledrónico, y sólo un ciclo de quimioterapia, debido a la intolerancia y a los efectos colaterales. La paciente sobrevivió 25 años después del diagnóstico original, lo que excedió en mucho la sobrevida mediana de menos de 15 años. La paciente murió 26 meses después del postoperatorio debido a la progresión de la enfermedad. El hecho de la metástasis para columna haber ocurrido después de 20 años del diagnóstico es bastante raro y se debe considerar en el diagnóstico diferencial de un paciente con una historia de feocromocitoma

[1]BS, Kansas City University of Medicine and Biosciences – Kcumb – Kansas City (MO), United States.
[2]MD, FACS, Professor of Neurosurgery, University of Kansas Medical Center – Kumc – Kansas City (KS), United States.
[3]BS, Department of Neurosurgery, University of Kansas Medical Center – Kumc – Kansas City (KS), United States.

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DESCRIPTORES: Feocromocitoma/diagnóstico; Paraganglioma; Vértebras torácicas; Metástasis de la neoplasia, Compresión de la médula espinal; Diagnóstico diferencial; Sobrevida; Informes de casos

INTRODUCTION

Pheochromocytomas are catecholamine-secreting tumors that arise from chromaffin cells of the adrenal medulla, though they may also arise as paraganglioma in the extra-adrenal sympathetic nervous system[1]. The reported incidence is approximately one case per 100 thousand person-years[2-4]. Only about 10% of pheochromocytomas are malignant, and the presence of metastasis is the only criterion for malignancy[2,4,5]. The most common locations for metastasis include bone, liver, lymph node, lung[2,4,6] and spleen[7]. Although bones are the most common site for metastases, vertebral involvement is rare with only a few cases reported[7-18]. The prognosis for metastatic pheochromocytoma is poor with few cases of long term survival[2,7,19,20]. The authors reported a case of malignant pheochromocytoma metastatic to the thoracic spine 22 years after initial presentation that was managed by tumor resection, spinal stabilization, radiation therapy, and chemotherapy.

CASE REPORT

A 34-year-old female with a history of metastatic pheochromocytoma first diagnosed at age 12 presented with circumferential back pain for 5 months. Work-up including computed tomography (CT) and positron emission tomography (PET) scans revealed a T9 destructive lesion of the right posterior vertebral body, posterior elements, pedicle, rib head, and lamina, with associated cord compression (Figure 1).

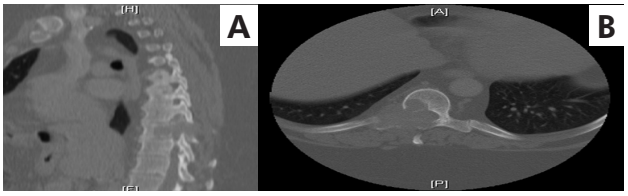

Figure 1
Sagittal (A) and axial (B) CT of the thoracic spine show tumor invading the right pedicle, lamina, and body of T9 with spinal cord compression.

The patient had received no radiation or chemotherapy prior to the bony invasion of her thoracic spine. After pretreating her hypertension for two weeks with the alpha-adrenergic blocker phenoxybenzamine, she was taken to surgery six weeks later for a posterior decompression with long segment pedicle screw fixation (Figure 2). A T9 extradural tumor was resected. Surgical pathology revealed pheochromocytoma (Figure 3).

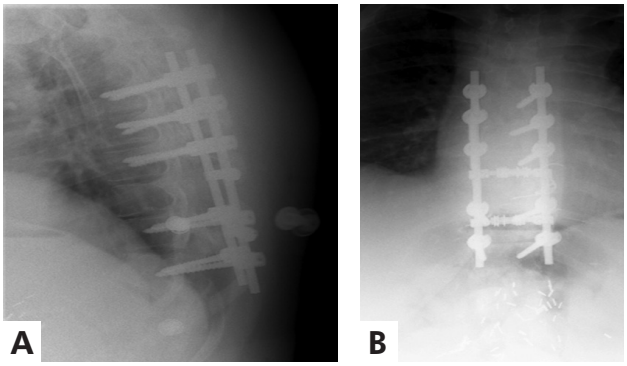

Figure 2
Postoperative X-rays show fixation and fusion (A and B).

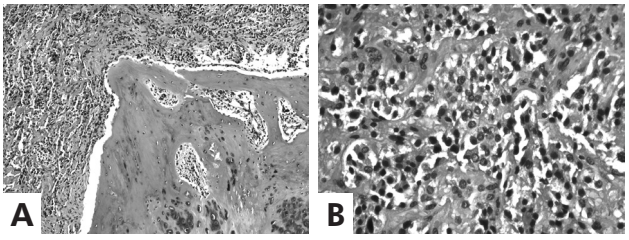

Figure 3
A reticulin stain highlights the nested "zellballen" configuration, as is typical forparagangliomas. Immunohistochemical stains supportive of the diagnosis include strong diffuse staining with antibodies to synaptophysin and chromogranin. Rare cells show immunoreactivity to S-100 antisera. Weak staining is seen with antibodies to serotonin. No staining is seen with anti-CD45, pan-cytokeratin, or neurofilament antibodies (A and B). [original magnification 10x (3A); 40x (3B)].

