Original article

Cross Effect of Neurofibromatosis type 1

by
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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 cases born to affected mothers or the female cases born to affected fathers have extremely possibility of having malignant tumors.
The male cases born to affected fathers or the female cases born to affected mathers or those who were new mutations didn't have malignant tumors. They were all benign.
"When the tumor is found in the male cases born to affected mothers or female cases born to affected fathers, it is extremely possible that the tumor is malignant."
I newly name it "cross effect".

【key words】neurofibromatosis type 1, cross effect, maternal effect, malignant tumor

【firstly】

When a male patient of the neurofibroma type 1 more derived from mother than the 1930s was seriously ill, and a tumor was found, it has been said that the probability that was a malignant tumor was very high as for it. When a male patient of the neurofibroma type 1 derived from mother was seriously ill, and a tumor was surely found when the writer took the statistics of 27 neurofibroma type 1, it became clear that malignant probability

was very high as for it. When a female patient of the neurofibroma type 1 derived from father was seriously ill, and a tumor was found in the same way, it became clear that the probability that it was malignant was very high. It became clear that the malignant thing might not have a female patient derived from mother, a male patient derived from father and proband even if a tumor was caught in the neurofibroma type 1 of the patient. However, this is consideration about 27 that the writer collected and needs a following supplementary examination.

[case]

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[example as follows derived from mother for men]

<< case 1 >> Mother origin, man, 38 years old

There are a few neurofibromas, but the occipital bone has a bone defect. It is healthy by nature. An iris nodule (+).

In about last September, nystagmus appears at the time of fatigue. It is October, and nystagmus becomes strong. I have a tumor of the hemisphere of cerebellum pointed out in head CT. The craniotomy tumor enucleation enforcement. It was a pleomorphic glioblastoma pathologically. The abnormality is not discovered by the examination of chromosome.

It was two brothers, and there was an older brother of the neurofibroma type 1, but I slept, but it was discovered in futon what died in the evening after the older brother learned strong fatigue at noon, and he came back from the workshop in 43 years. The cause of death was settled concerning heart failure. It was healthy, and this older brother has not had heart problem pointed out by nature, too. The dissection to check the cause of death was not performed. This older brother is thought to have been more likely to be a tumor of cerebellum or the brainstem, too.

<< case 2 >> Mother origin, man, 24 years old

I recognize cafe au lait spot on the back, the buttocks from time for childhood. An iris nodule (+).

It takes effect, and, on October 2, 1984, there is no head CT in the views that should mention specially. There are no views that should mention specially in the brain waves. A flexible mass (-).

The older brother who is 2 years old older intelligence quotient 32 (sb type). After being going to wake you up in the morning, during House of nursing hospitalization, he died in 12 years. As a result of dissection, it was brainstem malignant neurologic sheath tumor.

<< case 3 >> Mother origin, man, 19 years old

It enforces four times of tumor enucleation of the left orbit bottom at time for childhood. An iris nodule (+).

On November 13, 1987, I extract a right clavicle superior fovea tumor. It was a malignant star cell tumor pathologically.

On December 7, 1987, I extract a right elbow joint part tumor. Similarly it was a malignant star cell tumor.

On January 10, 1988, I extract left orbit bottom tumor. This was a malignant star cell tumor in the same way, too.

I introduce a university hospital in the reposition purpose of the brain lump with the loss of the left orbit wing this time.

<< case 4 >> Mother origin, man, 33 years old

Mother has several things like the small cafe au lait spot (it is said that she appeared from 40 seasons and years).

There is one older sister, but I am operated on by dislocation of the hip joint and take effect.

There is a tumor to the right hemisphere of cerebellum. An iris nodule (+). It is a bone defect to the right suboccipital region. I protrude the right back of the head. The left side is approximately totally blind. It was a malignant star cell tumor (grade 3) by a craniotomy operation pathologically.

<< case 5 >> Mother origin, man, 7 years old

Five countrymen. Three older sisters are healthy. The older brother switches over from pneumonia to meningitis in 1 year and dies.

A congenital aqueduct of midbrain obstruction is unidentified. An iris nodule (+). Is both sides eyesight drop; the eyesight drop is a tendency to progress.

<< case 6 >> Mother origin, man, 1 year old

Mind campaign development delay, congenital heart disease, an iris nodule (+). It is a lot of cafe au lait spot to a lower part of the body after life right more. In head CT brain atrophy (+), a tumor (-).

Two countrymen. As for the older sister, spotted dark brown on the left buttocks (4*4cm).

<< case 7 >> Mother origin, man, 14 years old

There is more left fibula false joint than the young time. An iris nodule (+). In 14 years, appeal for dizziness; the next House. In head CT, there is a tumor to the left hemisphere of cerebellum. Craniotomy tumor enucleation takes effect in a university hospital. It was a pleomorphic glioblastoma pathologically.

