Case report of a patient with multifocal high-grade glioma associated with Li-Fraumeni syndrome

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This is a case report of a 13 years old girl with genetically confirmed Li-Fraumeni syndrome treated for very early recurrence of a high-grade multifocal CNS tumor affecting both cerebellar hemispheres.

The girl's diagnosis was preceded by two weeks of headache, followed by an acute presentation with severe headache and vomiting under the picture of hemorrhage into a lesion of the right cerebellar hemisphere and decompensated obstructive hydrocephalus. Extraventricular drainage was introduced and diagnostic MRI was completed with the finding of two separate expansions in both cerebellar hemispheres. Resection of both expansions was performed in two periods with no macroscopic residue. She presented clinically with a very early recurrence of the tumor already after one month. Radical removal of the tumor recurrence was performed with the small macroscopic residue on MRI.

Histopathology revealed a diffuse high-grade glioma of pediatric type, H3-wildtype and IDH-wildtype, CNS WHO grade 4. We performed panel next-generation sequencing with the finding of TP53 mutation R175H. This mutation was present also in the germline genetic material and thus Li-Fraumeni syndrome was confirmed. Epigenetic methylation array analysis classified the tumor into a class glioblastoma, IDH wildtype, subclass RTK II with low score (0.54). Comprehensive molecular biological testing revealed a low mutational load, a variant in the NF1 gene and loss of the CDKN2A/B gene.

Due to the diagnostic conclusion and the genetic predisposition already considered initially because of the multifocal tumor finding, we indicated the patient for proton radiotherapy and concomitant chemotherapy Temozolomide. At the time of its start another neurosurgical intervention with VP shunt introduction was performed for the development of intracranial hypertension on the basis of postoperative cyst enlargement.

In view of such a rare and unfavorable diagnosis, we consulted the patient within the ERN tumor board with other European colleagues. In particular, we wanted to discuss the next treatment steps after the end of proton radiotherapy. The patient is now continuing chemotherapy with Temozolomide, Metformin has been added, because of her genetic predisposition, and the treatment with MEK-inhibitor is planned. The patient's family has also been under the care of the palliative care team since the beginning of treatment.