Abstract
I statistically analyzed 40 examples of neurofibromatosis type 1. Since before it has been said that the neurofibromatosis type 1 originated from mother is very serious. It is called "maternal effect". It has been said since 1930's. But many are against the opinion. The result of my examination is as follows.

The case from mother or father were more serious and self-originated cases were less.

The male case from mother and the female case from father have extremely much possibility of having malignant tumors.

The female case from mother, the male case from father, the case from self didn't have malignant tumors. They were all benign.

"When the tumor is found in the male case originated from mother or female case originated from father, it is very possible that the tumor is malignant."

I newly name it "cross effect".

key words : neurofibromatosis type 1, cross effect, maternal effect, malignant tumor
Introduction
Since the 1930s, it has been said that male patients with maternal neurofibromatosis type 1 are severely affected and if a tumor is found, it is very likely to be a malignant tumor. When I wrote the statistics of 40 cases of neurofibromatosis type 1, it is clear that a male patient with maternal neurofibromatosis type 1 was severely affected, and if a tumor was found, it was very likely to be malignant. Turned out to be high. Similarly, female patients with neurofibromatosis type 1 from the father were also severe, and if found, had a very high probability of being malignant. It turned out that female patients of maternal origin, male patients of paternal origin, and the proband with their own neurofibromatosis type 1 were rarely severe and could not be malignant if a tumor was found. However, this is a study of the 40 cases collected by the author, and requires further examination.

Case

[The following is a male example from mother]

<< Case 1 >> Derived from mother. male 38-year-old.
Neurofibromatosis are slight but have bone defects in the occipital bone. Innate, healthy. Lisch nodule(+).
Nystagmus appeared during fatigue last September. In October, nystagmus becomes stronger. Head CT shows a tumor in the cerebellar hemisphere. Craniotomy tumor resection was performed. Pathologically, it was glioblastoma multiforme. No abnormalities were found by chromosome examination.
He had two brothers, a brother with neurofibromatosis type 1, but at the age of 43, he returned to work after a day when he returned from work after feeling very tired and slept on a futon but died in the evening. Was discovered. The cause of death was cleared up for heart failure. He was
also healthy by nature, and had no indication of heart disease. No dissection was performed to determine the cause of death. It is likely that his brother was also a cerebellar or brainstem tumor.

<< Case 2 >> Derived from mother. male 24-year-old. Café-au-lait spots on the back and buttocks since childhood. Lisch nodule(+).
Head CT was performed on October 2, 1984, and no special findings were noted. Brain waves are not to be noted. Soft mass (−).
The older brother, 2-year-old, has an intelligence index of 32 (sb formula). He died while trying to get up in the morning at the age of 12 while in a nursing home. Dissection revealed malignant schwannoma of the brainstem.

<< Case 3 >> Derived from mother. male 19-year-old. From the childhood, remove the tumor in the bottom of the left orbit four times. Lisch nodule(+).
On November 13, 1987, the right supraclavicular tumor was removed. Pathologically, it was malignant astrocytoma.
On December 7, 1987, a tumor was removed from the right elbow joint. Similarly, it was a malignant astrocytoma.
On January 10, 1988, the left orbital tumor was removed. This was also a malignant astrocytoma.
This time, I was introduced to a university hospital for the purpose of reducing the cerebral aneurysm associated with the loss of the left orbital wing.

<< Case 4 >> Derived from mother. male 33-year-old. The mother has several small café-au-lait spots (it appeared at the age of 40).
Surgery was performed due to dislocation of the hip joint.
There is a tumor in the right cerebellar hemisphere. Lisch nodule(+). Bone defect in right lower occipital region. Right occipital bulge. The left side is almost completely blind. Craniotomy revealed pathological malignant
astrocytoma (grade 3).

<< Case 5 >> Derived from mother. male 7-year-old.
Five siblings. Three older sisters are healthy. His brother died at the age of one from pneumonia to meningitis.
Congenital aqueduct obstruction, unknown cause. Lisch nodule(+). There is bilateral vision loss, and vision loss tends to progress.

<< Case 6 >> Derived from mother. male 1-year-old.
Psychomotor retardation, congenital heart disease, Lisch nodule(+).
Many café-au-lait spots on lower body immediately after birth.
Head CT showed cerebral atrophy (+) and tumor (-).
Two brothers. Older brother had brown spots (4 x 4 cm) on the left hip.

