Fluvoxamine 2 cases of stuttering that became mild after long-term use

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[Abstract]

We experienced 2 cases of mild stuttering caused by long-term use of Fluvoxamine. Both cases had stuttering since childhood. Case 1 develops social anxiety disorder in the third year of high school. Case 2 recently develops a depressive disorder. In both cases, stuttering was mildly caused by long-term use of flvoxamine for those diseases (social anxiety disorder, depressive disorder). Case 1 took 10 months to recognize mildness of stuttering, and Case 2 took 7 months. Both cases have been more than 15 years since the stuttering of the stuttering, but stuttering continues to be mild enough to be remission.

Treatment of stuttering is particularly difficult in severe cases, and there are many social dropouts and social recluses. Since pharmacotherapy for stuttering is almost unknown in Japan, we report here.

[Key words] stuttering, fluvoxamine, serotonine selective reuptake inhibitor, long-term taking

[Introduction]

Stuttering is classified into repetitiveness that repeats the first first sound and difficulty that the first first sound does not come out, and both are often mixed at a certain rate. Childhood is often only repetitive, and it is common for it to become difficult to develop as an adult grows. Repeated stuttering is more common in young children and has weak subjective symptoms. However, it is often the target of “bullying” such as being imitated. Intractable stuttering is more common than in high school students, and there are few objective symptoms, but subjective symptoms are strong, and people often struggle to understand.

吃 Stuttering is widespread throughout the world without racial and regional differences, and it is estimated that about 1% of adults are affected. There are many literature that many men have a male to female ratio of 3: 1.

Most of the stuttering manifestations occur at the age of 2-7 years, and about 75% of stuttering manifestations of 2-7 years of age will naturally heal by puberty without any treatment. Playing roaring is counterproductive, and on the contrary it makes habits habitual. It is important not to speak even if you speak, and to grow up gently. In other words, it is important that children are not aware of stuttering4).

Currently, people with stuttering are sometimes seen in “Tojikomori”. Suicides suffering from stuttering are sometimes seen, and there is a college student who was a player of the Olympic men's hurdles as famous in Japan. And although not a suicide, a young monk who set fire to Kinkakuji was stuttering.

It is also said that parents are too harsh, too harsh, unwarming home environment, which makes them nervous and creates stuttering children. And in many adolescents, it often becomes severe with stress. Currently, gene-level research is actively conducted in Europe and the United States, and several roaring loci have been found from studies of frequent cases in families. However, multiple factors are considered to be involved. The frequency of stuttering between parents is more than three times that of the general population. In addition, studies on monozygotic twins indicate that heredity is greater than the environment16). *

吃 Stuttering often occurs after head injury, cerebral infarction, cerebral hemorrhage, encephalitis, etc., represented by traffic accidents, but this mechanism has not yet been unified. There are theories that the center of language has been destroyed, and that the center of the autonomic nerve has been destroyed18). Currently, stuttering tends to be perceived as a syndrome caused by various causes4). *

Research on stuttering has been actively conducted in the West. However, there is little research on stuttering in Japan. And there are no reports of stuttering treatment with drugs in Japan. In

Europe and the United States, stuttering is established as a disease unit and is regarded as important, but in Japan, stuttering is still simply referred to as “stuttering” and “bad habits” or “bad habits have become established”. It is thought that this is because it tends to not be identified as a disease unit.
The existence of pharmacotherapy for stuttering is hardly recognized by Japanese clinicians. Treatment is left to the speech therapist and speech practice is still mainstream. .
DSM-Ⅲ-R and DSM-IV-TR had Stuttering stuttering, but the American Psychiatric Association 2013 DSM-5 1) Childhood-Onset Fluency Disorder (Stuttering) Childhood-onset Fluency (stuttering) / Childhood-onset fluency disorder (stuttering) and expression changed.

[Case] (Some corrections were made in the life history of the case, and anonymity was taken into consideration. In both cases, stuttering was severe and difficult to treat. (I still grab it.)

