Li-Fraumeni syndrome

Rare (< 400 families identified) inherited autosomal dominant disorder of children and young adults with predominant soft tissue sarcomas, osteosarcomas, breast cancer intracranial metastases, and adrenocortical carcinoma.

Usually caused by a germline mutation in the TP53 tumor suppressor gene on chromosome 17p13. There are 3 main sets of criteria for diagnosing Li-Fraumeni-like syndrome: LFL-E2 definition, LFL-B definition & the Chompret criteria.

CNS tumors show a bimodal age distribution: 1) in children (primarily medulloblastomas & related embryonal tumors), and 2) in age 20–40 (primarily astrocytic neoplasms).

Patients with this syndrome may develop multiple malignant neoplasms, including brain tumors.

It was named after two American physicians, Frederick Pei Li and Joseph F. Fraumeni, Jr., who first recognized the syndrome after reviewing the medical records and death certificates of 648 childhood rhabdomyosarcoma patients.

This syndrome is also known as the Sarcoma, breast, leukaemia and adrenal gland (SBLA) syndrome.

The syndrome is linked to germline mutations of the TP53 tumor suppressor gene

The mutations can be inherited, or can arise from de novo mutations early in embryogenesis, or in one of the parent's germ cells.

Malignant astrocytomas occur in approximately 10% of persons with Li-Fraumeni syndrome

The vast majority of gliomas associated with Li-Fraumeni syndrome occur prior to 40 years of age.

2014

Lechien et al. report on a family in which segregation of a TP53 mutation in two generations was associated with two brain tumours, a leiomyosarcoma and a thyroid carcinoma in four male patients. The main patient presented with seizures revealing several primary brain tumours [1)].

Case reports

Hosoya et al. report the first case of Li-Fraumeni syndrome in which development of supratentorial anaplastic ependymoma led to difficulty in terms of selecting the optimal postoperative therapeutic protocol.

A 7-year-old boy experiencing a convulsive attack was brought to our institute. He underwent surgical

tumor resection, and magnetic resonance imaging of the head revealed a tumor-like lesion in the right parietal lobe. Although adjuvant radiotherapy was performed after total tumor resection, a focal recurrent lesion appeared soon afterward. We initiated chemotherapy with bevacizumab after resection of the recurrent lesion, but bevacizumab was unable to control tumor progression. At this writing, he remains bedridden and requires tube feeding and artificial ventilation.

Since Li-Fraumeni syndrome is a genetic disease that is caused by mutation of the tumor suppression gene TP53, patients should generally not be treated with radiotherapy or alkylating agents that induce DNA damage. However, if the prognostic benefit of postoperative adjuvant therapies is thought to surpass the risk of long-term secondary cancer, it is appropriate to consider these therapies after consultation with the patient and family. Postoperative treatment protocols are controversial, and their role should be further explored in cases of Li-Fraumeni syndrome complicated with malignant gliomas [2].

2013

A 28-year-old man presented with osteosarcoma of the occipital bone 16 years after 24 Gy of craniospinal irradiation for acute lymphocytic leukemia. The tumor had both intra- and extra-cranial components. However, the affected skull appeared to be normal on imaging because of permeative infiltration by the tumor. Subtotal resection was achieved and the tumor was verified histologically as an osteosarcoma. The residual tumor soon showed remarkable enlargement and disseminated to the spinal cord. Both of the enlarged and disseminated tumor masses were treated by surgical intervention and chemotherapy. However, the patient deteriorated due to the tumor regrowth and died 11 months after the initial diagnosis. This patient had previously developed a leukemia, a colon cancer, a rectal cancer and a hepatocellular carcinoma. His brother also died of leukemia. The patient had a heterozygous TP53 germ-line mutation of codon 248 in the exon 7. In conclusion, Yoshimura et al. consider the present tumor to be a rare example of radiation-induced skull osteosarcoma in a member of the cancer-prone family with TP53 germ-line mutation which is associated with Li-Fraumeni syndrome [3].

1)
Lechien JR, Brotchi J, Van Maldergem L, Costa de Araujo P, Bruninx G, Hilbert P, Nubourgh Y. Li-Fraumeni syndrome: multiple distinct brain tumours in two brothers. Neurochirurgie. 2014 Feb-Apr;60(1-2):51-4. doi: 10.1016/j.neuchi.2013.11.005. Epub 2014 Mar 14. PubMed PMID: 24636404.
2)
Hosoya T, Kambe A, Nishimura Y, Sakamoto M, Maegaki Y, Kurosaki M. A pediatric case of Li-Fraumeni syndrome complicated with supratentorial anaplastic ependymoma. World Neurosurg. 2018 Sep 6. pii: S1878-8750(18)31989-2. doi: 10.1016/j.wneu.2018.08.203. [Epub ahead of print] PubMed PMID: 30196175.
3)
Yoshimura J, Natsumeda M, Nishihira Y, Nishiyama K, Saito A, Okamoto K, Takahashi H, Fujii Y. [Radiation-induced intracranial osteosarcoma after radiation for acute lymphocytic leukemia associated with Li-Fraumeni syndrome]. No Shinkei Geka. 2013 Jun;41(6):499-505. Japanese. PubMed PMID: 23732761.