Cranial nerve deficit caused by skull metastasis of prostate cancer: three Japanese castration-resistant prostate cancer cases

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CRANIAL NERVE DEFICIT CAUSED BY SKULL METASTASIS OF PROSTATE CANCER: THREE JAPANESE CASTRATION-RESISTANT PROSTATE CANCER CASES

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ABSTRACT

We report 3 Japanese patients with cranial nerve deficit caused by skull metastasis of prostate cancer (PCa). Case 1 was a 75-year-old patient with a chief complaint of diplopia. The cause of diplopia was right oculomotor nerve palsy from the skull metastasis. External beam radiation therapy (EBRT) to the whole brain, 40 Gy in 20 fractions, was performed and the diplopia improved. Case 2 was a 72-year-old patient with a chief complaint of facioplegia. Bone scintigraphy and computed tomography (CT) of the head revealed right occipital bone metastasis of PCa resulting in right facial nerve palsy. EBRT to the right occipital bone, 50 Gy in 25 fractions, with daily oral dexamethasone (DEX) was performed and facioplegia showed complete recovery. At 12 months after onset, the patient was followed with no symptoms. Case 3 was a 74-year-old patient with a chief complaint of diplopia. Diffusion weighted magnetic resonance imaging (MRI) and positron emission tomography (PET) showed right petrous bone metastasis resulting in right abducent nerve palsy. EBRT to the right petrous bone, 44 Gy in 22 fractions, with oral DEX was performed and diplopia showed complete recovery. At 13 months after onset, the patient was followed with no symptoms. MRI and PET may detect PCa metastasis in the skull base more clearly than other imaging modalities. EBRT with 40 – 50 Gy in 20 – 25 fractions in association with corticosteroid administration may be a reasonable treatment modality in the treatment of patients with metastatic PCa who develop cranial nerve dysfunction.

Key words: cranial nerve palsy, prostate cancer, skull metastasis, external beam radiation therapy

INTRODUCTION

PCa is the most frequently diagnosed cancer in men and is the second leading cause of cancer-related death in the USA.[1] Although hormone therapy is useful for advanced PCa, its effects are limited and PCa cells become castration-resistant after several years.[2, 3] Skeletal metastasis occurs in approximately 80% of patients with advanced PCa, and no curative therapies are available for bone metastatic castration-resistant PCa (CRPC).[4, 5] Although cranial nerve dysfunction syndromes caused by skull metastasis of PCa have been reported, such as Collet-Sicard syndrome,[6] the skull base is a less common site of PCa metastasis. Cranial nerve palsy severely impacts the quality of life of the patient and treatment should be performed as soon as possible after diagnosis. Here, we report 3 Japanese cases of cranial nerve palsy caused by skull metastasis of PCa.

CASE REPORTS

Case 1

A 75-year-old male patient was diagnosed as having PCa with multiple bone and lymph nodes metastases and underwent combined androgen blockade (CAB) for 3 years followed by anti-androgen alternative therapy (AA) and estramustine phosphate (EMP), and developed diplopia. Abduction of the right eye was observed and prostate-specific antigen (PSA) at this time was 190 ng/mL. Bone scintigraphy and head CT showed no apparent evidence of skull metastasis. Docetaxel (DTX) with daily oral prednisone at a dose of 10 mg was started. Diplopia improved gradually after starting DTX and PSA decreased to 80 ng/mL after 7 cycles of DTX. After 9 cycles of DTX, diplopia deteriorated again and subsequently an unconsciousness attack occurred. Head CT revealed multiple brain metastases (Fig. 1A) and osteoblastic bone metastasis in the right processus clinoideus posterior (Fig.1B). It was concluded that abduction of the right eye was caused by oculomotor nerve palsy from the skull metastasis. Extent of disease on bone scintigraphy (EOD), which was proposed by Soloway *et al*. was group 4.[7] PSA increased to 203 ng/mL and DTX was withdrawn. EBRT to the whole brain, 40 Gy in 20 fractions, was performed. Subsequently, diplopia gradually improved and PSA decreased to 79 ng/mL. After EBRT, the patient was discharged and changed hospital.