[Case 1] 49-year-old male

(History) None to be noted
(Current medical history) My mother told me that I had stuttering since childhood. However, there was no knowledge of stuttering in the case.
】 First year in high school, the time of modern Japanese language, when reading a book, the first first sound does not come out and experience the trouble. It starts from this time and begins to suffer from stuttering. In other words, it was the first manifestation of the pathologic insight. And there is an episode that reading books in the time of modern Japanese language became painful and caused school refusal.
Developed social anxiety disorder in the third year of high school. However, he did not visit the hospital.
When she was 22 years old, she visited otolaryngology and neurology to treat stuttering, but she was introduced to psychiatry. And he knows that his stuttering is drastically reduced while taking bromazepam, cloxazolam, diazepam, etizolam, benzodiazepine anxiolytics prescribed for social anxiety disorder. The same benzodiazepine anti-anxiety drugs alprazolam 6), flutoprazepam, and flunitrazepam are known to cause stuttering temporarily but severely.
In this case, social anxiety disorder is also effective for benzodiazepine anti-anxiety drugs, but not as strong as stuttering. Therefore, social anxiety disorder was a major problem in cases.
In the case of a case, we find a document that clomipramine works for social anxiety disorder and take clomipramine. The first dose was on Saturday night, but until Sunday night, I fell awake without any awakening, and severely stuttering became severe enough to talk for almost two days. . The administration of clomipramine was completed once. I also found literature that

carbamazepine is effective for stuttering, but on the other hand, stuttering became so severe that it was discontinued after several doses (case is a doctor).
· Start taking fluvoxamine simultaneously with the release of flvoxamine. There was no nausea, but at the same time as taking fluvoxamine, she began to feel intense fatigue. The next day after the dose of fluvoxamine was reduced, the side effect of fluvoxamine was considered due to mild fatigue. However, since fluvoxamine was the only SSRIs released in Japan at that time, he continued to withstood his intense fatigue with the desire to ameliorate social anxiety disorder (clomipramine, an antidepressant, ameliorated social anxiety disorder) Because I was reading overseas papers). In the case of fluvoxamine, the patient feels strong fatigue, and taking it in the morning and noon is considered to be an impediment to work, so take the entire daily dose one hour before going to bed. Also, “morning wake-up difficulty” begins a little later.
In the case of fluvoxamine, the patient was forced to heal the social anxiety disorder while presuming that he was feeling tired because he was taking fluvoxamine. The holiday was almost in bed.
In the case, there was no depression, self-worthiness, thoughts of death, awakening in the early morning, and insomnia, but only morning difficulty and daytime fatigue. Therefore, the case was self-diagnosed as suffering from “disease similar to chronic fatigue syndrome”.
In the seventh month of taking the medicine, for a moment, the idea of rare death emerged and recognized for the first time that he was a depressive disorder.
When 10 months have passed after taking flvoxamine, I noticed that I was talking without inconvenience over the phone without taking benzodiazepine anxiolytics. In other words, we recognize that stuttering is becoming milder as it is closer to remission. Until now, it was almost impossible to talk on the phone without dissolving tension in the oral cavity such as etizolam. The case was empirically known that the effect was rapidly manifested when the benzodiazepine anxiolytic was absorbed through the oral mucosa and pharyngeal mucosa. He was always taking benzodiazepine anxiolytics during work. The ability to talk on the phone without taking benzodiazepine anti-anxiety drugs has been almost unrecognizable since high school. However, in cases, stuttering can be sufficiently surpassed by taking benzodiazepine anxiolytic drugs, but social anxiety disorder cannot be sufficiently surpassed by taking benzodiazepine anxiolytic drugs. It was. I learned that it was possible to talk without inconvenience without taking benzodiazepine anxiolytics, but the case was not very happy.
吃 Stuttering has been mild for about 16 years since the awareness of mildness. Social anxiety disorder continues without mildness.

