INTRODUCTION

- Gorlin Syndrome - Most cases caused by a pathogenic variant of PTCH1, which plays a role in the Sonic Hedgehog (SHH) signaling pathway.
- Affected patients have developmental anomalies, multiple basal cell carcinomas, and an increased risk of developing a medulloblastoma in early childhood.
- The case presented here is a 19-year-old Hispanic female patient with Gorlin Syndrome due to a pathogenic variant of PTCH1, which plays a role in the Sonic Hedgehog (SHH) signaling pathway.
- Mainstay treatment of MB consists of a combined-modality approach utilizing RT, but this is not recommended in patients with Gorlin Syndrome due to the increased risk of developing basal cell carcinomas.
- Vismodegib is an SHH signaling pathway inhibitor recently FDA approved for treating the basal cell carcinomas in Gorlin Syndrome. This case study discusses the use of Vismodegib as a targeted therapy for SHH+ medulloblastoma (MB).
- The use of Vismodegib as targeted therapy in our patient was initially promising, but the tumor still progressed.
- We present this case to raise awareness to the potential complications of treating MB in those with Gorlin syndrome and to discuss the possible benefit of Vismodegib for these patients.
- Multi-institutional studies are required to determine whether the drug should be included in a comprehensive treatment plan for patients with Gorlin syndrome and SHH+ MB.

PATIENT PRESENTATION

- Presentation:
  - Hypertelorism, large birth weight, missing right pupil and lens with associated strabismus, developmental delay
  - Worsening ataxia, beginning Nov. 2015
  - Imaging:
    - PET scan positive at left mandible & left pelvis
- Genetic Testing:
  - Positive PTCH1 gene mutation, consistent with diagnosis of Gorlin Syndrome
- Molecular profile: SHH+/p53-
- Molecular profile: SHH+/p53-
- Pathology of posterior fossa tumor
  - Nodular/desmoplastic morphology with large cell/anaplastic changes
  - Pathology of left mandible biopsy showing infiltrative small cell malignancy
- Recurrent widespread metastatic disease:
  - Begin radiation now, as benefit outweighs risk.
- Post RT: no evidence of residual disease
- Evidence of recurrent, metastatic, extraneural SHH+ MB
- Initial therapy:
  - 5 cycles of chemores per COG-95223
  - Avoid radiation therapy due to increased risk of developing basal cell carcinomas

PATIENT PRESENTATION - FIGURES

- Figure 1: Clinical Manifestations of Gorlin Syndrome
- Figure 2: Vismodegib's role in SHH pathway
- Figure 3: 2015;5:14
- Figure 4: Pathology of posterior fossa tumor
- Figure 5: Biopsy stained with synaptophysin, consistent with metastatic medulloblastomas
- Figure 6: Nov 2015 - Original posterior fossa tumor
- Figure 7: Feb 2019 - Mandibular recurrence of tumor

IMAGING

- MRI photos courtesy of Dr. Linda Margraf, MD

CONCLUSION

- Mainstay treatment of MB consists of a combined-modality approach utilizing RT, but that is risky in patients with Gorlin syndrome.
- The use of Vismodegib as targeted therapy in our patient was initially promising, but the tumor still progressed.
- We present this case to raise awareness to the potential complications of treating MB in those with Gorlin syndrome and to discuss the possible benefit of Vismodegib for these patients.
- Multi-institutional studies are required to determine whether the drug should be included in a comprehensive treatment plan for patients with Gorlin syndrome and SHH+ MB.

REFERENCES

- Pathology Imaging courtesy of Dr. Linda Margraf.
- MRI photos courtesy of Dr. Sibo Zhao.

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