Case 2

A 72-year-old patient, who was diagnosed as having PCa with multiple bone metastases underwent CAB for 2 years followed by AA, EMP, and zoledronate (ZOL), developed right facioplegia. PSA at this time was 405 ng/mL and bone scintigraphy revealed right occipital bone metastasis (Fig. 2A) and group 3 on EOD. Head CT also revealed right occipital osteoblastic bone metastasis compressing the perpendicular part of the facial nerve (Fig. 2B). Therefore, it was concluded that the symptoms were due to facial nerve palsy. Daily oral DEX at a dose of 2 mg was started and EBRT to the right occipital bone, 50 Gy in 25 fractions, was performed. The symptoms disappeared at 1 week after starting EBRT. At 6 months after onset, although the findings of head CT were the same as those at onset (Fig. 2C), PSA was decreased to 10 ng/mL. At 12 months after onset, DEX administration was continued and the patient was followed-up with no symptoms as an outpatient.

Case 3

A 74-year-old male patient was diagnosed as having PCa with multiple bone metastases underwent CAB for 2 years followed by AA and EMP, and developed diplopia. Adduction of the right eye was observed. Head CT showed slight osteolytic changes of the right petrous bone (Fig. 3A), and diffusion weighted MRI showed a high signal intensity in the right petrous bone (Fig. 3B). Furthermore, bone scintigraphy revealed bone metastasis in the right petrous bone (Fig 3C) and group 3 on EOD. PET showed a high-density signal (standardized uptake value = 4.5) in the right petrous bone (Fig. 3D). PSA at this time was 34 ng/mL. It was concluded that adduction of the

right eye was due to abducent nerve palsy caused by right petrous bone metastasis. Monthly ZOL infusion and daily oral DEX at a dose of 2 mg in addition to EBRT to the right petrous bone, 44 Gy in 22 fractions, were performed. After EBRT, adduction of the right eye showed complete recovery. Subsequently, DTX was started and the patient was discharged after 2 cycles of DTX. At 13 months after the onset of diplopia, PSA was decreased to 17 ng/mL. The patient was treated with DTX with no symptoms as an outpatient.

DISCUSSION

Cranial nerve palsy is an infrequent complication of metastatic PCa, and skull base metastasis is difficult to find radiologically. In a study of skull base metastasis caused by various malignancies, radiological confirmation of metastatic spread to the skull base was found in only 77% of patients.[8] It was reported that bone scintigraphy was the most sensitive method for investigation.[9] Bone scintigraphy, however, cannot clearly show the localization of the metastasis. In case 3, diffusion weighted MRI and PET could clearly detect the metastatic lesion. These may be crucial modalities for making regional diagnosis of skull base metastasis of PCa.

There have been few reports with regard to cranial nerve palsy caused by skull base metastasis of PCa due to its rarity. As patients with metastasis in distal bone had a poorer prognosis than those with metastatic lesions in the pelvis or dorsal vertebrae,[10] when advanced cancer causes cranial nerve palsy it may indicate a poor prognosis. O'Sullivan *et al*. reported that EBRT to the skull base combined with corticosteroids was a valuable treatment modality in the treatment of patients with metastatic PCa who develop cranial nerve dysfunction, and that the optimum radiation treatment schedule was 20 Gy in 5 fractions because of the very poor prognosis in a total of 32 patients. The median survival following skull base radiotherapy was 3 months with only 14 patients (44%) living < 2 months in their study. However, the percentage of complete response was only 25%.[9] McDermott *et al*. reported that palliative EBRT for 15 patients with either 20 Gy in 5 fractions to the skull base or 30 Gy in 10 fractions to the whole brain achieved complete response in