[Case 2] 49-year-old male
(History) From the 4th grade of elementary school, a friend told me that he was “odd” (meaning

that he was restless and jumpy). The case itself had no awareness of being “odd”, and the case had the awareness that it was nervous and its annoyance.
(Current medical history) Stuttering developed at least in the third grade of elementary school. She was worried about her mother and was treated by a speech therapist at an otolaryngology department at a university hospital, but only a slight reduction in stuttering was observed. She was aware of stuttering, and since she was in elementary school, her mother was worried about stuttering and was consulting with her teacher. Therefore, there was no “bullying” from teachers and classmates due to stuttering at school. Case 1 and high school friend. Coincidentally, a severe stuttering person of the same class was in the same athletic club.
From Case 1, “There are drugs that are effective against stuttering. I have to take it for at least one year with a drug called SSRIs. ”
I have been suffering from a depressive disorder and have been taking medication for about a year. Depression was the main symptom. Cases self-analyzed that their depressive disorder developed under severe stress due to stuttering. The prescription at the visit was mainly amoxapine, and fluvoxamine was never given at that time.
Personality was bright and social, and social adaptation was relatively good. However, there were unclean fears and confirmation threats. When I went to work in the morning because of a confirmation threat, I sometimes went back and forth at the entrance of the apartment for more than 30 minutes. In the worst case, I went back and forth at the entrance for an hour and a half. When the filthy fear was terrible, I returned home from the company and washed my hands for three hours.
From the first day of visit, start taking fluvoxamine 150 mg daily for 1 hour before going to bed. There was no nausea, but he felt moderate fatigue. This fatigue continues until you stop taking fluvoxamine. Benzodiazepine anti-anxiety drugs are said to aggravate stuttering, and administration is discontinued after 1 month. *
Stuttering is said to be "lightening" by the surroundings about 7 months after taking. The patient has little awareness of mild stuttering, and is not aware of it until it is pointed out by the surroundings. Continue to take fluvoxamine 150mg daily for 1 hour before going to bed.
Five months after recognizing the mildness of stuttering, the depressive disorder that lasted for two years is in remission. The case has been taking fluvoxamine for 12 months. I had fallen into complete erectile dysfunction for 12 months while taking fluvoxamine. Erectile dysfunction did not exist when amoxapine-based treatment was used in the House.
吃 Stuttering disease has been in progress for over 15 years since the symptom of mildness, but no seriousness has been observed. Unclean fears and confirmation threats persisted with milnacipran hydrochloride and paroxetine without being mild, and the visit stopped.

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[Discussion]

In 1997, dopamine overactivity was demonstrated in the brain of stuttering patients 23), and the effectiveness of risperidone 12) and olanzapine 13) was shown in a double-blind study. Risperidone has been shown to start at 0.5 mg / day and up to 2 mg / day, and olanzapine is to be taken in small doses of 2.5 mg or 5 mg / day. However, because risperidone and olanzapine have strong side effects, they are limited to use in severe cases, and there is a strong opinion that SSRIs with relatively weak side effects are the first choice4,11).

There are many reports of stuttering treatment by SSRIs by paroxetine 13), and reports of stuttering treatment by other SSRIs are only reported by sertraline 3) and fluoxetine 11). There are no reports other than these three drugs. Daniel C et al.4) cite paroxetine and sertraline as representatives of SSRIs with pharmacotherapy for stuttering.

The report of the treatment of stuttering by SSRIs mainly consisting of these paroxetine is faster than the above two cases. However, when he stopped taking it, he relapsed. Long-term efficacy has not been shown. In Europe and the United States, research on stuttering is thriving, and weak temporary mildness tends to be a case report.

It is recommended to take SSRIs that are effective for social anxiety disorders for a long period of more than 1 year22). However, long-term administration of SSRIs over 1 year has not been shown for stuttering. Case 1 told Case 2 “There are drugs that work for stuttering. The phrase “must be taken with SSRIs for at least one year” was a confusion between stuttering and social anxiety disorder. It can be said that Case 1 suffered from social anxiety disorder so that it was confused. *

The treatment of stuttering can be noticeably mild in elementary school children and younger children only with pronunciation therapy by a speech auditor, but it is difficult to see the effect for junior high school students and older. More effective than high school students 4).

Also, stuttering people suffer a lot of stress in their social life. Therefore, people with stuttering are susceptible to secondary depression and anxiety disorders4).

