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Case Report

Cerebellopontine angle metastatic melanoma mimicking schwannoma in a sexagenarian: Case report

Hui-Min Xie[1], Li Li[2], Seidu A. Richard[2,3], Zhigang Lan[2]*, Yuekang Zhang[2]

[1]*Department of Radiology, West China Hospital, Sichuan University; 37 Guo Xue Xiang Road, Chengdu, Sichuan, 610041. P. R. China*

[2]*Department of Neurosurgery, West China Hospital, Sichuan University; 37 Guo Xue Xiang Road, Chengdu, Sichuan, 610041. P. R. China*

[3]*Department of Medicine, Princefield University, P. O. Box MA 128, Ho-Volta Region, Ghana, West Africa*

Corresponding authors: Zhigang Lan, Email: 158075478@qq.com

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ABSTRACT

Introduction: Metastasis of melanomas to the cerebellopontine angle (CPA) are very rare. Dissemination via blood, cerebrospinal fluid and/or leptomeninges may be the principal pathway for metastatic spread of malignant melanomas to the CPA. **Case presentation:** A 68-years old man presented with two years history of hearing lost in the right ear with associated dizziness and headaches. A skin lesion was seen on the patient's right forearm. MRI revealed a nodular abnormal signal intensity at the right CPA which was resected and pathology revealed metastatic melanoma. **Conclusion:** Aggressive treatment regime comprising of a combination of surgery, chemotherapy and radiotherapy is very efficacious in prolonging the survival of patients with metastatic melanomas to the brain especially the metastasis to the CPA.

INTRODUCTION

Metastasis of melanomas to the cerebellopontine angle (CPA) are very rare[1, 4]. Metastasis of melanoma to the CPA constitutes about 0.2-0.7% of the lesions found at this site of the brain because most CPA lesions are benign[4]. Dissemination via blood, cerebrospinal fluid (CSF) and/or leptomeninges may be the principal pathway for metastatic spread of malignant melanomas to the CPA[9]. Metastatic melanomas at the CPA often present with a syndrome of rapid succession of symptoms such as hearing loss, vertigo, and/or facial palsy[4].

Characteristically, on T1-weighted magnetic resonance imaging (MRI), CPA melanomas are often seen as hyperintense lesions and hypo-, iso-, or hyperintense lesions on T2-weighted images[1, 5, 7]. They are often enhanced after gadolinium administration[5, 7]. However, amelanotic melanomas are often isointense on T1-weighted images as well as hyperintense on fluid attenuated inversion recovery (FLAIR) sequences[5, 7]. The optional treatment modalities for melanoma metastasis to the CPA includes, stereotactic radiosurgery, surgical resection as well as systemic chemotherapy[3, 4, 9]. We present a case of CPA metastatic melanoma in a sexagenarian which mimicked schwannoma.

CASE REPORT

A 68-years old man presented with two years history of hearing lost in the right ear. He also experienced dizziness and headaches but no tinnitus. Two weeks prior to admission, his dizziness worsen with associated nausea and vomiting. Right forearm internal fixation was done due to a fracture in the right humerus 4 years prior to the above symptomatology. General physical examination revealed a skin lesion on the patient's right forearm (Figure 1). Cranial nerves examination revealed no anomalies in all cranial nerves expect a deficit in CN VIII. Webber and Renner tests revealed a mixed hearing loss in the right ear. Routine Chest X-ray and electrocardiogram (ECG) were essentially normal. Also, routine laboratory investigations were grossly normal.

Head MRI revealed a nodular abnormal signal intensity measuring about 3.4 x 2.7 x 1.6 cm at the right CPA extending to the jugular foramen area (Figure 2A-C). The lesion also showed uneven enhancement. Also, right internal auditory meatus was enlarged. The radiological finding above made us implicate a schwannoma arising from inferior cranial nerves. Computer tomographic angiography did not

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show any vascular abnormalities. Based on the MRI finding above, we decided to operate.

The patient was put in the park-bench position with the head fixed in the Mayfield three keys after general anesthesia. Auditory brainstem responses (ABRs) and electromyographic (EMG) were utilized to monitor the inferior cranial nerves. The modified retrosigmoid approach was used to resect the lesion. Intraoperatively, the tumor was located at the right CPA extending into the right jugular foramen area. The tumor was solid and tough in consistency. It was bright white with clear boarders and rich blood supply. Also, the tumor was adhering as well as exerting compressive effects on the auditory nerve, facial never, vagus nerve, glossopharyngeal nerve. The tumor was carefully dissected from the above nerves. We achieved complete resection of the tumor and complete preservation of the inferior cranial nerves above.