<< Case 7 >> Derived from mother. male 14-year-old.
Since childhood, left fibula pseudoarthrosis. Lisch nodule(+). At the age of 14, she complained of dizziness and visited the hospital. Head CT shows tumor in left cerebellar hemisphere. Craniotomy tumor removal was performed at a university hospital. Pathologically, it was glioblastoma multiforme.

<< Case 8 >> Derived from mother. male 11-year-old.
There are café-au-lait spots on the three younger brothers (two younger brothers) and the younger sister.
He visited our hospital about 2 years ago because of nausea and headache. On head CT, there was a tumor that appeared to be astrocytoma on the left temporal parietal region. The tumor grows in size and is referred to a university hospital. Craniotomy performed. The pathological finding was malignant astrocytoma. Lisch nodule(+).

<< Case 9 >> Derived from mother. male 23-year-old.
café-au-lait spots occur throughout the body from birth. There is a soft mass under the back. He was diagnosed with neurofibroma type 1 at a biopsy last year. Lisch nodule(+).
At the age of 23, he noticed the presence of a brain tumor on head CT. Tumor size is increasing. Schedule for craniotomy.

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[The following are examples of women from mothers]

<< Case 10 >> Derived from mother. female 23-year-old.
Three females and one male child. Two older sisters are healthy.
My brother died of a spinal cord tumor at the age of 15 (this brother also has neurofibromatosis type 1).

<< Case 11 >> Derived from mother. female 42-year-old.
Simple mass and café-au-lait spots occur throughout the body since childhood.
Café-au-lait spots on all three children (one male and two female).

<< Case 12 >> Derived from mother. female 43-year-old.
Bilateral congenital hip dislocation. There are more than a dozen café-au-lait spots on the trunk.

<< Case 13 >> Derived from mother. female 38-year-old.
Cerebral palsy, neuropathic bladder. she was able to walk alone until junior high school. At the age of 37, he developed back pain and became paralysed in both lower limbs. CT showed a tumor shadow in the lumbar spine. Pathologically benign tumor.

<< Case 14 >> Derived from mother. female 29 years old.
Eight years ago, a soft mass appeared in the right iliac bone and she underwent resection. Pathologically benign tumor.
Five years ago, a soft mass with tenderness appeared on the flexed side of the right upper arm.
[The following is a male example from father]

<< Case 15 >> Derived from father. male 27-year-old.
When he is a junior high school student, he notice that there is a soft mass on the trunk. After that, the number gradually increased, so he visited our hospital 9 years ago and were diagnosed with neurofibroma type 1. My sister died of childhood asthma.
No abnormalities in head CT. Cauda equina tumor present. The cauda equina tumor was pathologically a benign tumor.

<< Case 16 >> Derived from father. male 32-year-old.
Three siblings (all male) have absence seizures.
There is a tumor shadow on the right side of the head CT. Craniotomy was a benign astrocytoma.

<< Case 17 >> Derived from father. male 31-year-old.
Left pulsatile astigmatism, left orbital bone defect.

<< Case 18 >> Derived from father. male 18-year-old.
Bone defect (3.5 × 3.5cm) on midline of occiput. Language disorders since childhood.
Visit to the medical examination for SDF enlistment.

<< Case 19 >> Derived from father. male 2-year-old.
Right Turkish saddle enlarged (J type). Enlargement of the right middle ear canal. Elevation of right pterygium.
Enlargement of the right eye nerve tract. Enlarged orbit.

<< Case 20 >> Derived from the father. male. 11-month.
<< Case 21 >> Derived from father. male 10-year-old.

1 More than a dozen café-au-lait spots appear on the trunk and limbs from one month after birth. There is no increase in the number and size of café-au-lait spots. Neurofibromas appeared on the entire back, centered on the lumbar region one year ago, but began to regress from around summer (natural regression). At the time of our first visit to our hospital (September 5, 1992), the swelling slightly increased in the lumbar region. There were only six soft tumors. At the time of hospitalization (December 16, 1992), the same site had almost disappeared to the extent that it could not be confirmed.

We are hospitalized this time for various tests for neurofibroma. No special note on head CT.

Café-au-lait spot on father. My brother has two older sisters, but there is no abnormality at present.