Depressive disorder is a disease with a high morbidity rate in developed countries, and fluvoxamine has been used for a long time among SSRIs22). However, no report has been found that fluvoxamine was effective in stuttering. Since fluvoxamine has a slow onset effect on stuttering, it seems most appropriate to think that there is no report of mild stuttering until now. It is also speculated that there were very few cases of long-term administration such as the above two cases, although what seemed to be strong side effects

occurred. In Europe and America, SSRIs have been used for a long time, and SSRIs have a wide choice in many countries. It is common to change to other SSRIs or antidepressants if what appears to be a strong side effect. In the above two cases, fluvoxamine was the only SSRIs in Japan.

SSRIs, unlike tricyclic antidepressants, have a strong inhibitory effect on the CYP450 enzyme. SSRIs have different CYP450 enzyme inhibition depending on the drug7). For example, fluvoxamine has a high inhibitory action on CYP1A2. Only fluvoxamine has this inhibitory action among SSRIs21). There is a report that the administration of fluvoxamine increases the half-life of caffeine from 5 hours to 31 hours9). Moreover, it has a high inhibitory action of CYP2D6 as a characteristic of paroxetine 2). Thus, SSRIs tend to have special effects for each individual drug.

Case 1 recognizes mild stuttering at 10 months after taking fluvoxamine and Case 2 at 7 months after taking fluvoxamine. Case 1 wanted to cure social anxiety disorder, and stuttering was not very much in mind. Case 2 suffered from depressive disorder and thought that stuttering would not be mild unless taken for more than one year. Therefore, it seems that neither of the two cases was able to recognize their mild stuttering. *

In both cases, fluvoxamine was continued even after recognizing stuttering. Case 1 was taken for another 8 months and Case 2 was taken for another 5 months. Case 1 is taken continuously for 18 months, and Case 2 is taken continuously for 12 months.

In both cases, more than 15 years have passed since the mildness of stuttering has been reduced, but stuttering has been maintained as mild as remission. From at least these two cases, it is speculated that long-term use is necessary for long-term mildness and remission of stuttering. It is unclear whether it is common to SSRIs or unique to flvoxamine.

There is a strong opinion that benzodiazepine anxiolytics are not used in the treatment of stuttering4). This is largely due to the idea of the Western medical community who strongly dislikes the dependence of benzodiazepine anxiolytics, and alprazolam, which is frequently used for panic disorder, on the contrary, temporarily exacerbates stuttering 6). Seem.

A report that meprobamate succeeded in 14 out of 18 cases was made in 1958 17). There are at least four reports of meprobamate mitigation of stuttering. .

Currently, pagoclone, which is considered to be a non-benzodiazepine selective GABA receptor agonist and effective for panic disorder, has been the topic of discussion, but its evaluation is not good 8,14).

(At least alprazolam, flutoprazepam, and flunitrazepam, which are benzodiazepine anxiolytics, cause stuttering temporarily but severely. Alprazolam is referred to as "severe stuttering because it has the same action as a tricyclic antidepressant, ie, an anticholinergic

action" 6). This is because carbamazepine also has an anticholinergic effect, and the same mechanism as stuttering disease temporarily became severe when carbamazepine was taken in case 1.
However, benzodiazepine anxiolytics such as bromazepam, cloxazolam, diazepam, and etizolam are often effective for stuttering. The success of these benzodiazepine anxiolytics is considered to be a neurotic case with very strong tension. *
"The" Tounkai ", a self-help group for people with stuttering in Japan, will practice desensitization speech, that is, give a speech in front of all attendees, and will have various discussions with all attendees. However, there are many stuttering people who only attend once, saying, "Practicing vocalization for desensitization therapy has nothing to do". *
Also, when the "Funyukai" learns about the existence of children and students who have fallen into "Tojikomori" due to stuttering, they visit the house and discuss how to get out of "Tojikomori".
Currently, the "Funyukai" stands on a negative view of drug therapy. The negative view is stubborn, which is thought to be a prejudice against psychiatry. .
The

[Conclusion]

The suffering of stuttering is stronger than I expected. Speech therapy may be sufficient if it is mild. However, if it is severe, social relics are inevitable without drugs.
The author is convinced that denying drug therapy and stubbornly forcing or neglecting speech therapy will only create social relics due to roaring today, where "bullying" is prevalent.
In Europe and the United States where stuttering is actively studied, there is a strong opinion that stuttering is a brain dysfunction, and there is a tendency toward the need to take medicine.
From now on, I believe we should actively incorporate "long-term use of SSRIs" for severe stuttering. *
The
---------- Dedicated to people with stuttering ----------
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Fluvoxamine 長期服用によって軽症化した吃音症の２例