Immunohistochemistry evaluation of the CPA tumor sample and the cutaneous lesion revealed positivity for S-100 and human melanoma black-45 (HMB-45) **(Figure 3A &B).** Nevertheless, glial fibrillary acidic protein (GFAP), oligodendrocyte transcription factor (Oligo-2), creatine kinase (CK), chromogranin A (CgA), synaptophysin (Syn), thyroid transcription factor-1 (TTF-1), human leukocyte common antigen (LCA), P63, CD1a, CD3, CD20 and CD30 were negative. Also, BRAF(V600E) gene mutation as well as telomerase reverse transcriptase (TERT) initiation at site 250 mutation was detected. Thus, a definitive diagnosis of CPA metastatic melanoma was established.

Postoperative MRI revealed total resection of the lesion **(Fig. 4A-C).** Postoperative examination before discharge revealed a resolution of his symptomatology and no neurological deficits. The patient was discharged home two weeks after admission in the hospital. The patient was further treated with temozolamide and radiotherapy at our hospital's oncology department. Two years follow-up revealed no recurrence of the lesions and he is well. Nevertheless, he is still being followed closely to detect any recurrence.

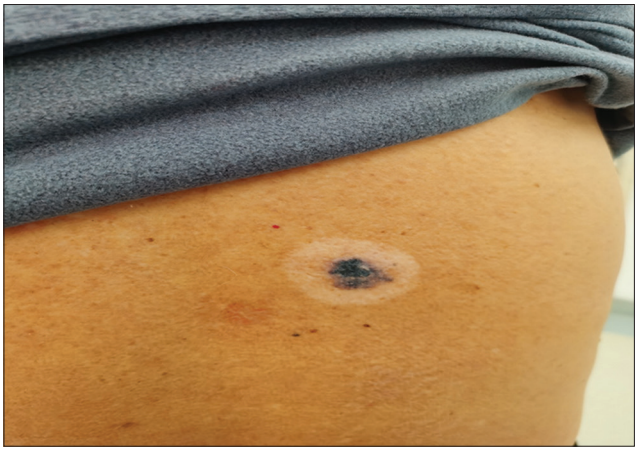

Figure 1: Show a skin lesion on the patient's right forearm

DISCUSSION

Melanomas comprise of 11.7% of all cerebral metastases[7, 17]. They can be solitary or multiple, and are naturally found in the gray matter or subcortically at the gray matter-white matter junction[7, 17]. They are often the main cause of morbidity as well as mortality[4, 15]. Metastatic melanomas to the central nervous system often cause death in as many as 95% of the patients[9]. The average duration from treatment of skin melanoma to the detection of CPA metastasis was 7.7 years, varying from 1.5-17 years[4].

The detection of metastatic melanoma is our case was incidental because the patient was not a known melanoma patient. Incidentally, we saw a skin lesion on the right forearm which was consistent with skin melanoma. Histopathology evaluation of samples of the resected CPA lesion and skin lesion confirmed that the CPA lesion was metastatic melanoma. Nevertheless, we also have a strong convincing that, the initial surgery at forearm could have triggered the cutaneous melanoma in the right forearm which subsequently metastasis to the CPA. Though malignant melanomas have extreme tendency to metastasize to the brain, involvement of the CPA is exceptionally rare[2, 9]

There are numerous potential means via which metastatic melanoma invade the CPA[9]. Dissemination via the CSF and/or leptomeningeal may be the principal pathway for metastatic spread to the CPA[9, 18]. Kingdom postulated that, hematogenous dissemination of malignant melanoma cells

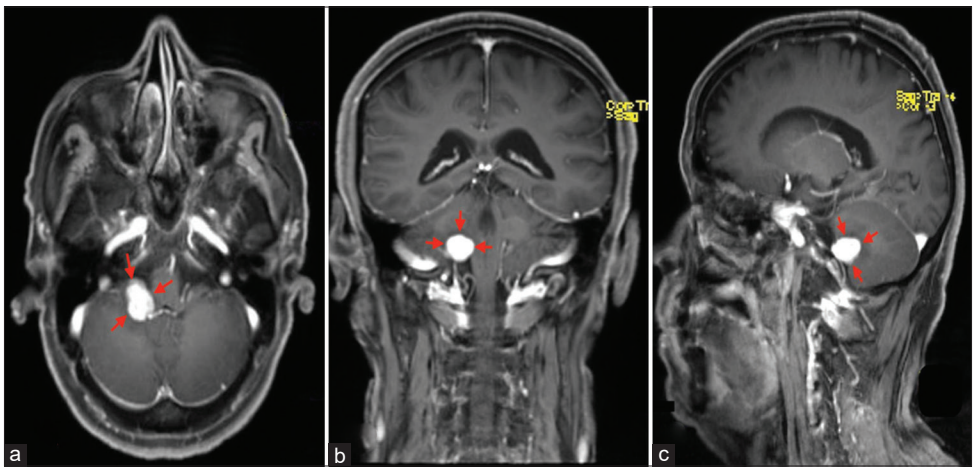

Figure 2: a-b Are preoperative MRI showing a nodular abnormal signal intensity at the right cerebellopontine angle (CPA)
a = Axial, b = Coronal, c = Sagittal. Red arrows = lesion

from the internal carotid artery into the internal auditory canal and successive progression into the CPA leading to early neurovascular invasion as well as extension may be the pathway via metastatic melanoma invade of the CPA[11]. Clinically, patients with metastatic melanoma to the CPA presents with hearing loss, headache, vertigo or imbalance, and/or facial weakness as a result of lower cranial nerves invasion[1, 4]. Our patient presented with the above symptomology.