A reticulin stain highlighted the nested "zellballen" configuration typical for paragangliomas, whether of adrenal medulla (pheochromocytoma) or of extramedullary origin. The histological appearance was similar, although more monomorphous, than the earlier tumors of 1986 and 1992, thus suggestive of metastatic pheochromocytoma. However, it was also highly possible that the thoracic tumor represented a new extra-adrenal paraganglioma originating in this location or at another site, because of: the long tumor-free interval (12.5 years since the liver

lobectomy despite vascular and capsular invasion, and more than 20 years since the original tumor diagnosis); and the other imaging abnormalities noted. Furthermore, pheochromocytomas in children are less likely malignant (the patient was a child when originally diagnosed); therefore, extra-adrenal pheochromocytomas or multiple paragangliomas could be possible over time. The patient survived 25 years after original diagnosis, far exceeding the average survival of less than 15 years. The patient died 26 months postoperatively due to progression of disease.

DISCUSSION

Pheochromocytomas are paragangliomas of the adrenal medulla; the incidence is approximately one case per 100 thousand person-years[2-4]. Only about 10% of these tumors occur in children[3,4], thus the incidence of malignant pheochromocytoma in children is exceedingly rare. Although pheochromocytomas are more likely to be malignant in adults[21,22], only about 10% of pheochromocytomas are malignant[2-5]. Spinal cord compression secondary to metastatic pheochromocytoma has been documented in only a few reports[6,12,15,23,24].

Histological examination to determine malignancy in pheochromocytoma is difficult, because the general malignant features such as giant cells, mitosis, and nuclear pleomorphism can be present in the benign tumors as well[2,6]. Therefore, malignancy in pheochromocytoma is defined as the presence of metastasis at a site that would not otherwise have chromoffin tissue[5,25].

After diagnosis of metastatic disease, the survival rate has been estimated at less than three years[2,4,13,26]; the five-year survival rate has been estimated at about 44%[2,4,7,27]. In 2009, Nomura et al. reported the first survival curve analysis by the Kaplan-Meier method in patients with malignant pheochromocytoma[1]. They confirmed a variable but long average survival period, with a 10-year survival rate of 61% from the time of initial diagnosis. In addition, this survival curve declines continuously and linearly from the time of initial diagnosis through 20 years. From the time of diagnosis of metastasis, the curve was linear for the first 10 years then became flat, indicating that about 19% of patients with malignant pheochromocytoma have an extremely long survival time[1]. The patient of this case report falls into this very small group of patients.

In our case, the patient had been battling recurrent metastases for over 22 years after her initial adrenalectomy at age 12. Despite regular surveillance work-ups including radionucleotide scans and urinary catecholamine testing, her initial presenting sign indicating thoracic metastasis was progressively worsening back pain. While bony metastasis from pheochromocytoma generally responds well to radiation therapy alone[16], the posterior and middle column destruction was too extensive for non-operative management. The patient had received no radiation or chemotherapy prior to the rare bony invasion of her thoracic spine. Despite this patient's negative test for urinary catecholamines, the patient was pre-treated for two weeks with the alpha-adrenergic blocker phenoxybenzamine prior to surgery, as many tumors of this type tend to be hormonally active with hemodynamic instability occurring during resection[15,28].

Isolated metastatic spread of pheochromocytoma to vertebral bodies is extremely rare[29]. There are only a few reports in the literature of vertebral metastases[7-18]. Our patient's presentation of an extradural thoracic pheochromocytoma is an uncommon occurrence.

To date there is no established therapy for metastatic pheochromocytoma with spinal cord compression; however, the therapy of choice is considered to be surgical decompression followed by external beam radiation[8,29,30]. Chemotherapy can provide temporary regression and palliation of metastases, especially with the cyclophosphamide, vincristine and dacarbazine (CVD) regimen[29,31]. In 1987, Olson et al. recommended that radiation therapy should be used if a spinal lesion is causing only pain or only radiculopathy. Surgical decompression should be used (depending on the patient's overall condition) if the patient experiences neurologic deterioration during or after radiation treatment, or develops myelopathy, sphincteric dysfunction, or hypertension[12]. This treatment strategy has been endorsed in subsequent reports[15,32].

A high degree of suspicion is needed to diagnose metastatic pheochromocytoma in a patient with a spinal lesion, especially those patients with a previous history of pheochromocytoma[14]. Sahdev et al. advocate screening for patients at risk of developing paragangliomas due to predisposing genetic factors or a previous diagnosis of paraganglioma[33]. For those patients in whom the tumors were not completely removed, long-term follow-up is mandatory[34], and regular and periodic screening may be beneficial even in patients with sporadic lesions[7]. Patients who have undergone tumor resection should have indefinite screening[35], and for these same patients, Kasliwal recommends periodic screening with whole body imaging, even when abdominal imaging is normal, due to the risk of metachronous metastasis[7]. Screening modalities include serial levels of plasma and urinary metanephrine, CT, PET, somatostatin receptor imaging apart from MRI and MIBG, and blood pressure measurement[7,35]. Preoperative and intraoperative precautions should be taken to prevent hemodynamic instability due to the vascular nature of the tumor.

CONCLUSION

Early diagnosis and aggressive surgical treatment may significantly improve the survival of patients with spinal metastases from pheochromocytoma.

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Correspondence

Paul M. Arnold

University of Kansas Medical Center, 3,901

Rainbow Blvd, Mail Stop 3021

Kansas City KS 66160 USA

Phone: 913-588-7587

Fax: 913-588-7596

E-mail: parnold@kumc.edu