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【抄録】

Fluvoxamine 長期服用によって吃音症の軽症化が起こった症例を２例経験した。２症例とも幼年時より吃音症に罹患していた。症例１は高校３年次、社交不安障害を発症する。症例２は最近、うつ病性障害を発症する。２症例とも、それらの疾患（社交不安障害、うつ病性障害）に対し fluvoxamine を長期服用することにより、吃音症の軽症化が偶発的に起こった。症例１は吃音症軽症化を認識するまで１０ヶ月、症例２は７ヶ月を要した。２症例とも吃音症の軽症化より１５年以上を経ているが、吃音症は寛解と言えるほど軽症化した状態を保ち続けている。

吃音症の治療は特に重症に於いては困難を極めており、社会的脱落者、社会的隠遁者も多い。吃音症の薬物治療は本邦に於いてはほとんど知られていないため、ここに報告する。

【key words】 stuttering, fluvoxamine, serotonine selective reuptake inhibitor)、long-term taking)

【緒言】

吃音症は最初の第一音を連発する連発性と、最初の第一音が出て来ない難発性とに区別され、その両者がある程度の割合で混合していることが多い。幼年期は連発性のみであることが多く、大人になるにつれ難発性に変化してゆくことが一般的である。連発性吃音症は幼年者に多く自覚症状が弱い。しかし真似をされるなど“いじめ”の対象になることが多い。難発性吃音症は高校生以上に多く、他覚症状は少ないが自覚症状が強く人知れず悩み抜くことが多い4)。

吃音症は世界中に人種差、地域差なく遍満しており成人の１%程が罹患しているとされる。男性に多く男女比は３：１としている文献が多い 4)。

吃音症はほとんどが２～７歳で発現し、２～７歳発現の吃音症は７５%程が何の治療を行わなくても思春期までに自然治癒してゆく。吃音を叱ることは逆効果であり、却って吃音を習慣付けることになる。吃っても叱らず、のびのびと育てることが重要である。すなわち、子供に吃音を自覚させないことが重要である 4)。

現在は “とじこもり”に時おり吃音症者が見られる。吃音症を苦にしての自殺者も時おり見られ、本邦では有名なものとしてオリンピック男子ハードルの選手だった大学生が存在する。そして自殺者ではないが、金閣寺に放火した若い僧侶が吃音症であった。

また厳し過ぎる親の躾、厳し過ぎる環境、暖かみのない家庭環境、それらが子供を神経質にさせ、吃音症の子供を造ると言われる。そして多感な思春期にストレスとともに重症化することが多い。現在は遺伝子レベルの研究が欧米で盛んに行われており、家系内多発例の研究から吃音の遺伝子座も幾つか見つかっている。しかし多因子が関与するものとされている。親兄弟間の吃音症の発生頻度は一般の３倍以上である。また一卵性双生児の研究から環境よりも遺伝が大きく作用するとされている 16)。

交通事故を代表とする頭部外傷、脳梗塞、脳出血、脳炎などの後、吃音症が起こることが頻繁にあるが、この機序は未だ統一した見解は成されていない。言語中枢に破壊が及んだ故という説、自律神経の中枢に破壊が及んだ故という説などがある 18)。現在、吃音症は様々な原因で起こる一つの症候群として捉えられる傾向が出てきている 4)。

欧米に於いて吃音症の研究は盛んに行われている。しかし本邦では吃音症の研究はほとんど行われていない。そして薬物による吃音症治療の報告は本邦に於いて見つからない。欧米では吃音症が一つの疾患単位として確立化され重要視されているが、本邦に於いて吃音症は未だ単に「吃音」と呼ばれ「悪い習癖」または「悪い習癖が定着化したもの」と考えられており、一つの疾患単位として見成されていない傾向にある故と思われる。