<< case 8 >> Mother origin, man, 11 years old

Because there are nausea, a headache from approximately two years ago, I consult our House. In head CT, there is tumor which seems to be a star cell tumor to left both sides of the head parietal area. Size increases, and tumor introduces a university hospital. The craniotomy operation enforcement. It was a malignant star cell tumor pathologically. An iris nodule (+).

There is cafe au lait spot for a little younger sister in three brothers (two younger sisters) immediately.

<< case 9 >> Mother origin, man, 23 years old

It is cafe au lait spot more-prone to a whole body than straight bottom time. There is the back in a flexible mass subcutaneously. I had a diagnosis of neurofibroma type 1 by biopsy of the last year. An iris nodule (+).

In 23 years, it is noticed the existence of the brain tumor in head CT. The volume of tumor is a tendency to increase. The plan of the craniotomy operation.

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[example as follows derived from mother for women]

<< case 10 >> mother origin, woman, 23 years old

Three women, Sueko of the one man. Two older sisters are healthy.

A right-sided auditory nerve tumor. It is a benign tumor pathologically. Both sides blindness. Sense of smell suffers a loss with right and left.

The older brother dies of a spinal cord tumor at 15 years old (as for this older brother, type 1 a neurofibroma).

<< case 11 >> mother origin, woman, 38 years old

Cerebral infantile paralysis, neurogenic bladder.

I came by walking alone until junior high school time. Low back pain develops and, in 37 years, becomes both lower limbs paralysis. In CT, there is tumor shadow to a lumbar part. It is a benign tumor pathologically.

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[example as follows derived from father for men]

<< case 12 >> father origin, man, 27 years old

Though the human trunk has a flexible mass, in a junior high student, I notice. I

gradually write 増数 and consult our House nine years ago and have a diagnosis of neurofibroma type 1 afterwards. An older sister dies by asthmatical bronchitis.

There is no abnormality in head CT. There is a cauda equina nerve tumor. Cauda equina nerve tumor was a benign tumor pathologically.

<< case 13 >> father origin, man, 32 years old

There are three countrymen (all man), absence attacks.

In head CT, there is tumor shadow on the right head. Craniotomy was a benign star cell tumor though I was operated on.

<< case 14 >> father origin, man, 31 years old

Left pulsatility drawing of the eyes with marking dots, left orbit bottom bone defect.

<< case 15 >> father origin, man, 18 years old

On back of the head midline a bone defect (3.5*3.5cm). From the young time a speech impediment.

It is the next House for a medical examination for Self-Defense Forces enlistment.

<< case 16 >> father origin, man, 2 years old

Right sella turcica expansion (J type). The expansion of the ear canal in the right. The elevation of the right wing-like scale.

The expansion of the right eye nerve way. Expansion of the orbit.

<< case 17 >> father origin, man, 11 months

There is the right cranial bones loss. There is not the neurologic loss. There is a tumor to cervical vertebrae. It is a benign tumor pathologically.

<< case 18 >> father origin, man, 10 years old

The cafe au lait spot of 10 several appears to a human trunk, limbs from one month after birth. There are not increase of the number of cafe au lait spot and the expansion of the size. The neurofibroma developed in the whole back mainly on hips for one year, but six elasticity tumors which began to resolve in the summer from the time (natural regression), and slightly rose to hips at the time of this House outpatient department first medical examination on (September 5, 1992) existed. Almost none of the parts could confirm it at the time of hospitalization on (December 16, 1992), too and resolved.

I am hospitalized for the inspection of the neurofibroma this time. In head CT, there are no views that should mention specially.

Cafe au lait is spotted for father. The countryman has an older sister in two people, but there is no abnormality now.

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[example as follows derived from father for women]

<< case 19 >> father origin, woman, 34 years old

It was noticed cafe au lait spot from the small time. However, there was a little cafe au lait spot, and there were not most of the flexible masses. An iris nodule (+). Appeal for a headache; a senior Pope next House. The bone defect was not clear, but there is a tumor to the left hemisphere of cerebellum. A university hospital introduction. Craniotomy was operated on, but a pathologically malignant star cell tumor. After an operation, he dies.

<< case 20 >> father origin, woman, 21 years old

The right parietal area, a right back of the head ache develop from about October, 1992. When a pain is strong, there are feeling like vomiting, a radiation ache to the right shoulder. I do not recognize it in head CT abnormally. A neurofibroma of the right cervical vertebrae transverse process is diagnosed. An iris nodule (+).

