Abstract: P2253

Title: THE APPLICATION OF MINIGENE TRANSCRIPTION ANALYSIS IN THE DIAGNOSIS AND TREATMENT OF INFANTILE MYOFIBROMATOSIS (IM) WITH HEMOPHILIA A

Abstract Type: e-Poster Presentation

Topic: Bleeding disorders (congenital and acquired)

Background:

Infantile myofibromatosis (IM) is a rare childhood myofibroblastic disorder with various inheritance patterns. It's characterized by the formation of nodules in the skin, muscle, bone, and, more rarely, visceral organs. According to the location and number of lesions, there are three different forms: solitary, multicentric without visceral involvement, and multicentric with visceral involvement. IM is regarded as a benign tumor, and cases without visceral involvement tend to spontaneously regress, but multicentric disease with visceral involvement carries a poor prognosis. In IM with visceral involvement, the most common treatment is chemical regimens such as intravenous application of vinblastine and methotrexate. There are also reports that cases associate with mutations in PDGFRB are sensitive to TKI such as imatinib, etc.

Aims:

Assist in confirming the diagnosis of IM in the child and provide reasonable recommendations for clinical treatment.

Methods:

We admitted a 19-month-old male patient with a facial mass. Upon admission, he presented with oral bleeding. Subsequently, he underwent head CT, head MRI, chest CT, coagulation function screening, biopsy of the mass, and for further diagnostic clarification, whole-genome sequencing was performed. To validate its functionality, we performed Minigene transcription analysis.

Results:

The head CT and MRI revealed a mass in the right temporal fossa area, while chest CT showed multiple localized emphysematous changes in both lower lung lobes. A complete set of coagulation factors indicated an F8 activity of 15.9%. Pathological biopsy results suggested proliferative fibrous tissue lesion, indicating the possibility of intermediate or low-grade fibrous tumor. Whole-genome sequencing revealed mutations in F8 (c.6900+4105 G>T, p.?) and PDGFRB (c.2024-39G>A, p.?), both inherited from the mother and not reported previously. Hemophilia A and infantile myofibromatosis (IM) were considered. Due to the patient's history of trauma and low coagulation factor activity, the possibility of pseudotumor in hemophilia could not be ruled out. To validate the functionality of the PDGFRB gene mutation, Minigene transcription analysis was conducted. Results of Minigene in vitro transcription experiments indicated that the mutation c.2024-39G>A would affect the normal splicing of the PDGFRB mRNA. Hemostasis was achieved through factor VIII infusion. During this period, abnormal signals were observed in the left lip area on MRI monitoring, which later resolved spontaneously. Six months after the diagnosis, the patient is being closely followed up in outpatient clinics. MRI revealed a reduction in the size of the mass in the right temporal fossa compared to previous imaging.

Summary/Conclusion:

We report a case of infantile myofibromatosis (IM) in a patient with concomitant hemophilia A. Whole-genome sequencing revealed novel intronic mutations in the F8 and PDGFRB genes. Through Minigene transcription analysis, we validated the impact of the PDGFRB gene intronic mutation on PDGFRB gene function, further confirming the diagnosis of IM. We also suggest that if the patient's condition progresses, TKI therapy could be considered.

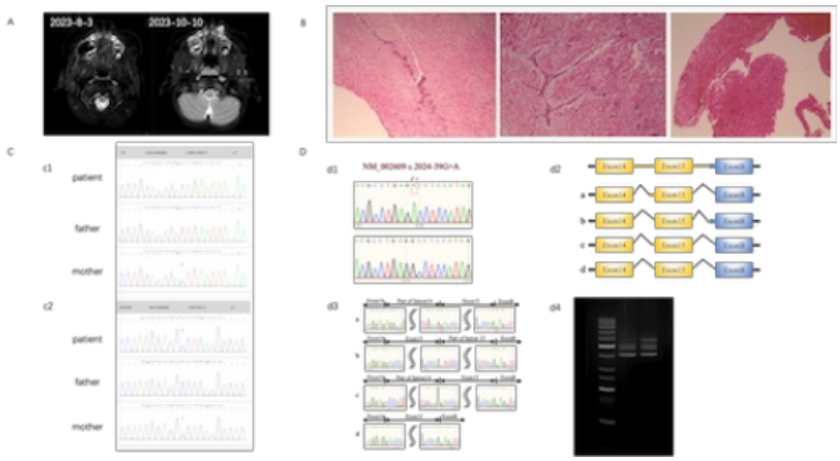

Figure 1 Imaging examinations, biopsy, and whole-genome sequencing

A Imaging examinations□B Biopsy□C Genome sequencing□F8 and PDGFRB; D Minigene transcription analysis

Keywords: Tumor, Pediatric, PDGFRB, Hemophilia A