吃音症に薬物療法が存在することは本邦の臨床医師に於いてほとんど認識されていない。治療は言語聴覚士に委ねられ発声練習が未だ主流になっている。

DSM-Ⅲ-R、DSM-IV-TR では Stuttering 吃音症 であったが、米国精神医学会 2013 年発表 DSM-5　1)では Childhood-Onset Fluency Disorder (Stuttering) 小児期発症流暢症（吃音）/小児期発症流暢障害（吃音） と表現が変更された。

【症例】（症例の生活歴に於いては若干の訂正を加え、匿名性に配慮してある。また、２症例とも吃音症は重症で難発性であった。２症例とも年賀状により状況は現在も掴めている。）

［症例１］４９歳、男性

（既往歴）特記すべきものなし

（現病歴）幼年時より吃音症であったと母親から言われていた。しかし症例に吃音症の病識は存在しなかった。

高校１年次、現代国語の時間、本を読むとき最初の第一音が出て来ず困り抜く経験をする。このときより始めて吃音症に悩むようになる。すなわち、吃音症の病識の最初の発現であった。そして現代国語の時間に本を読まされることが苦痛となり登校拒否を起こしたというエピソードがある。

高校３年次、社交不安障害を発症する。しかし病院受診は行わないでいた。

２２歳時、吃音症を治療する目的で耳鼻咽喉科、神経内科を受診するが精神科を紹介される。そして自身の吃音症が社交不安障害に対して処方されたベンゾジアゼピン系抗不安薬である bromazepam、cloxazolam、diazepam、etizolam を服用している間は劇的に軽症化することを知る。また同じベンゾジアゼピン系抗不安薬である alprazolam 6)、flutoprazepam、flunitrazepam は吃音症を一時的ながらも重症化させことを知る。

この症例に於いて、社交不安障害もベンゾジアゼピン系抗不安薬に効能が見られるが、吃音症のような強い効能は見られない。それ故、症例に於いては社交不安障害が大きな問題であった。

症例は clomipramine が社交不安障害に効くという文献を見つけ、clomipramine を服用する。初回の服用は土曜日の夜であったが、日曜日の夜まで全く覚醒せずに眠ってしまい、しかも激しく吃音症が重症化し、２日間ほど、ほとんど話をすることができなくなったという経験を持つ。clomipramine の服用は１回で終了した。また carbamazepine が吃音症に効くという文献も見つけ服用したが、却って吃音症は重症化するため数回の服用で中止した（症例は医師である）。

fluvoxamine の発売と同時に fluvoxamine 服用を開始する。悪心はなかったが fluvoxamine 服用開始と時を同じくして激しい倦怠感を自覚し始める。fluvoxamine の服用量を減量した翌日は倦怠感が軽い故に fluvoxamine の副作用が考えられた。しかし当時、本邦に於いて発売されていたＳＳＲＩｓは fluvoxamine のみであったため、社交不安障害を寛解させたい一心でその激しい倦怠感に耐え続けた（抗うつ薬である clomipramine が社交不安障害を寛解させた海外の論文を読んでいたためである）。症例は fluvoxamine を服用すると強い倦怠感に襲われるため朝昼に服用することは仕事に差し支えると考え、就寝１時間前に一日量全てを服用する。また少し遅れて「朝の起床困難」も始まる。

症例は fluvoxamine 服用故の強い倦怠感と推測しながらも社交不安障害を治したい一心で、就寝１時間前 fluvoxamine 150mg の服用を続ける。休日はほとんど臥床状態であった。

症例には、抑うつ、自己の無価値感、希死念慮、早朝覚醒および不眠などが存在しなく、朝の起床困難と昼間の倦怠感のみであった。それ故、症例は「慢性疲労症候群に似た疾患」に罹患していると自己診断していた。

