



BASELINE TUMOR IMAGING CHARACTERISTICS IN MEDULLOBLASTOMA PATIENTS WITH EXTRANEURAL METASTASIS: A CASE CONTROL STUDY

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BACKGROUND

- Medulloblastoma is a malignant posterior fossa tumor, which comprises approximately 20% of all pediatric brain tumors and <1% of all adult brain tumors.
- Metastatic stage at presentation significantly impacts prognosis and is determined by Chang's M staging system:
 - M0 - Localized to the posterior fossa without evidence of dissemination in cerebrospinal fluid (CSF), or on brain or spine MRI
 - M1 - Tumor cell dissemination in CSF but no MRI evidence of tumor dissemination in the CNS
 - M2 – MRI evidence of tumor dissemination in the brain
 - M3 – MRI evidence of tumor dissemination in the spine
 - M4 – Imaging evidence of metastatic disease outside the CNS i.e. extraneural metastases.
- M4 disease accounts for only 1-2% of all medulloblastoma cases with a drastically lower survival rate as compared to the M0-M3 stages.
- M4 disease is usually not present at initial diagnosis but instead develops during or after completion of treatment.

CLINICAL QUESTION AND STUDY HYPOTHESIS

- This represents a valuable period for surveillance and early intervention.
- The baseline, pretreatment brain MRI routinely performed in all patients before surgical resection is an important resource in understanding tumor characteristics in this patient population.
- What we do know: Patients with M4 disease have a higher frequency of genetic aberrations e.g. *MYC* and *MYCN* gain or amplification.
- What we do not know: Do patients with M4 disease also have more aggressive baseline tumor imaging characteristics?
- **Study hypothesis:** Medulloblastoma patients with extraneural metastases will have more locally aggressive baseline imaging characteristics as compared to age-, sex- and immunophenotype-matched controls without extraneural metastases.

STUDY METHODOLOGY

- **Study type:** Case-control study
- **Cases:** Medulloblastoma patients with extraneural metastases at presentation or developed extraneural metastases during or after treatment.
- **Controls:** Age-, sex-, immunophenotype- and M stage (M0 vs M+) controls were matched in a 3:1 ratio to cases.
- **Inclusion criteria:** Age 1-25 years, treatment at SJCRH over the past 20 years on a clinical trial, the availability of baseline MRI in PACS, and additional modality-specific imaging for extraneural metastasis.
- **Exclusion criteria:** Patients over 25 years old, non-availability of baseline brain MRI, or non-diagnostic baseline brain MRI due to motion artifact or susceptibility artifact from braces.

STUDY METHODOLOGY

- **Demographic and clinical data:** Age and sex, histopathology and immunophenotyping of tumors and extraneural metastases, additional genetic aberrations, including *TP53*, *MYC*, and *MYCN* status, M stage at presentation and date of death or last follow-up.
- The date of baseline MRI for both cases and controls were obtained from the PACS system.
- For cases, additional imaging, including extremity radiographs, chest, abdominal, and pelvic CTs, abdominal ultrasound, and nuclear medicine positron emission tomography (PET) CTs, was reviewed.

STUDY METHODOLOGY

- Tumor volume was calculated using an automated segmentation tool on MINT by an advanced imaging processing specialist and quality controlled by a Pediatric Neuroradiologist (SNP).
- Invasion of the brainstem and brachium pontis, and extension through the outflow tracts of the 4th ventricle (foramina of Luschka and Magendie) were determined on the axial T2 sequences by a Pediatric Neuroradiologist (SNP) blinded to the diagnosis of extraneural metastases.

RESULTS

- 11 cases of medulloblastoma with extraneural metastases were identified, who were diagnosed based on FDG PET imaging. 1 patient did not have a baseline MRI and was therefore excluded from the analysis.
- 1 of the 10 cases presented with extraneural metastases, with the remaining 9 cases developing extraneural disease between 3-46 months (median 3.5 months) from initial diagnosis.
- Bone was the most common site of extraneural metastases (90%) followed by lymph node (50%) and liver metastases (30%).
- The median age at presentation was 7 years in both cases and matched controls (age range: 2-22 years), with a 50% female distribution in each group.