In 1992, I have star cell tumor doubt pointed out by left both sides of the head parietal area in head CT. Size increases, and tumor enforces a craniotomy operation. A pathologically malignant star cell tumor.

<< case 21 >> father origin, woman, 28 years old

There was cafe au lait spot from time for childhood and hemispheric flexible masses occurred frequently more systemically than 16 years old and came to increase. An iris nodule (+). Right ear mixture characteristics hearing loss.

There is a stenosis in rectum. However, tumor marker (-).

There is the flexura which is a whit to lower part thoracic vertebra. There is no abnormality in blood, biochemistry.

I recognize calcification and low-attenuation foci to hemisphere of cerebellum in head CT. With contrast media a reinforcement effect (-), a cerebellum symptom (-). I have a diagnosis of cerebellum atrophy or arachnoid cyst and become the follow-up without the need of the operation.

Nystagmus appears and, in head CT, has a tumor pointed out by hemisphere of cerebellum, and a craniotomy operation takes effect recently. A pathologically pleomorphic glioblastoma.

<< case 22 >> father origin, woman, 16 years old

A countryman has two older brothers, younger brother one, but cafe au lait spot or the flexible mass are not detected. I detected large-scale cafe au lait spot and the elasticity mass of the part from the back to the buttocks after life more immediately. An iris nodule (+). I operate for a flexible mass in S General Hospital plastic surgery. It is the next House

by looking at the both eyes, and having dripped down from 2.0 in 0.9 recently. In head CT, there is a tumor to occipital lobe. I look at the both eyes more and fall in 0.1 recently. I introduce me and am operated on, and it is taken effect to a university hospital. A pathologically malignant star cell tumor.

<< case 23 >> father origin, woman, 13 years old

There is an epilepsy attack to a younger brother. An older sister until about 7 years old febrile convulsion (do abnormally now). Purpura (I do abnormally now) allergic as for the older brother.

There is almost cafe au lait spot to a whole body. A number and the area are tendencies to increase. The flexible mass is recently, too

"Case 23" Father-derived, female, 13 years old

My younger brother has epileptic seizures. My older sister is fever seizures (now no abnormality) until about 7 years old. My older brother has allergic purpura (now there is no abnormality).

Most of the body has caffe ore spots. The number and area tend to increase. Recently, a soft mass begins to appear. Iris nodule (+).

I have a stomachache since March this year. There are 2 clots of bloody stools in June. Laparotomy surgery is enforced. Pathologically, it was a colon tumor with a high degree of malignancy.

No particular noticeable findings on head CT.

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

Unknown from "Case 24", Male, 57 years old

Cafe aule plaque and soft tumor mass are remarkable. At the age of 30, a lumbar soft mass reconstruction was performed.

We have undergone surgery 12 years ago, 11 years ago, 8 years ago under diagnosis of hydronephrosis in bilateral kidney 12 years ago. Pathologically, benign hamartoma.

Strong left side vision disorder continues from 10 years ago, but it has not progressed.

No abnormality was found by chromosome examination.

August last year, nystagmus, appearance. Similar nystagmus, emergence in September (however, nystagmus only occurred once in August, September). It is pointed out suspected astrocytoma which is performed partly on the right side parietal region by MRI. Suspected astrocytoma in the right parietal region was excised by craniotomy but the part considered to be a tumor that was imaged by MRI was a benign tumor with no vascular hyperplasia and neuroglial tumorigenesis.

Unknown from "Case 25", Male, 39 years old

There is a cafe au lait on the left buttocks at birth. Emergence of soft tumor from 4 to 5 years ago. Two years ago I noticed a hard, marginally clear, movable hardening with a diameter of 8 mm on the left third intercostal sternum left edge. The soft mass of the left buttocks is (7 × 4 cm) large soft-type, pigmented. There is abnormal electroencephalogram in the back of the head. There is abnormal shadow in the basal ganglion of the cerebrum, on the head CT.

Unknown from "Case 26", Male, 21 years old
Sister is SLE. When I was in elementary school, I noticed brown spots on the upper right lip. It was a cafe au lait. In case
When a junior high school student, the abdomen, notice the light brown spots of both upper limbs. In July 1985, a brain tumor was found in the head CT, and the tumor was excised. Pathologically, the tumor was benign.
In case
Unknown from "Case 27", Male, 14 years old
At the age of 5, emergence of soft tumor in upper left arm. A soft mass exists also in the right neck, right wrist. Brown spot on front chest from early childhood. It is diagnosed as cafe aule spot in dermatology.
At the age of 13, left upper arm soft tissue mass extraction.
At the age of 15, surgery was performed on the extramedullary tumor of the third cervical vertebra and fifth cervical vertebra. Pathologically, it was a benign tumor. There is also cerebral sinus meningioma (fibrous).