服用７ヶ月目、一瞬、希死念慮が湧き、初めて自身がうつ病性障害であることを認識する。

fluvoxamine の服用が１０ヶ月を経過した頃、ベンゾジアゼピン系抗不安薬の服用なしに電話で不自由なく話をしていることに気付く。つまり吃音症が寛解に近いほど軽症化していることを認識する。今までは etizolam などの口腔内溶解を行い緊張を解さないと電話で話をすることはほとんど不可能であった。症例は口腔内溶解し口腔粘膜や咽頭粘膜からベンゾジアゼピン系抗不安薬を吸収させるようにすると効果が早く発現することを経験的に知っていた。仕事中は常にベンゾジアゼピン系抗不安薬を服用していた。ベンゾジアゼピン系抗不安薬の服用なしに電話で不自由なく話ができることは症例には高校時代以降はほとんど記憶のないことであった。しかし症例は吃音症はベンゾジアゼピン系抗不安薬の服用に依って充分に凌げるが、社交不安障害はベンゾジアゼピン系抗不安薬の服用に依っても充分に凌ぐことができない故に社交不安障害に強く悩んでいた。もはやベンゾジアゼピン系抗不安薬を服用しなくとも不自由なく話をすることが可能であることを知ったが症例はあまり喜ばなかった。

吃音症は軽症化の自覚より約１６年以上経過するが軽症化を維持している。社交不安障害は軽症化せずに続いている。

［症例２］４９歳、男性

（既往歴）小学４年次より「オドオドしている（落ち着きなく、びくびくしている、という意）」と友人より言われていた。症例自身には「オドオドしている」という自覚はなく、症例は自身が神経質であるという自覚とその煩悶があった。

（現病歴）少なくとも小学３年次には吃音症が発症していた。母親が心配し、大学病院の耳鼻咽喉科にて言語聴覚士による治療を受けたが、吃音症の軽症化は僅かに認められたのみであった。本人にも吃音症の自覚があり、小学校時代より吃音症ということで母親が心配し担任の教師などに相談していた。それ故、学校にて吃音症による教師およびクラスメートなどからの“いじめ”はなかった。症例１と高校時代の友人である。偶然に同級の重度の吃音症者が同じ運動部であった。

症例１より『吃音症に効く薬がある。ＳＳＲＩｓという薬で少なくとも１年間は服用しなければならない』と知らされて来院する。

来院１年ほど前よりうつ病性障害を発症し投薬治療を受けていた。抑うつ感が主な症状であった。症例は自身のうつ病性障害は吃音症故の強いストレス状況下に発症したと自己分析していた。来院時処方は amoxapine が主体であり、fluvoxamine の投与はその時点では受けたことがなかった。

性格は明るく社交的で社会適応は比較的良好であった。しかし不潔恐怖、確認脅迫が存在した。確認脅迫のため朝、会社へと出掛けるときに三十分以上、アパートの玄関で行き戻りを繰り返すことが時折あった。最も酷いときは１時間半、玄関で行き戻りを繰り返したことがある。不潔恐怖も酷いときは会社から帰ってきて三時間、手を洗い続けたことがある。

来院初日より fluvoxamine １日 150mg 就寝１時間前服用を開始する。悪心はなかったが中等度の倦怠感を覚える。この倦怠感は fluvoxamine 服用を中止するまで続く。ベンゾジアゼピン系抗不安薬は却って吃音症を重症化させると言い、投与は１ヶ月間で中止する。

吃音症は服用７ヶ月後頃「軽くなっている」と周囲より言われる。症例には吃音症軽症化の自覚はほとんどなく、周囲より指摘されて始めて気付く。その後も fluvoxamine １日 150mg 就寝１時間前服用を続ける。

吃音症軽症化に気付いて５ヶ月後、２年間続いたうつ病性障害が寛解する。症例は１２ヶ月間 fluvoxamine を服用したことになる。fluvoxamine を服用していた１２ヶ月間は完全な勃起不全に陥っていた。勃起不全は前院に於いて amoxapine を主体とした治療が行われていたときには存在しなかった。

吃音症は軽症化の自覚より１５年以上経過するが重症化は認められない。不潔恐怖、確認脅迫は milnacipran hydrochloride, paroxetine に依っても軽症化せず存続し、来院は途絶えた。

【考察】

１９９７年、吃音症者の脳にドーパミン過活動が証明され 23)、 二重盲検試験で risperidone 12)、olanzapine 13)の有効性が示された。risperidone は 0.5mg/日より始めて最大 2mg/日 まで、olanzapine は 2.5mg または 5mg/日の少量服用が示されている。しかし risperidone、olanzapine は副作用が強いため重症例の使用に限られ、副作用が比較的弱いＳＳＲＩｓが第一選択であるとの意見が強い 4,11)。

