More Than Meets the Eye: Constitutional Mismatch Repair Deficiency Presenting with Multiple Primary Malignancies in Childhood

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Introduction

Constitutional Mismatch Repair Deficiency (CMMRD) is a rare autosomal recessive cancer predisposition syndrome associated with early-onset multiple malignancies.

Case Presentation

A 10-year-old girl presented with headache, vomiting and ataxia, with multiple melanocytic naevi, hypopigmented skin lesions and parental consanguinity. She underwent posterior fossa mass resection, histopathology confirmed SHH-activated, TP53-wildtype medulloblastoma. Subsequent imaging demonstrated recurrent posterior fossa disease and a synchronous left frontal IDH-mutant, WHO grade 2 diffuse glioma (without 1p/19q codeletion). MSH6 loss on immunohistochemistry established CMMRD. Subsequent colonoscopy for rectal bleeding revealed multiple tubular adenomas, also showing MSH6 loss.

Fig 1 – Baseline MRI

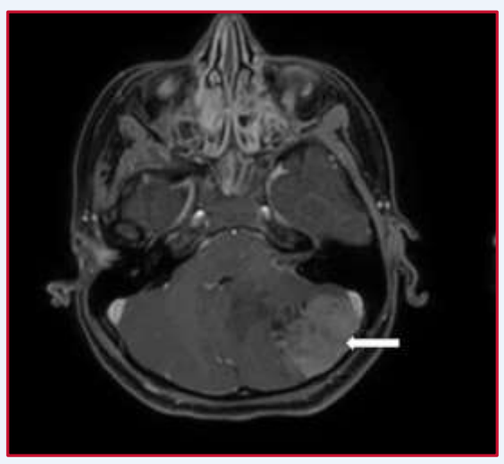


Fig 2 – Posterior fossa recurrence

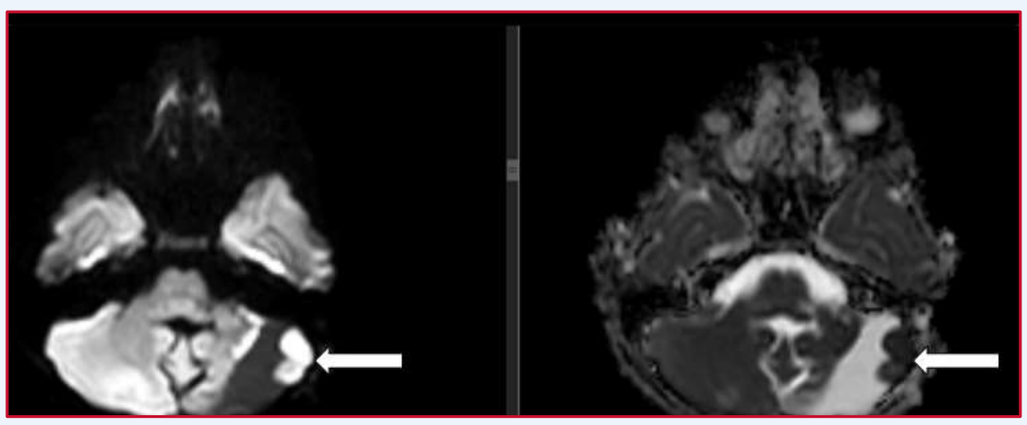


Fig 1: *Pre-operative axial MRI showing the posterior fossa mass (arrow).*

Fig 2: *Recurrent posterior fossa disease on DWI [a] and ADC [b] (arrows).*

Fig 3 – Fontal glioma

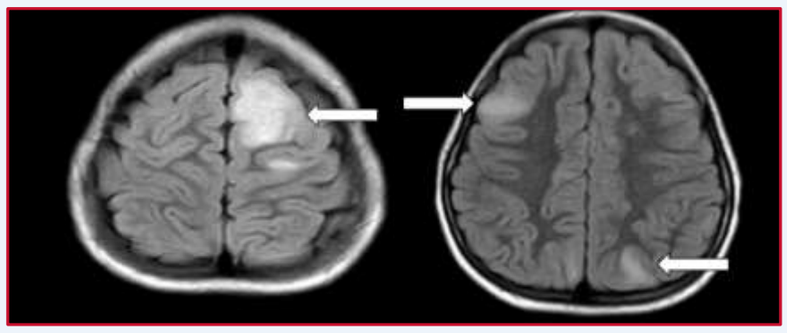


Fig 4 – Colonic polyps

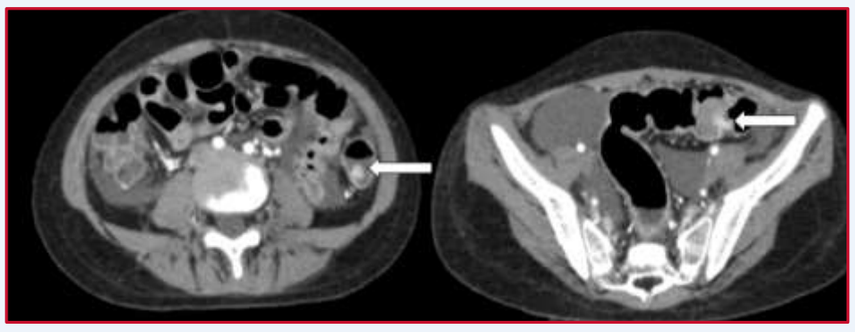


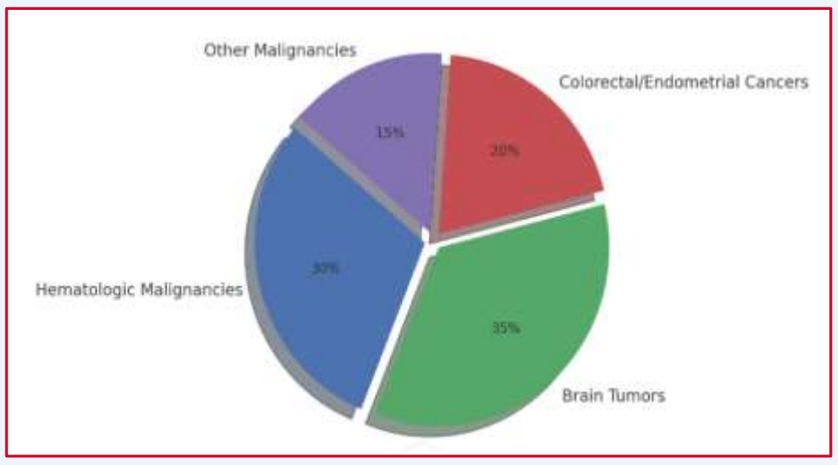
Fig 3: *Axial FLAIR MRI showing the right and left frontal gliomas (arrows).*

Fig 4: *CT showing colonic polyps (arrows).*

Discussion

Concurrent medulloblastoma and diffuse glioma required multimodality treatment with chemotherapy and craniospinal radiotherapy. Follow-up imaging raised suspicion of disease progression, highlighting the aggressive course and need for vigilant surveillance.

Fig 5 – CMMRD malignancies



Teaching Points

1. Suspect CMMRD in children with multiple primary malignancies, characteristic skin lesions and parental consanguinity.
2. Mismatch repair immunohistochemistry and clinicoradiological correlation facilitate diagnosis.
3. Early recognition guides treatment, lifelong malignancy surveillance and genetic counselling is required.
4. Multidisciplinary management is essential.