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[The following is unknown origin. That is, the case itself is a proband woman]
1 case none

【Summary of cases】

[Example of male from mother]
Case 1 died of glioblastoma multiforme (38 years old), older brother died (43 years old) in the tumor (suspicion) of the brain stem
In case 2, the elder brother died of brain stem malignant schwannoma (12 years old), the patient himself was alive (24 years old) on the head CT, tumor (-)
Case 3 is malignant astrocytoma (19 years old)
Case 4 is a malignant astrocytoma (grade 3) (33 years old), although one has an older sister, he undergoes surgery with hip joint dislocation.
In case 5, older brother dies after transitioning from pneumonia to meningitis at 1 year of age. The patient himself is congenital midbrain water obstruction obstruction, vision deterioration

tends to progress (7 years old), three older sisters health
Case 6 is delayed psychomotor development, congenital heart disease (1 year old)
Case 7 is glioblastoma multiforme (14 years old)
Case 8 is malignant astrocytoma (11 years old)
Case 9 is an increasing trend of brain tumor (23 years old)

[Example of female from mother]
Case 10 is right auditory nerve tumor (benign) (23 years old), older brother died of spinal cord tumor at age 15
Case 11 shows a soft tumor (38 years old)

[Example of male from father]
Case 12 is a cauda equina neoplasm (benign) (27 years old), older sister died of childhood asthma
Case 13 is astrocytoma (benign) (32 years old)
Case 14 was left orbital bottom bone defect and left pulsating eyestrain (31 years old)
Case 15 was bone loss (3.5 x 3.5 cm) on the medial line of the occipital region, language disorder (18 years old) from young age,
Case 16 shows right Turkish saddle expansion (J type), enlargement of right middle ear canal, elevation of right winged scales (2 years old)
Case 17 was tumor (benign) in the cervical spine (11 months)
In case 18, neurofibroma appeared all around the back centering around the lumbar region from 1 year ago but it disappeared (spontaneous withdrawal) (10 years old) from around the summer
In case
[Examples of female from father]
Case 19 died of malignant astrocytoma (34 years old)
Case 20 was malignant astrocytoma with surgery (21 years old)
Case 21 is surgery (28 years old) with glioblastoma multiforme
Case 22 was malignant astrocytoma with surgery (16 years old)
Case 23 is a colorectal tumor with a high degree of malignancy (13 years old)

[Cases themselves are male cases of probands]
Case 24 is a benign brain tumor (57 years old)
Case 25 shows abnormal shadow (39 years old) in basal ganglia of the cerebrum,
Case 26 is a benign brain tumor (21 years old)
Case 27 is an extramedullary tumor (benign) of the third cervical vertebra and fifth cervical vertebra (14 years old)

[Case itself is a female example of a proband]

I could not find one case

【Discussion】

There are few references in which origin is clearly described in brain tumors of type 1 neurofibroma. There is a literature of a malignant brain tumor in which the origin was specified, but it was a case of multiple malignant schwannoma and was derived from a mother, and the patient was a male. In case

In addition, there is a case in which another origin is clearly stated, which is a document that suggested spontaneous resolution of the orbital glioblastoma multiforme of a 2 - year - old father-born girl [5].

When examining 27 cases, neurofibroma 1 type of a male-derived male patient tends to be malignant. And female patients from fathers also have a strong tendency to malignant to the same extent.

Mother-derived effects in neurofibroma 1 type, that is, maternal effect 6, 7, 8, 10, 11, 13) have been conventionally mentioned. However, there are also many objections 1, 2, 3, 12, 16), and unification of opinion has not been made. I propose a new cross effect, here a cross effect.

Mother-derived effects exist reliably in this survey. It is strongly related whether neurofibroma type 1 is a father-derived female patient, a mother-derived male patient, or another case for canceration. As described above, malignant tumors are highly likely to develop in male patients and father-derived female patients in neurofibroma 1 type, and mother-derived female patients, male-derived male patients, and patients themselves are probands I believe that the absence of malignant tumors will give great implications for cancer gene therapy.

In case

【Reference】

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---------- Summary ---------- -

Cross effect of neurofibroma 1 type

Statistical analysis of 27 neurofibroma 1 types was performed.
Patients with mother-derived neurofibroma 1 type have been said to be more severe than in the past. This is called maternal effect. However, there are many objections. As a result of my investigation, it is very likely that a tumor is malignant in a mother-derived male patient or a father-derived female patient, and if a mother-derived female patient, a father-derived female patient, or a case where the mother is a proband It was never malignant, all were benign.
"When a tumor is found in a mother-derived male patient, a father-derived female patient, the possibility that it is malignant is extremely high." This is called a new cross effect.