10 patients (67%). However, 10 patients (67%) died within 3 months after EBRT and only 3 patients (20%) survived at 12 months after EBRT.[11] Although hypofractionation with high daily dose and low fractions can promptly improve symptoms, it cannot maintain focal control for a long time, and increases late onset toxicities. The survival times in those studies were extremely short. Therefore, hypofractionation with 20 Gy in 5 fractions or 30 Gy in 10 fractions may be permitted. DTX resistant CRPC patients tend to show short survival and severe pain is a significant predictor of overall survival with metastatic CRPC.[12] Hypofractionation may be considered in such cases. However, Japanese CRPC patients may show longer survival than those in other countries because several salvage therapies are often performed, such as AA, EMP, DEX, and ethinylestradiol.[13-17] The reports of O'Sullivan and McDermott were retrospective studies with small sample sizes and unclear ethnic backgrounds. To our knowledge, there have been no reports of cranial nerve deficit caused by skull metastasis of PCa in Japanese patients in the English literature. In case 1, EBRT to the whole brain was performed and long survival time was not confirmed. This case should not be considered as the same condition as other 2 cases and might be an indicative case of hypofractionation because metastatic spread of PCa to the parenchyma of the brain implies short survival time.[18] In cases 2 and case 3, survival time for more than 12 months with complete response was confirmed. These patients were administered daily oral corticosteroid as did in previous studies.[9, 11] Although efficacy of low-dose DEX in CRPC were reported,[19] there have been no reports of efficacy of DEX alone for cranial nerve deficit caused by skull bone metastasis of PCa. On the other hand, role of systemic corticosteroids in the management of malignant spinal cord

compression were also reported,[20] corticosteroids may be needed when EBRT to the skull base metastasis from PCa is performed. On the basis of these results, EBRT with 40 – 50 Gy in 20 – 25 fractions to the skull base metastasis in association with corticosteroid administration may be a reasonable treatment modality for maintenance of focal control of cranial nerve deficit and prevention of late onset toxicities in Japanese CRPC patients.

CONCLUSIONS

MRI and PET may detect PCa metastasis in the base of the skull more clearly than other imaging modalities. When the long survival time of the patient is predicted, EBRT with 40 – 50 Gy in 20 – 25 fractions in association with corticosteroid administration may be a reasonable treatment modality in the treatment of patients with metastatic PCa who develop cranial nerve dysfunction.

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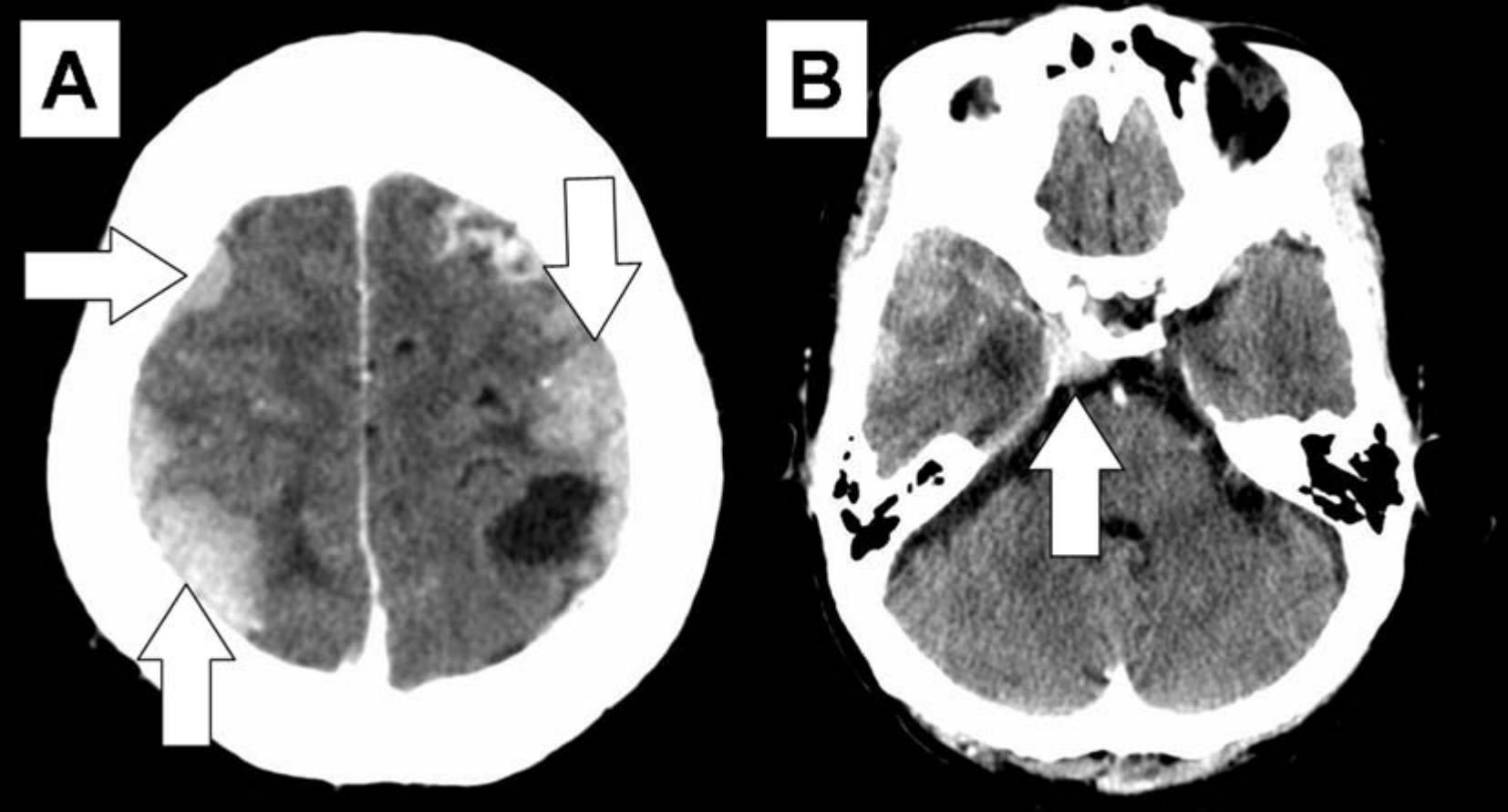
Legends to illustrations