Studies have demonstrated that, whole-body 18F-2-fluoro-2-deoxy-D-glucose (FDG)-PET is often beneficial in distinguishing between metastatic brain tumors from primary brain tumors[9]. The 18F-FDG-PET modality has a sensitivity of about 90-97% in identifying melanoma metastasis[9]. We did not utilize this modality during our initial evaluation because the lesion in our patient mimicked schwannoma. Several studies have demonstrated that, most metastatic melanomas mimic acoustic neurinomas and meningiomas during radiological evaluation[9, 16].

On CT, most cerebral metastatic melanomas display pre-contrast hyperintensity[1, 4]. Studies have established that, the augmented T1 as well as reduced T2 signals are as a result of intratumoral blood products like hemorrhage or hematoma formation[4]. Also, histopathologic comparison with CT scan imaging established that, melanin was predominantly accountable for the shorten T1 and T2 signals, as well as the augmented density appearance on CT scan[4, 5].

Several studies have demonstrated that, metastatic melanomas characteristically exhibit shorten T1 as well as T2 relaxation time on MRI[1, 4, 5]. Studies have shown that, melanotic or pigmented melanoma characteristically appears hyperintense on T1-weighted sequence just like lipomatous choristoma or lipoma but with no reduction in signal during fat suppression sequences compare to lipoma and appears hypointense or isointense on T2-weighted sequences[4, 5]. On the other hand, amelanotic or nonpigmented metastatic melanomas appears isointensity or hypointensity on T1-weighted as well as hyperintensity or isointensity on T2-weighted sequences[4].

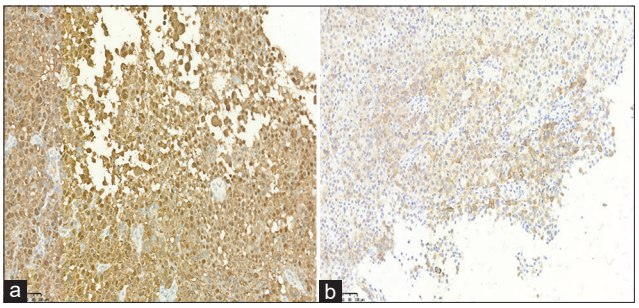

Figure 3a&b: Are immunohistochemistry images of the CPA tumor sample and the cutaneous lesion. *A = S-100, B = HMB-45*

Gerganov et al indicated that, surgical resection of the CPA metastatic melanoma lesions via the retrosigmoid approach with protection of the facial nerve function as well as hearing, combined with treatment of the systemic disease, offers a near normal quality of life for their patient for at least 42 months after the diagnosis of the primary melanoma[7]. We achieved complete resection of the tumor and complete preservation of the inferior cranial nerves such as the auditory nerve, facial never, vagus nerve, glossopharyngeal nerve with the aid of intraoperative ABRs and EMG monitors. The patient was further treated with temozolamide and radiotherapy at our hospital's oncology department. Fernandez et al indicated that, a more rigorous as well as systematic regime of therapy, combining surgery with other treatment modalities like radiation as well as chemotherapy, may yield a more favorable clinical outcome[6].

Pangiotou et al observed that, melanoma patients with single brain metastases treated via surgery and gamma knife radiosurgery (GKR) comparatively survived longer, with a median of 12 months, while patients treated with GKR as well as chemotherapy survived only 5 months[15]. Thus, they recommended that solitary lesions be resected[15]. Systemic treatment regime for melanoma often comprises of a combination of chemotherapy as well as immune modulating therapy[4, 8]. However, clinical outcomes from the current melanoma agents are poor. Currently, temozolomide, cisplatin, vinblastine as well as doxorubicin are the commonly used chemotherapy agents while interferon α and interleukin 2 are adjuvant immunotherapy agents[4, 8]. Gonzalez et al observed that, only 20-32% out of 34 patients of their patients responded to the combined treatment modality above with a median survival of 10 months[8].