Someone please translate it into English. You can post to a foreign medical journal. It is useless in Japan. I am not good at English very much. Thanking you in advance.

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I am a psychiatrist now and also a doctor of brain surgery before.

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Currently 56 years old
Born on November 26, 1961

【原著】

神経線維腫１型の交差効果

誰か、英語に翻訳して、海外の医学学術専門雑誌に投稿してください。これはノーベル賞、間違いないのです。しかし、海外の医学学術専門雑誌に載せないと評価されません。
宜しくお願いします。

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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.
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The male cases born to affected fathers or the female cases born to affected mathers or those who were new mutations didn't have malignant tumors. They were all benign.
"When the tumor is found in the male cases born to affected mothers or female cases born to affected fathers, it is extremely possible that the tumor is malignant."
I newly name it "cross effect".

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key words：neurofibromatosis type 1, cross effect, maternal effect, malignant tumor

【はじめに】

１９３０年代より、母親由来の神経線維腫１型の男性患者は重症であり、腫瘍が見つかった場合、それは悪性腫瘍である確率が非常に高いと言われてきた。筆者が２７例の神経線維腫１型の統計を取ったところ、確かに、母親由来の神経線維腫１型の男性患者は重症であり、腫瘍が見つかった場合、それは悪性である確率が非常に高いことが判明した。同じように父親由来の神経線維腫１型の女性患者も重症で

あり、腫瘍が見つかった場合、それは悪性である確率が非常に高いことが判明した。母親由来の女性患者、父親由来の男性患者および発端者が患者自身の神経線維腫１型は腫瘍が見つかっても悪性であることは有り得ないことが判明した。しかし、これは筆者が収集した２７例についての考察であり、以降の追試を必要とする。

【症例】

[以下は母親由来の男性例]

《症例１》母親由来、男性、３８歳
神経線維腫は僅かであるが後頭骨に骨欠損がある。生来、健康。虹彩結節（＋）。
昨年９月頃、疲労時、眼振が出現。１０月になり眼振が強くなる。頭部ＣＴにて小脳半球の腫瘍を指摘される。開頭腫瘍摘出術施行。病理学上、多形性膠芽腫であった。染色体検査では異常は発見されず。
２人兄弟であり、神経線維腫１型の兄が居たがその兄が４３歳時、昼、強い疲労感を覚え仕事場から帰ってきた後、布団に寝ていたが夕方、死亡しているのが発見された。死因は心不全ということで片付けられた。この兄も生来健康であり心臓疾患など指摘されたことはなかった。死因を調べるための解剖は行われなかった。この兄も小脳あるいは脳幹部の腫瘍であった可能性が高いと思われる。

《症例２》母親由来、男性、２４歳
幼少時より背部、臀部にカフェオレ斑を認める。虹彩結節（＋）。
昭和５９年１０月２日、頭部ＣＴ施行し、特記すべき所見なし。脳波も特記すべき所見なし。軟性腫瘤（−）。
２歳年上の兄は知能指数 32(sb 式)。養護院在院中、１２歳時、朝、起こそうとしたところ死亡していた。解剖の結果、脳幹部悪性神経鞘腫であった。

《症例３》母親由来、男性、１９歳
幼少時より左眼窩底部の腫瘍摘出術を４回施行する。虹彩結節（＋）。
昭和６２年１１月１３日、右鎖骨上窩腫瘍摘出。病理学上、悪性星細胞腫であった。
昭和６２年１２月７日、右肘関節部腫瘍摘出。同じく、悪性星細胞腫であった。
昭和６３年１月１０日、左眼窩底部腫瘍摘出。これも同じく、悪性星細胞腫であった。
今回、左眼窩翼の欠損に伴う脳瘤の整復目的で大学病院紹介。

《症例４》母親由来、男性、３３歳
母親には小さなカフェオレ斑らしきものが数個あり（４０歳時より出現したという）。

姉が一人いるが股関節脱臼で手術施行。
右小脳半球に腫瘍あり。虹彩結節（＋）。右後頭下部に骨欠損。右後頭部膨隆。左側はほぼ全盲。開頭手術にて病理学上、悪性星細胞腫(grade 3)であった。

《症例５》母親由来、男性、７歳
同胞５人。姉３人は健康。兄は１歳時、肺炎から髄膜炎に移行して死亡。
先天性中脳水道閉塞症、原因不明。虹彩結節（＋）。両側視力低下あり、視力低下は進行傾向。

《症例６》母親由来、男性、１歳
精神運動発達遅滞、先天性心疾患、虹彩結節（＋）。生後すぐより下半身にカフェオレ斑多数。頭部ＣＴにて脳萎縮(＋)、腫瘍（−)。
同胞２人。姉は左臀部に茶褐色斑(4×4cm)。

