

Review

Cross effects of neurofibromatosis type 1

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Abstract

I statistically analyzed 27 patients with neurofibromatosis type 1. Since the 1930's, it has been said that the neurofibromatosis type 1 born to affected mothers is very serious. It is called "maternal effect". But many are against the opinion. The result of my examination is as follows.

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

The male cases from affected father and the female case from affected mother and those who were sporadic case didn't have malignant tumors. They were all benign.

"When the tumor is found in the male case from affected mother or female case from affected father, it is extremely much possibility of having malignant tumors."

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 maternally derived neurofibromas type 1 are severely ill, and if a tumor is found, there is a very high probability that it is a malignant tumor. When the author obtained statistics on 27 cases of neurofibromatosis type 1, I found, indeed, that male patients with maternally derived neurofibromatosis type 1 are very sick and, if a tumor is found, there is a very high probability that it is a malignant tumor. Similarly, female patients with paternally derived neurofibromatosis type 1 were found to be severely ill and, if a tumor was found, it was found to be very likely to be malignant. It was found that female patients of maternal origin, male patients of paternal origin, and sporadic case neurofibroma type 1 could not be malignant even if a tumor was found. However, this is a discussion of 27 cases collected by the author and requires further investigation.

Case

-----[The following is a male case of maternal origin]

(Case 1) Maternal origin, male, 38 years old.

Neurofibromas are slight, but there is a bone defect in the occipital bone. Healthy by nature. Lisch nodule (+).

Nystagmus appeared around September last year when he was fatigued; nystagmus became stronger in October. A tumor in the cerebellar hemisphere was pointed out on CT scan of the head. An open craniotomy was performed. Pathologically, the patient had a glioblastoma multiforme. Chromosome examination did not reveal any abnormalities.

He had two brothers and an elder brother with neurofibromatosis type I. The elder brother became very fatigued at noon, came home from work, and was found dead in the evening. The cause of death was ruled out as heart failure. The brother had been healthy by nature and had never been diagnosed as having a heart problem. No autopsy was done to determine the cause of death. There is a high probability that he, too, had a tumor in the cerebellum or brain stem.

(Case 2) Maternal origin, male, 24 years old.

Café-au-lait spots on the back and buttocks since childhood. Lisch nodules (+).

A CT scan of the head was performed on October 2, 1984, and there was no evidence of any special note. An EEG was also performed on October 2, 1984, and there was no significant finding. A soft mass (-).

His brother, who was two years older than him, had an intelligence quotient of 32 (sb formula). While at the nursing home, at age 12, he died when we tried to wake him up in the morning. An autopsy revealed a malignant schwannoma of the brain stem.

(Case 3) Maternal origin, male, 19 years old.

Since childhood, he has undergone four rounds of tumor removal from the left orbital floor. Lisch nodule (+).

Tumor excision of the right supraclavicular fossa on November 13, 1987. Pathologically, it was a malignant astrocytoma.

On December 7, 1987, a tumor was removed from the right elbow joint. It was also a malignant astrocytoma.

On January 10, 1988, a tumor was removed from the left orbital floor. It was also a malignant astrocytoma.

This time, he was referred to the University Hospital for the purpose of revision of a brain mass associated with a defect in the left orbital wing.

(Case 4) Maternal origin, male, 33 years old.

His mother had several small café-au-lait spots (which appeared since she was 40 years old).

He has one sister who underwent surgery for a dislocated hip.

Tumor in the right cerebellar hemisphere. Lisch nodule (+). Bony defect in the right lower occipital region. Right occipital bulge. Almost total blindness on the left side. On craniotomy, pathology revealed a malignant astrocytoma (grade 3).

(Case 5) Maternal origin, male, 7 years old.

Five compatriots. Three sisters are healthy. Brother died at 1 year of age, transitioning from pneumonia to meningitis.

Congenital midbrain water supply obstruction, cause unknown. Lisch nodules (+). Bilateral vision loss is present, vision loss is progressive.

(Case 6) Maternal origin, male, 1 year old.

Delayed psychomotor development, congenital heart disease, Lisch nodules (+). Multiple café-au-lait spots on the lower half of his body soon after birth. Brain atrophy (+) and tumor (-) on CT scan of the head.

Two compatriots. Sister had a brownish-red spot (4 x 4 cm) on her left hip.

(Case 7) Maternal origin, male, 14 years old.

Left fibula pseudoarthrosis since childhood. Lisch nodule(+). He came to the hospital at age 14, complaining of dizziness. CT scan of the head revealed a tumor

in the left cerebellar hemisphere. Open craniectomy was performed at a university hospital. Pathologically, it was glioblastoma multiforme.

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(Case 8) Maternal origin, male, 11 years old.

He came to our clinic because of nausea and headache for 2 years. On CT scan of the head, there was a tumor on the left side of the parietal region that looked like an astrocytic tumor. The tumor grew in size and the patient was referred to a university hospital. The patient was referred to the university hospital. Pathologically, it was a malignant astrocytoma. Lisch nodule (+).

He had a café-au-lait spot on her younger sister.

(Case 9) Maternal origin, male, 23 years old.

Multiple café-au-lait spots over the body since birth. There was a soft mass under the dorsal skin. A biopsy last year diagnosed neurofibroma type 1. Lisch nodules (+).

At the age of 23 years old, the presence of a brain tumor was noticed on CT scan of the head. The size of the tumor is increasing. Scheduled for a craniotomy.

----- [The following is a female case of maternal origin]

(Case 10) Maternal origin, female, 23 years old.

The youngest of three females and one male. Two sisters are healthy.

Right-sided vestibular schwannoma. Pathologically, benign tumor. Bilateral blindness. Olfactory deficiency on both sides.