Radiotherapy is one of the most common treatment modalities for patients with malignant melanoma with brain

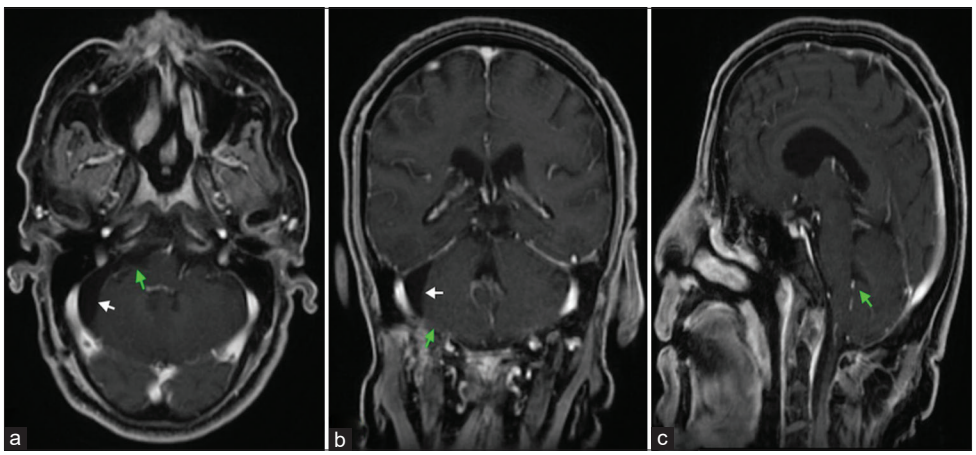

Figure 4a-c: Are postoperative MRI showing total resection of the lesion at the right cerebellopontine angle (CPA). *a = Axial, b = Coronal, c = Sagittal. Green arrow = no lesion. white arrow = CSF in the operative defect*

metastases[3, 10]. Treatment regimens of 3,000 cGy alienated into ten equal 300-cGy fractions over 2 weeks have been generally accepted for patients with metastatic brain melanomas[9, 14]. In case of multiple metastatic melanoma brain lesions, whole brain radiotherapy is often adopted. Hofmann et al observed that, temozolamide in combination with radiotherapy is an efficaciously treatment modality for malignant melanoma patients with brain metastases because, augmented survival was notice in their patients [10].

The diagnosis of CPA melanoma metastases was established based on CSF evaluation, neuroimaging, or postmortem examination, rather on histopathological evaluation of resected tumor[7]. Nevertheless, postoperative histopathological evaluation using immunohistochemical staining's such as S100 protein, vimentin as well as antimelanin antibody staining and electron microscopy, are often obligatory to aid in differentiating melanomas from melanocytic meningiomas as well as other pigmented lesions[2, 9]. Immunohistochemistry evaluation of the tumor sample in our patient revealed positivity for S-100 and HMB-45 which are key diagnostic biomarker for melanoma. We also detected BRAF(V600E) gene mutation as well as TERT initiation at site 250 mutation.

Mastorakos et al reported that, BRAF mutation status appears to be a potent prognostic factor in melanoma patients with brain metastasis[13]. Lade-Keller et al found TERT mutation in 67% of examined melanoma samples[12]. Studies have shown that, patients with melanoma brain metastasis often present with poor outcome with a median survival time varying from 2-10 months[9, 10, 14]. Our patient is still alive after 2 years follow-ups because of our aggressive treatment regime comprising of a combination of surgery, chemotherapy and radiotherapy. We are still following him up via out-patients department.

CONCLUSION

Metastasis of malignant melanomas to the CPA is exceptionally rare although melanomas have higher tendency to metastasize to the brain. Aggressive treatment regime comprising of a combination of surgery, chemotherapy and radiotherapy is very efficacious in prolonging the survival of patients with metastatic melanomas to the brain especially the metastasis to the CPA. ABRs and EMG monitoring of the inferior cranial nerves is very crucial in CPA metastatic melanoma surgery.

ABBREVIATION LIST

Auditory brainstem responses = ABRs, Cerebellopontine angle = CPA, Cerebrospinal fluid = CSF, Electromyographic = EMG, Fluid attenuated inversion recovery = FLAIR, Gamma knife radiosurgery = GKR, Human melanoma black-45 = HMB-45, Magnetic resonance imaging = MRI, Telomerase reverse transcriptase = TERT.

DECLARATION

Ethics approval and consent to participate

This case was reported or written in accordance to ethical committee of West China Hospital criteria for reporting or writing case reports. The patient and relatives were informed about our intension to involve him in a case study and they agreed to partake in the study.

CONSENT FOR PUBLICATION

The patient and relatives were duly informed about our intention to publish his case and they fully concerted to the use of these documents. A written informed consent was obtained. A written concern for publication was signed. The hospital also concerted to the use of this information for publication.

AUTHOR CONTRIBUTIONS

All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work. Seidu A. Richard wrote the final paper.

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