《症例７》母親由来、男性、１４歳
幼い頃より左腓骨偽関節あり。虹彩結節（＋）。１４歳時、目眩を訴え来院。頭部ＣＴ上、左小脳半球に腫瘍あり。大学病院にて開頭腫瘍摘出術施行。病理学上、多形性膠芽腫であった。

《症例８》母親由来、男性、１１歳
２年ほど前より吐気、頭痛があるため当院受診。頭部ＣＴ上、左側頭頭頂部に星細胞腫らしき腫瘍あり。腫瘍は大きさが増大してゆき大学病院紹介。開頭手術施行。病理学上、悪性星細胞腫であった。虹彩結節（＋）。
３人兄弟（妹２人）ですぐ下の妹にカフェオレ斑あり。

《症例９》母親由来、男性、２３歳
生下時より全身にカフェオレ斑多発。背部皮下に軟性腫瘤あり。昨年の生検にて神経線維腫１型と診断された。虹彩結節（＋）。
２３歳時、頭部ＣＴにて脳腫瘍の存在に気付かれる。腫瘍の大きさは増大傾向。開頭手術の予定。

[以下は母親由来の女性例]

《症例１０》母親由来、女性、２３歳
３人女性、１人男性の末子。姉２人は健康。
右側聴神経腫瘍。病理学上、良性腫瘍。両側盲目。左右とも嗅覚欠損。
兄は１５歳で脊髄腫瘍で死亡（この兄も神経線維腫１型)。

《症例１１》母親由来、女性、３８歳

脳性小児麻痺、神経因性膀胱。
中学時までは独歩できた。３７歳時、腰痛出現し両下肢麻痺となる。ＣＴ上、腰椎部に腫瘍陰影あり。病理学上、良性腫瘍。

[以下は父親由来の男性例]

《症例１２》父親由来、男性、２７歳
中学生時、体幹に軟性腫瘤があるのに気付く。その後、徐々に増数したため９年前に当院受診し、神経線維腫１型と診断される。姉が小児喘息で死亡。
頭部ＣＴで異常なし。馬尾神経腫瘍あり。馬尾神経腫瘍は病理学上、良性腫瘍であった。

《症例１３》父親由来、男性、３２歳
同胞３人（全て男性)、欠神発作あり。
頭部ＣＴ上、右側頭部に腫瘍陰影あり。開頭手術するも良性の星細胞腫であった。

《症例１４》父親由来、男性、３１歳
左拍動性突眼、左眼窩底部骨欠損。

《症例１５》父親由来、男性、１８歳
後頭部正中線上に骨欠損(3.5×3.5cm)。幼い頃より言語障害。
自衛隊入隊のための健康診断に来院。

《症例１６》父親由来、男性、２歳
右トルコ鞍拡大（Ｊ型)。右中耳道の拡大。右翼状鱗の挙上。
右眼神経道の拡大。眼窩の拡大。

《症例１７》父親由来、男性、１１ヶ月
右側頭骨欠損あり。神経学的欠損は無い。頚椎に腫瘍あり。病理学上、良性腫瘍。

《症例１８》父親由来、男性、１０歳
生後１ヶ月より体幹、四肢に１０数個のカフェオレ斑出現する。カフェオレ斑の数の増加や大きさの拡大は無い。神経線維腫は１年前から腰部を中心に背部全体に出現したが夏頃より消退し始め（自然消退）当院外来初診時（平成４年９月５日）には腰部に僅かに隆起する６つの軟性腫瘍が存在するのみであった。入院時（平成４年１２月１６日）には同部位もほとんど確認できない程度に消退していた。
今回、神経線維腫の諸検査のため入院する。頭部ＣＴ上、特記すべき所見なし。
父にカフェオレ斑。同胞は２人で姉が居るが現在、異常なし。

[以下は父親由来の女性例]

《症例１９》父親由来、女性、３４歳
小さい頃よりカフェオレ斑に気付かれていた。しかし、カフェオレ斑は僅かであり、軟性腫瘤はほとんど無かった。虹彩結節（＋）。頭痛を訴え本院来院。骨欠損は明かではなかったが、左小脳半球に腫瘍が存在。大学病院紹介。開頭手術したが病理学上、悪性星細胞腫。手術後、死亡。

《症例２０》父親由来、女性、２１歳
平成４年１０月頃より、右頭頂部、右後頭部痛出現。痛みが強いときは嘔気、右肩への放散痛あり。頭部ＣＴで異常認めず。右頚椎横突起の神経線維腫と診断される。虹彩結節（＋）。
平成４年、頭部ＣＴにて左側頭頭頂部に星細胞腫疑いを指摘される。腫瘍は大きさが増大してゆき開頭手術施行。病理学上、悪性星細胞腫。

