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Vismodegib and physeal closure in a pediatric patient

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A 2 year old girl presented with several week history of sub-occipital headaches. Brain MRI revealed hydrocephalus and a large lateralized posterior fossa mass (Fig. 1a). She underwent a gross total resection which confirmed a WHO Grade 4 nodular desmoplastic medulloblastoma, Sonic Hedgehog subtype. Due to her young age, she was treated on an institutional protocol with chemotherapy to delay adjuvant radiation. She completed induction and consolidation chemotherapy but developed intracranial and thoracic spine leptomeningeal disease three months into the maintenance phase of oral chemotherapy. She was started on Vismodegib with evidence of treatment response on interval MRI at both 1 and 3 months after start of therapy. Four months into therapy with Vismodegib she developed bilateral knee pain which was evaluated with frontal and lateral radiographs of both knees. Physeal fusion of both the proximal tibial growth plates was noted relative to a pre-Vismodegib imaging evaluation (Fig. 1b). On subsequent radiographic evaluation three months later, the distal femoral growth plates were also noted to have signs of premature fusion. Re-imaging of the tibial and distal femoral growth plates showed progressive fusion (Fig. 1c). Physeal closure has been noted in animal studies at doses 20-40% of the adult dose¹. Others have reported physeal thickening² but to our knowledge this represents the first documented report of physeal closure in children.

References

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Fig. 1.

(A) T2-weighted axial brain MRI of patient at diagnosis shows a large lateralizing mass in the posterior fossa. (B) Pre-Vismodegib imaging evaluation of tibial physes. (C) Progressive physeal fusion of both tibial and distal femoral growth plates continues even after discontinuation of therapy.