Brother died of a spinal cord tumor at age 15 (this brother also had neurofibromatosis type 1).

(Case 11) Maternal origin, female, 38 years old.

Cerebral palsy, neurogenic bladder.

She was able to walk unaided until middle school; at 37 years of age, she developed back pain and became paralyzed in both lower limbs. Pathologically, she had a benign tumor.

----- [The following is a male case of paternal origin]

(Case 12) paternal origin, male, 27 years old.

When he was in middle school, he noticed a soft mass on his trunk. Subsequently, it gradually increased in number and he was diagnosed with neurofibroma type 1 nine years ago at our clinic. His sister died of childhood asthma.

Head CT scan is unremarkable. Tumors of the cauda equina is present. And it was pathologically benign.

(Case 13) paternal origin, male, 32 years old.

Three compatriots (all male), with absence seizures.

On CT scan of the head, there was a tumor shadow on the right side of the head. Craniotomy was performed, but it was a benign astrocytoma.

(Case 14) paternal origin, male, 31 years old.

Left pulsatile astigmatism, left orbital bone defect.

(Case 15) paternal origin, male, 18 years old.

Bone defect on the midline of the occipital region (3.5 x 3.5 cm). Speech disorder since childhood.

He came to the hospital for a medical examination to enlist in the Self-Defense Force.

(Case 16) paternal origin, male, 2 years old.

Enlargement of right sella turcica (type J). Enlargement of right middle ear canal. Elevation of the right pterygoid scale.

Enlargement of the right ocular nerve tract. Enlargement of the orbit.

(Case 17) paternal origin, male, 11 months.

Right temporal bone defect present. No neurological deficit. Tumor in the cervical spine. Pathologically, the tumor was benign.

(Case 18) paternal origin, male, 10 years old

More than a dozen café-au-lait spots appeared on the trunk and extremities from one month of age. There was no increase in the number of café-au-lait spots and no increase in their size. Neurofibromas had appeared in the lumbar region and the whole back one year before, but they began to disappear around summer (spontaneous disappearance).

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. He is hospitalized this time for various tests for neurofibroma. No special note on head CT.

Café-au-lait spot on the father. There were two siblings and an older sister who is currently clear.

-----[The following is a female case of paternal origin]

(Case 19) paternal origin, female, 34 years old.

She had been aware of café-au-lait spots since she was a child. However, the café-au-lait spots were slight and there were few soft masses. Lisch nodule (+). She came to our hospital complaining of a headache. No bone defect was evident, but a tumor was present in the left cerebellar hemisphere. Referred to a university hospital. The patient underwent craniotomy, but pathology revealed a malignant astrocytoma. Death after surgery.

(Case 20) paternal origin, female, 21 years old.

Since October 1992, right parietal and occipital pain appeared. When the pain was severe, nausea and radiating pain in the right shoulder were present. Head CT scan showed no abnormalities. Neurofibromas of the transverse process of the right cervical vertebrae were diagnosed. Lisch nodule (+).

In 1992, a CT scan of the head showed a suspicion of an astrocytoma in the left parietal region. The tumor grew in size and a craniotomy was performed. Pathologically, she had a malignant astrocytoma.

(Case 21) paternal origin, female, 28 years old.

She has had café-au-lait spots since childhood, and from the age of 16 years old, she began to have multiple and increasing hemispherical soft masses of systemic origin. Lisch nodules (+). Mixed hearing loss in the right ear.

Stenosis in the rectum. But tumor markers (-).

Slight curvature of the lower thoracic spine. No blood or biochemical abnormalities.

Head CT scan shows calcification and low absorption in the cerebellar hemisphere. Enhanced effect (-) and cerebellar symptoms (-) on contrast agent. Cerebellar atrophy or arachnoid cyst is diagnosed and the patient is followed up without surgery.

Recently, nystagmus was observed in the cerebellar hemisphere and a craniotomy was performed. Pathologically, the patient had glioblastoma multiforme.

(Case 22) paternal origin, female, 16 years old.

Two siblings and one younger sibling have no café-au-lait spots or soft masses. Immediately after birth, a large café-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 23) paternal origin, female, 13 years old.

An epileptic seizure exists at her younger brother. Her sister had febrile convulsions until she was about 7 years old. Her brother has allergic purpura (no

abnormalities at the moment).

There are café-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.

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

(Case 24) unknown origin, male, 57 years 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 25) unknown origin, male, 39 years 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 26) unknown origin, male, 21 years 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 was 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 27) unknown origin, male, 14 years 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).

Discussion

There are few documented cases of neurofibromatosis type 1 brain tumors with a stated origin; however, there is one documented case of a malignant brain tumor with multiple malignant schwannoma, of maternal origin, and of male patient 6).

There is one more case with a stated origin in the literature that presented spontaneous resolution of orbital glioblastoma multiforme in a 2-years-old girl of paternal origin⁵).

Considering 27 cases, neurofibromatosis type 1 in a male patient of maternal origin has a strong tendency to become malignant. And female patients of paternal origin were equally prone to malignant transformation.

The maternal effect^{6,7,8,10,11,13}) in neurofibromatosis type 1 has been widely recognized. However, there have been many objections (1,2,3,12,16) and no consensus of opinion has been reached. Newly I propose here “cross effect” .

The maternal effect is definitely present in the present study. It is largely related to whether neurofibromatosis type 1 occurs in female patients of paternal or maternal origin, or in other cases. Thus, the high incidence of malignant tumors in neurofibromatosis type 1 in male patients of maternal or paternal origin and the absence of malignant tumors in female patients of maternal or paternal origin, as well as in patients themselves, may provide some insight into the mechanism of cancer development. Possible.

Conflict of Interests

The authors declare that they have no conflict of interests.

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postscript

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



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