Fig. 1 – Head CT. (A) Arrows indicate brain parenchyma metastases. (B) The arrow indicates osteoblastic metastasis of the right processus clinoideus posterior.

Fig. 2 – (A) The arrow in the bone scintigraphy indicates isotope accumulation in the right skull. (B) The arrow in head CT before treatment indicates the perpendicular part of the right facial nerve compressed by the right occipital osteoblastic bone metastasis. (C) The arrow in head CT after treatment indicates the perpendicular part of the right facial nerve. There were no differences between head CT before and after treatment.

Fig. 3 – (A) The arrow in head CT indicates faint osteoclastic change of the right petrous bone. (B) The arrow in diffusion weighted MRI indicates high signal intensity in the right petrous bone. (C) The arrow in bone scintigraphy indicates isotope accumulation in the right skull. (D) The arrow in PET indicates a high density signal in the right petrous bone.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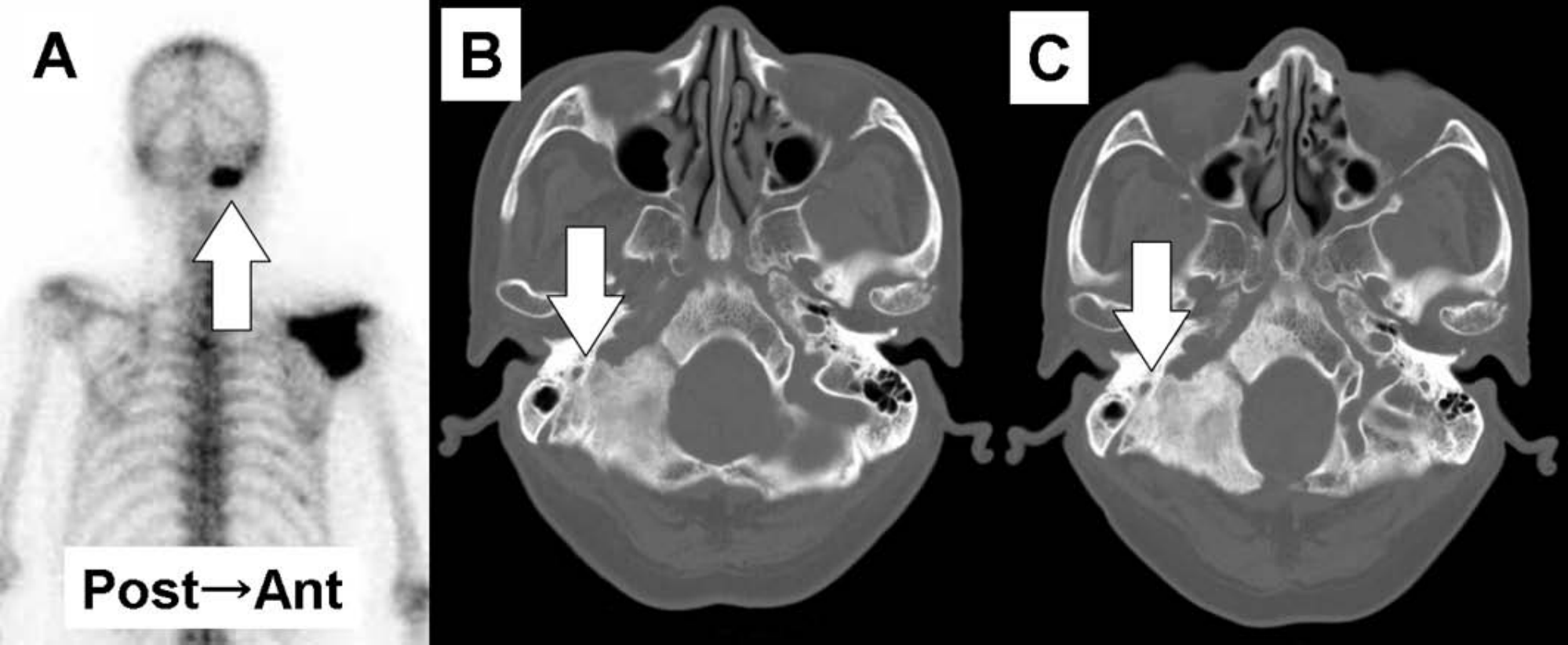
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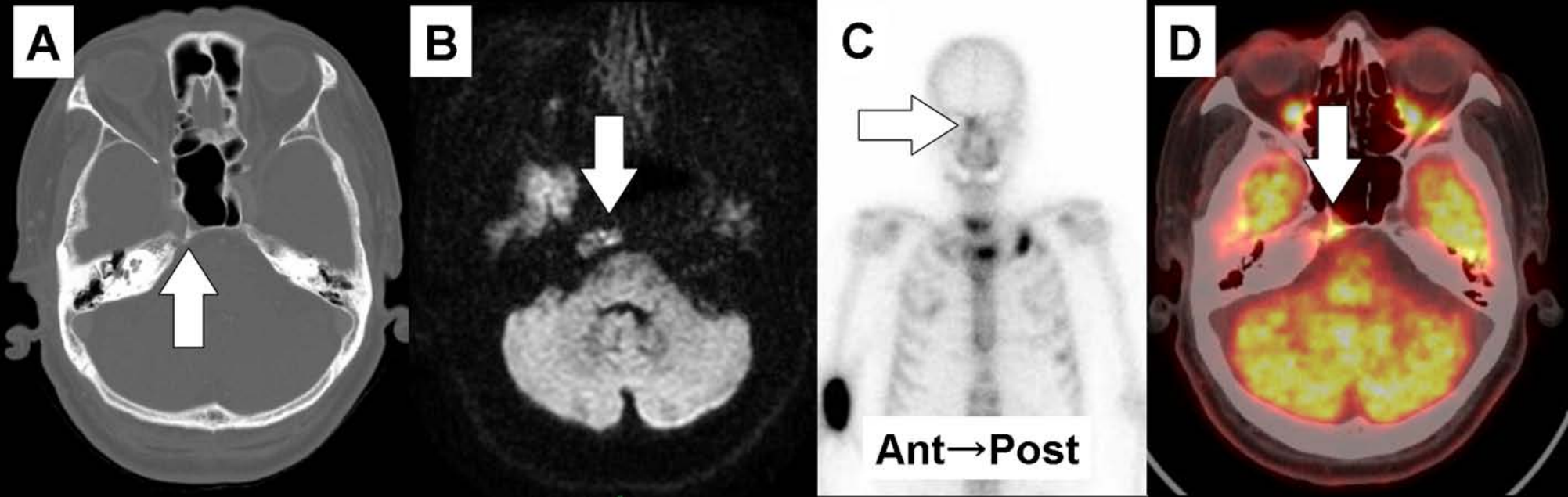
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