《症例２１》父親由来、女性、２８歳
幼少時よりカフェオレ斑があり、１６歳より全身性に半球状の軟性腫瘤が多発し増大してくるようになった。虹彩結節（＋）。 右耳混合性難聴。
直腸に狭窄あり。しかし腫瘍マーカー（−）。
下部胸椎に微少な彎曲あり。血液・生化学上異常なし。
頭部ＣＴにて小脳半球に石灰化と低吸収域を認める。造影剤にて増強効果（−）、小脳症状（−）。小脳萎縮またはクモ膜嚢胞と診断され手術の必要なく経過観察となる。
最近、眼振が出現し、頭部ＣＴ上、小脳半球に腫瘍を指摘され、開頭手術施行。病理学上、多形性膠芽腫。

《症例２２》父親由来、女性、１６歳
同胞に兄２人、弟１人いるがカフェオレ斑や軟性腫瘤などは認められない。生後すぐより背部から臀部にかけて大型のカフェオレ斑と同部の軟性腫瘤を認めていた。虹彩結節（＋）。Ｓ総合病院形成外科にて軟性腫瘤を手術。最近、両眼視 2.0 から 0.9 に落ちたことで来院。頭部ＣＴ上、後頭葉に腫瘍あり。最近、更に両眼視 0.1 へと落ちる。大学病院へ紹介し手術施行。病理学上、悪性星細胞腫。

《症例２３》父親由来、女性、１３歳
弟にてんかん発作存在。姉が７歳頃まで熱性痙攣（今は異常なし）。兄はアレルギー性紫斑病（今は異常なし）。
ほとんど全身にカフェオレ斑あり。数および面積は増大傾向。最近、軟性腫瘤も出現し始める。虹彩結節（＋）。
本年３月より腹痛あり。６月、２回血便あり。開腹手術施行。病理学上、悪性度

の強い大腸腫瘍であった。
　頭部ＣＴ上、特記すべき所見なし。

[以下は由来不明。すなわち症例自身が発端者の男性例]

《症例２４》由来不明、男性、５７歳
　カフェオレ斑と軟性腫瘤は著明。３０歳時、腰部軟性腫瘤切除術を施行。
　１２年前より両側腎に水腎症の診断の下、１２年前、１１年前、８年前と手術を行っている。病理学上、良性の過誤腫。
　強い左側視力障害が１０年前より続いているが進行はしていない。
　染色体検査で異常は発見されず。
　昨年８月、眼振、出現。９月にも同様の眼振、出現（しかし、眼振は８月、９月に１回づつ有ったのみである)。ＭＲＩ施行し右側頭頂部に一部造影される星細胞腫疑いを指摘される。右側頭頂部の星細胞腫疑いを開頭術にて摘出したがＭＲＩで造影されていた腫瘍と思われていた部分は血管増生があり神経膠の腫瘍化がなく、良性腫瘍であった。

《症例２５》由来不明、男性、３９歳
　出生時より左臀部にカフェオレ斑あり。４、５年前より軟性腫瘤出現。２年前より左第３肋間胸骨左縁上に直径８mm の硬く辺縁明瞭、可動性のある硬結に気付く。左臀部の軟性腫瘤は(7×4cm)大の柔房型、色素沈着あり。後頭部に異常脳波あり。頭部ＣＴ上、大脳基底核部に異常陰影あり。

《症例２６》由来不明、男性、２１歳
　妹がＳＬＥ。小学生時、右上口唇部に褐色斑があるのに気付く。カフェオレ斑であった。
　中学生時、腹部、両上肢の淡褐色斑に気付く。昭和５９年７月、頭部ＣＴにて脳腫瘍が見つかり、腫瘍摘出術施行。病理学上、腫瘍は良性であった。

《症例２７》由来不明、男性、１４歳
　５歳時、左上腕部軟性腫瘤出現。軟性腫瘤は右頚部、右手首にも存在。幼少時から前胸部に褐色斑あり。皮膚科にてカフェオレ斑と診断される。
　１３歳時、左上腕部軟性腫瘤摘出。
　１５歳時、第３頚椎・第５頚椎の髄外性腫瘍にて手術施行。病理学上、良性腫瘍であった。また脳鎌部髄膜腫（繊維性）あり。