[The following is an example of a female from her father]

<< Case 22 >> Derived from father. female 34-year-old.
She noticed café-au-lait spots when she was little. However, there were few café-au-lait plaques and almost no soft masses. Lisch nodule (+). Visited our hospital for headache. Bone defect was not clear, but tumor was present in left cerebellar hemisphere. University hospital introduction. Craniotomy was performed, but pathologically, malignant astrocytoma was found. He died after surgery.

<< Case 23 >> Derived from father. female 21-year-old.
Pain in the right head and right occipital region from around October 1992. Nausea when pain is severe, radiation pain to right shoulder. No abnormalities were recognized on the head CT. Diagnosis of neurofibroma of the right cervical spine. Lisch nodule(+).

In 1992, a CT scan revealed a suspected astrocytoma in the left parietal
region. The tumor grew in size and craniotomy was performed. Pathologically malignant astrocytoma.

<< Case 24 >> Derived from father. female 28-year-old. Cafe-au-lait spots since childhood, and hemispherical soft tumor masses increased systematically from the age of 16 and began to increase. Lisch nodule (+). Right ear mixed hearing loss. Stenosis in the rectum. But a tumor marker (−). There is a slight curvature in the lower thoracic spine. No abnormalities in blood or biochemistry. Head CT shows calcification and low absorption in the cerebellar hemisphere. Enhancement effect (−), cerebellar symptoms (−) with contrast agent. The patient is diagnosed with cerebellar atrophy or arachnoid cyst and is followed up without surgery. Recently, nystagmus appeared, and a tumor was pointed out in the cerebellar hemisphere on the CT of the head. Glioblastoma multiforme on pathology.

<< Case 25 >> Derived from father. female 16-year-old. Two siblings and one younger sibling have no cafe-au-lait spots or soft masses. Immediately after birth, a large cafe-au-lait spot and a soft mass in the same area were observed from the back to the buttocks. Lisch nodule (+). Surgery for a soft mass in plastic surgery at S General Hospital. Recently, she came to the hospital because her binocular vision dropped from 2.0 to 0.9. CT on head, occipital lobe tumor. Recently, it drops further to binocular 0.1. The patient was referred to a university hospital and surgery was performed. Pathologically malignant astrocytoma.

<< Case 26 >> Derived from father. female 13-year-old. An epileptic seizure exists at his younger brother. My sister had febrile convulsions until she was about 7-year-old. My brother has allergic purpura (no abnormalities at the moment). There are cafe-au-lait spots almost all over the body. Number and area are increasing. Recently, soft masses have also begun to appear. Lisch
nodule (+).

She have had stomachache since March this year. June: Bloody stool twice. Open surgery was performed. It was a colorectal tumor with a high degree of malignancy in pathology. No special note on head CT.

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[The following is unknown. That is, the case itself is a proband male case]

<< Case 27 >> Unknown origin. male 57-year-old. Café-au-lait spots and soft masses are prominent. At age 30, he underwent lumbar soft massectomy. Surgery has been performed 12 years ago, 11 years ago and 8 years ago under the diagnosis of hydronephrosis in both kidneys since 12 years ago. Pathological benign hamartoma. Severe left visual impairment has been occurring for 10 years, but has not progressed. No abnormalities were found by chromosome test. In August last year, nystagmus appeared. A similar nystagmus appeared in September. (However, nystagmus occurred only once in August and September.) MRI was performed, and astrocytoma suspected to be partially imaged on the right parietal region was pointed out. A suspected astrocytoma in the right temporal parietal region was removed by craniotomy, but the portion that was thought to be a tumor that had been imaged by MRI was a benign tumor without vascular hyperplasia and glioma neoplasia.

<< Case 28 >> Unknown origin. male 39-year-old. Café-au-lait spots on left buttocks since birth. A soft mass appeared 4 or 5 years ago. Two years ago, on the left edge of the left third intercostal sternum, 8 mm in diameter, a hard, clear, mobile induration

<< Case 29 >> Unknown origin. male 21-year-old.
His sister is SLE. When he was in elementary school, he noticed a brown spot on the upper right lip. It was a café-au-lait spot. When he are a junior high school student, notice light brown spots on the abdomen and both upper limbs. In July 1984, a CT scan revealed a brain tumor, and the tumor was removed. On pathology, the tumor was benign.