RESULTS

- The most common molecular subtype was the non-WNT non-SHH subtype (60%), followed by SHH (30%) and WNT (10%).
- The cases had a higher proportion of high-risk molecular aberrations including *MYC/MYCN* gain/amplifications and *TP53* mutations (30%) vs controls (10%).
- There was a positive association of invading branchium pontis with cases ($p=0.0488$).
- The patients with invading branchium pontis had 4.89 times having extraneural metastases (Cases) than those of no invading branchium pontis (Odds Ratio=4.8929).
- The associations of higher tumor volume, extending through the foramen of Luschka, and extending through the foramen of Magendie with cases (patients with extraneural metastases) were not detected.

FIGURE 1

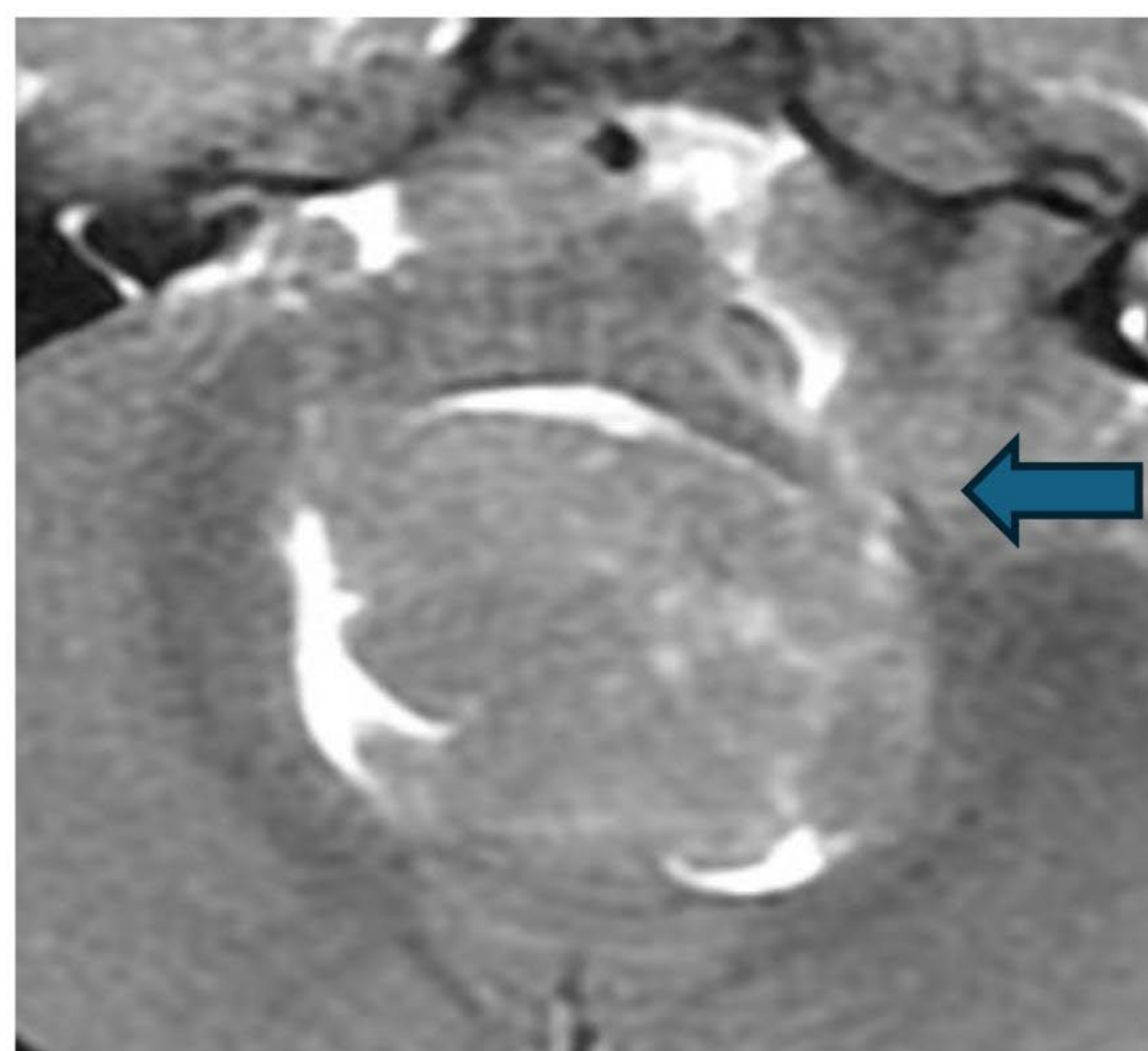


FIGURE 3

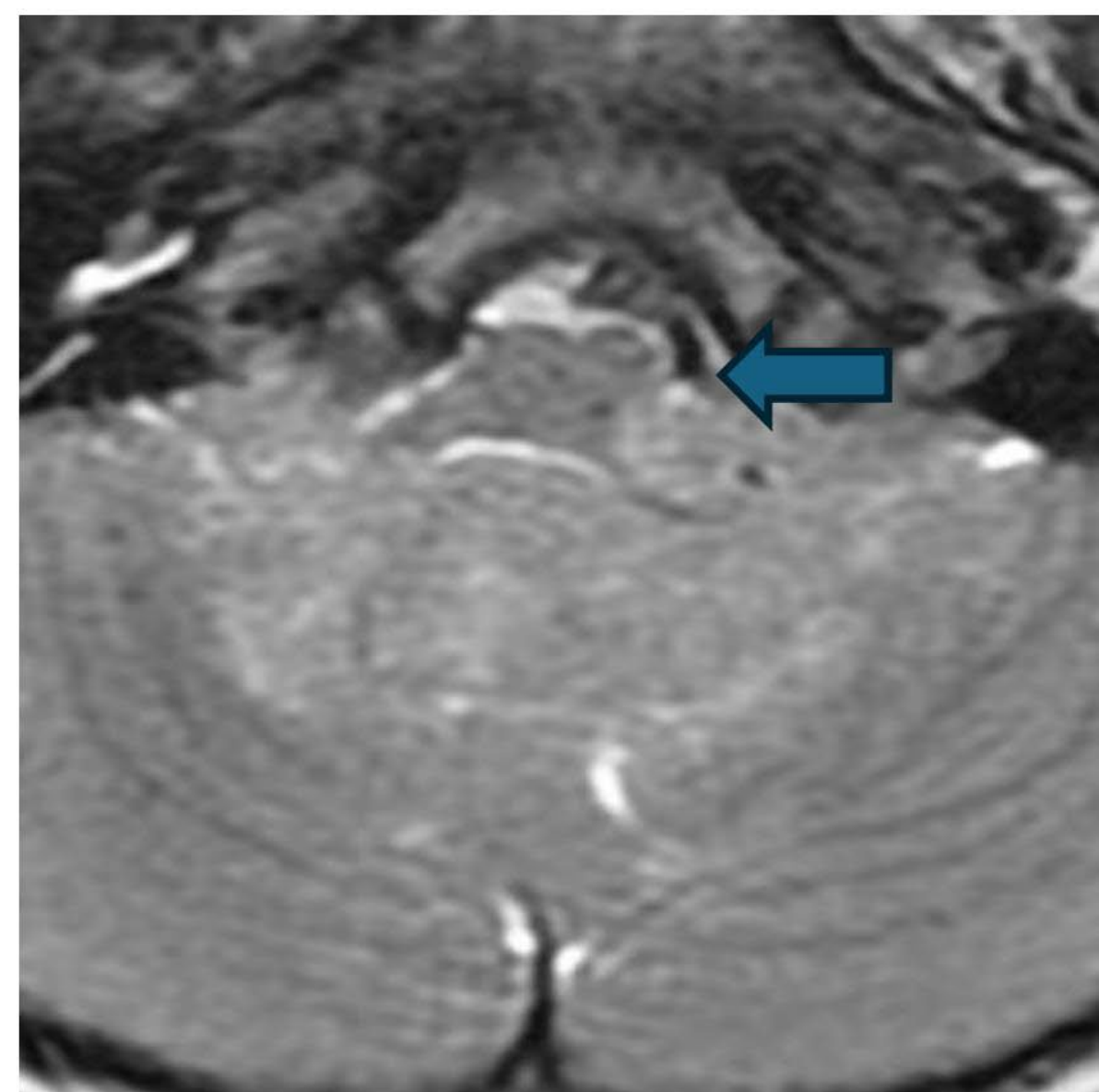
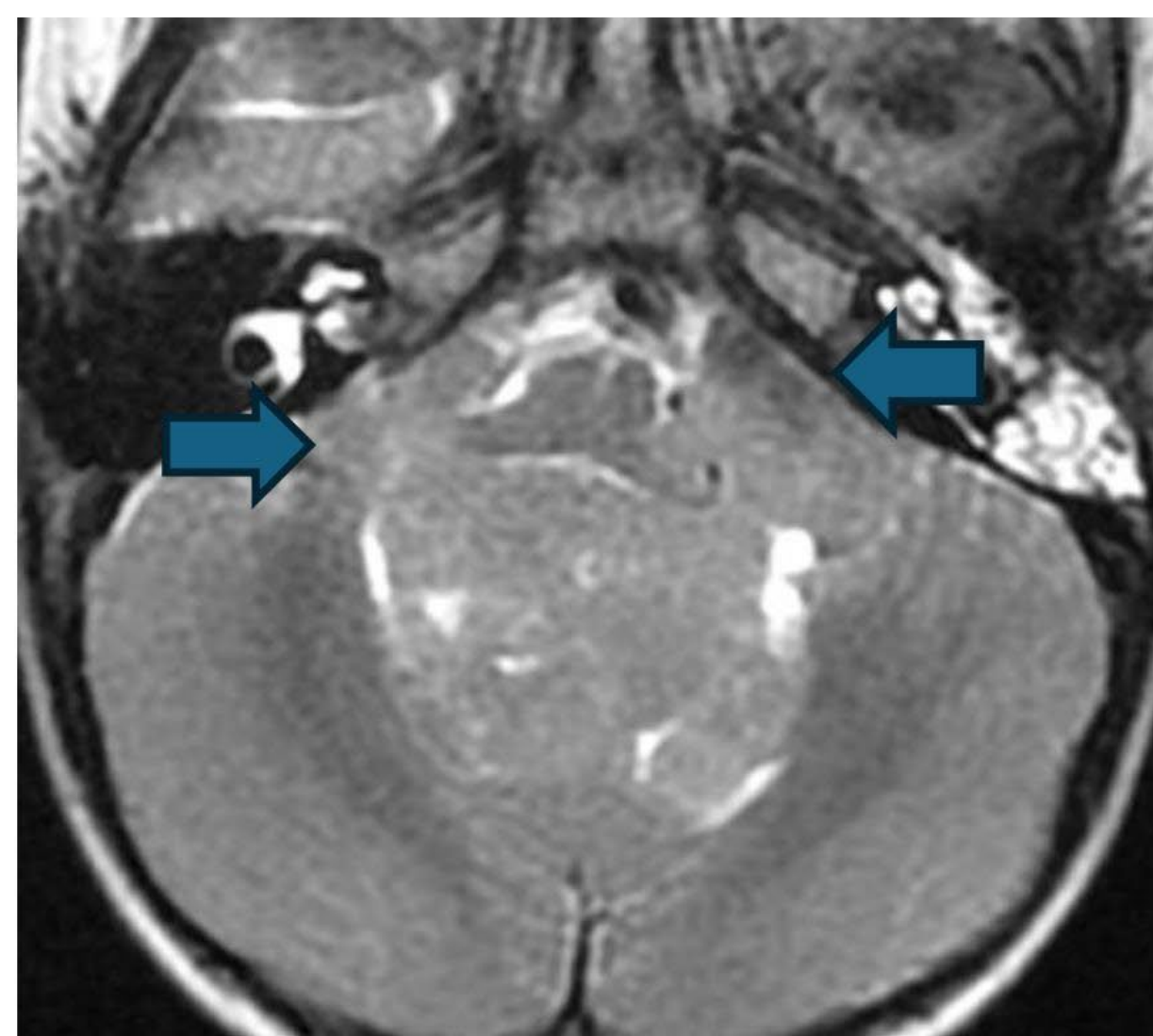


FIGURE 4



FIGURE 2



20-year-old male patient, presented with widespread osseous metastases 4 months after initial presentation. Axial T2 images; Figure 1 shows invasion of the brachium pontis on baseline MRI (arrow), Figure 2 shows extension through bilateral foramina of Luschka (arrows), Figure 3 shows brainstem invasion (arrow). Figure 4 shows numerous osseous metastases on FDG PET (arrows).

CONCLUSION

- Our study represents a novel approach to M4 medulloblastoma patients, with a focus on baseline imaging characteristics between patients with and without extraneural disease.
- While it is known that patients with extraneural metastases have an increased frequency of high-risk molecular aberrations e.g. *MYC/MYCN* amplification, it is possible that these tumors also have more aggressive imaging characteristics.
- Our study provides important preliminary data that warrants exploration in larger prospective studies investigating the association of both molecular and imaging features with the development of extraneural metastases.

REFERENCES

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