[以下は由来不明。すなわち症例自身が発端者の女性例]
　１例もなし

【症例のまとめ】
[母親由来の男性例]
症例１は多形性膠芽腫にて死亡（３８歳)、兄は脳幹部の腫瘍（疑い）にて死亡（４３歳）
症例２は兄が脳幹部悪性神経鞘腫にて死亡（１２歳)、本人は健在で（２４歳）頭部ＣＴ上、腫瘍（−）
症例３は悪性星細胞腫（１９歳）
症例４は悪性星細胞腫(grade 3) （３３歳)、姉が一人いるが股関節脱臼で手術施行。
症例５は兄が１歳時、肺炎から髄膜炎に移行して死亡。本人は先天性中脳水道閉塞症で視力低下は進行傾向（７歳)、姉３人は健康
症例６は精神運動発達遅滞、先天性心疾患（１歳）
症例７は多形性膠芽腫（１４歳）
症例８は悪性星細胞腫（１１歳）
症例９は増大傾向にある脳腫瘍（２３歳）

[母親由来の女性例]
症例１０は右側聴神経腫瘍（良性）（２３歳)、兄は１５歳で脊髄腫瘍で死亡
症例１１は幼児期より全身に軟性腫瘤（３８歳）

[父親由来の男性例]
症例１２は馬尾神経腫瘍（良性）（２７歳)、姉が小児喘息で死亡
症例１３は星細胞腫（良性）（３２歳）
症例１４は左眼窩底部骨欠損で左拍動性突眼（３１歳）
症例１５は後頭部正中線上に骨欠損(3.5×3.5cm)、幼い頃より言語障害（１８歳）
症例１６は右トルコ鞍拡大（Ｊ型)、右中耳道の拡大、右翼状鱗の挙上（２歳）
症例１７は頚椎に腫瘍（良性）（１１ヶ月）
症例１８は神経線維腫が１年前から腰部を中心に背部全体に出現したが夏頃より消退（自然消退）（１０歳）

[父親由来の女性例]
症例１９は悪性星細胞腫にて死亡（３４歳）
症例２０は悪性星細胞腫にて手術（２１歳）
症例２１は多形性膠芽腫にて手術（２８歳）
症例２２は悪性星細胞腫にて手術（１６歳）
症例２３は悪性度の強い大腸腫瘍（１３歳）

[症例自身が発端者の男性例]

症例２４は良性の脳腫瘍（５７歳）
症例２５は大脳基底核部に異常陰影（３９歳）
症例２６は良性の脳腫瘍（２１歳）
症例２７は第３頚椎・第５頚椎の髄外性腫瘍（良性）（１４歳）

[症例自身が発端者の女性例]
　１例も発見できず

【考察】

神経線維腫１型の脳腫瘍で由来が明記された文献は少ない。１例由来が明記された悪性の脳腫瘍の文献があるがそれは多発性悪性神経鞘腫の症例で母親由来のものであり、患者は男性であった 6)。

また、もう１例由来が明記された症例があるが、それは父親由来の２歳の少女の眼窩部多形性膠芽腫の自然消退を提示した文献である 5)。

２７例の症例を考察した場合、母親由来の男性患者の神経線維腫１型は悪性化の傾向が強い。そして、父親由来の女性患者も同程度に悪性化の傾向が強い。

神経線維腫１型における母親由来効果すなわち maternal effect6,7,8,10,11,13)は従来から言われてきたことである。しかし反論も多く 1,2,3,12,16)、意見の統一は成されていない。筆者はここに新しく交差効果すなわち cross effect を提唱する。

母親由来効果は今回の調査上、確実に存在する。癌化に神経線維腫１型が父親由来の女性患者であるか母親由来の男性患者であるか、それとも他の場合であるか、大きく関係している。このように神経線維腫１型において母親由来の男性患者、父親由来の女性患者に悪性の腫瘍が極めて発生しやすいこと、そして母親由来の女性患者、父親由来の男性患者、および患者自身が発端者の場合、悪性の腫瘍は発生しないことはがん遺伝子治療への大きな示唆を与えると確信する。

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----------要旨----------

神経線維腫１型の交差効果

２７例の神経線維腫１型の統計的分析を行った。
従来より母親由来の神経線維腫１型の患者は重症度が高いと言われてきた。これを maternal effect という。しかし、反対意見も多い。筆者が調べた結果、母親由来の男性患者、父親由来の女性患者に於いて腫瘍が悪性である可能性が極めて高く、母親由来の女性患者、父親由来の男性患者、自身が発端者である場合は悪性であることは無く、すべて良性であった。
「母親由来の男性患者、父親由来の女性患者に於いて腫瘍が見つかった場合、それが悪性である可能性は極めて高い」これを新しく交差効果（cross effect）と名付ける。

誰か、英語に翻訳して下さい。外国の医学雑誌に投稿できます。日本では駄目なのです。私は英語が物凄く苦手です。宜しくお願いします。