<< Case 30 >> Unknown origin. male 19-year-old.
He says he has had chickenpox a couple of times. Urinary retention and rash appeared with contrast agent. Right lower leg false joint. There are several café-au-lait spots on the trunk.

<< Case 31 >> Unknown origin. male 17-year-old.
About 7 or 8 years old, café-au-lait spots have frequently occurred mainly on the trunk. There is only one rice-sized soft mass on the back. In addition, since about 8 years of age, the bones of both lower legs have been enlarged.
From November 1990, the swelling of the lower left leg becomes prominent.
The same symptom appeared on the lower right leg from November 1991.

<< Case 32 >> Unknown origin. male 17-year-old.
At the age of 9, bilateral cervical lymphadenopathy appeared. At 12 years of age, resection of the soft mass in the back was performed.
At the age of 17, a soft back mass appeared again. Café-au-lait spots on the whole body.

<< Case 33 >> Unknown origin. male 14-year-old.
At the age of 5, a left upper arm soft tumor appeared. A soft mass is also present on the right neck and right wrist. Brown spots on the anterior chest from childhood. Dermatology diagnoses café-au-lait spots.
At 13 years of age, a soft mass in the left upper arm was removed.
At 15 years of age, surgery was performed for extramedullary tumors of the third and fifth cervical vertebrae. Pathologically, it was a benign tumor.
He had a sickle meningioma (fibrous).

<< Case 34 >> Unknown origin. male 14-year-old. Surgery was performed at the age of five for congenital partial loss of the left fibula. The same operation was performed at the age of eight. Under scrutiny for liver function decline for two years from age eight years. There is secondary glaucoma.

<< Case 35 >> Unknown origin. male 4-year-old. Gait disturbance, left neck bulge, spinal curvature, swallowing difficulties.

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[The following is unknown. That is, the case itself is a proband female case]


<< Case 37 >> Unknown origin. female 35-year-old. Soft mass and café-au-lait spots (appearing at age 35) throughout the body. No abnormalities in chromosome tests.

<<Case 38>> Unknown origin. female 22-year-old. Café-au-lait spots that occur frequently throughout the body. Recently, soft tumors protruding in a hemispherical shape of small coffee bean tend to occur more frequently.

<<Case 39>> Unknown origin. female 4-year-old. About a year ago, café-au-lait spots began to appear on both palms, and the number has increased. Soft mass (-).

<<Case 40>> Unknown origin. female 3-year-old. Irregular café-au-lait spots on the trunk and limbs, irregular in size smaller than the thumb head size, occur frequently. Soft mass (-).
Discussion

There are few documents that clearly specify the origin of neurofibromatosis type 1 brain tumors. There is a literature on malignant brain tumor that clearly indicate the origin of one case, but it was from a mother in a case of multiple malignant schwannoma, and the patient was a male 6).

In addition, there is another case in which the origin is specified, which is a document presenting natural disappearance of orbital glioblastoma multiforme in 2-year-old girl from a father 5).

Considering 40 cases, maternally derived male patients with neurofibromatosis type 1 have a strong tendency to become malignant. In addition, female patients derived from fathers have a similar tendency to malignancy.

The maternal effect in neurofibromatosis type 1, that is, the maternal effect 13) has been said so far. However, there have been many objections, and the opinions have not been unified. I propose here newly cross effect.

Maternal effects do exist in this survey. It is highly related to whether neurofibromatosis type 1 is a female patient derived from a father or a male patient derived from a mother, or otherwise. Thus, malignant tumors are extremely likely to occur in maternal male patients and paternal female patients in neurofibromatosis type 1.

Female patients of maternal origin, male patients of paternal origin, and patients themselves with the proband in the case of, the absence of a malignant tumor would provide one indication for the mechanism of cancer development.

Literature
17) Upadhyaya M, Ruggieri M, Maynard J et al: Gross deletions of the...
neurofibromatosis type 1 (NF1) gene are predominantly of maternal origin and commonly associated with a learning disability, dysmorphic features and developmental delay. Hum Genet 102 (5): 591-597, 1998

postscript
This is a result obtained 28 years ago, but it was not announced.

(home) 47-8 kuyamadai Isahaya-shi Nagasaki-prefecture, 854-0067  Japan
Toshiro Takami

mm82889@yahoo.co.jp