ＳＳＲＩｓによる吃音症治療の報告は paroxetine 13)によるものが多く、他のＳＳＲＩｓによる吃音症治療の報告は sertraline 3)、 fluoxetine 11) によるものが散見されるのみである。この３剤以外の報告は見当たらない。Daniel C ら 4)は吃音症の薬物療法によるＳＳＲＩｓの代表として paroxetine と sertraline を挙げている。

これら paroxetine を主とするＳＳＲＩｓによる吃音症治療の報告は上記２症例と異なり効果が早く現れている。しかし服用を中止すると再燃している。長期的な効能は示されていない。欧米では吃音症の研究が盛んであるため、弱い一時的な軽症化も症例報告となる傾向性がある。

社交不安障害には効果が見られるＳＳＲＩｓの１年を越える長期服用が推奨されている 22) 。しかし吃音症にはＳＳＲＩｓの１年を越える長期投与は示されていない。症例１が症例２に語った『吃音症に効く薬がある。ＳＳＲＩｓという薬で少なくとも１年間は服用しなければならない』という言動は吃音症と社交不安障害を混同したものであった。混同するほど症例１は社交不安障害に悩んでいたとも言える。

吃音症治療は小学生など幼少者に於いては言語聴覚士による発音療法のみで顕著な軽症化が得られる場合があるが、中学生以上では効果が見られ難くなる。高校生以上では更に効果が見られ難くなる 4)。

また吃音症者は社会生活上、多くのストレスを受ける。故に、吃音症者は二次的にうつ病性障害や不安障害に罹患し易い 4)。

うつ病性障害は先進諸国では罹患率の高い疾患であり、ＳＳＲＩｓのなかでも fluvoxamine は比較的古くから使用されてきた 22)。しかし fluvoxamine が吃音症に効果があったという報告は見つからない。fluvoxamine は吃音症への効果発現が遅い故に現在まで吃音症軽症化の報告が存在しないと考えるのが最も妥当と思われる。また、強い副作用と思われるものが起こりながらも上記２症例のように長期間、服用を続けた例は極めて少なかった故とも推測される。欧米では古くからＳＳＲＩｓが使用されており多くの国でＳＳＲＩｓの選択肢が広い。強い副作用と思われるものが起こったならば他のＳＳＲＩｓまたは抗うつ薬に変薬することが一般である。上記２症例のときは fluvoxamine が本邦で唯一のＳＳＲＩｓであった。

ＳＳＲＩｓは三環系抗うつ薬と異なりＣＹＰ４５０酵素に対する強い阻害作用を有する。そしてＳＳＲＩｓは各薬物によりＣＹＰ４５０酵素阻害が異なる7)。例えば fluvoxamine はＣＹＰ１Ａ２の高度な阻害作用を持つ。ＳＳＲＩｓの中でこの阻害作用を持つのは fluvoxamine のみである21)。 fluvoxamine 投与によりカフェインの半減期が５時間から３１時間に延長する9)などという報告がある。また paroxetine の特徴としてＣＹＰ２Ｄ６の高度な阻害作用を有している2)。 このようにＳＳＲＩｓは個々の薬剤ごとに特殊な作用を持つ傾向がある。

症例１は fluvoxamine 服用１０ヶ月にて、症例２は服用７ヶ月にて吃音症の軽症化を認識する。症例１は社交不安障害を治したい一心であり吃音症は余り念頭になかった。症例２はうつ病性障害に苦しんでおり、かつ、１年以上服用しないと吃音症の軽症化は起こらないと考えていた。それ故に２症例とも自身の吃音症軽症化を認識し得なかったと思われる。

そして２症例とも吃音症軽症化を認識してからも fluvoxamine の服用を続けた。症例１は更に８ヶ月間、症例２は更に５ヶ月間連続服用した。症例１は１８ヶ月間、症例２は１２ヶ月間連続服用したことになる。

２症例とも吃音症の軽症化より１５年以上を経ているが吃音症は寛解と言えるほどの軽症化を維持している。少なくともこの２症例より、長期服用が吃音症の長期的な軽症化および寛解に必要と推測される。それは ＳＳＲＩｓに共通することなのか、fluvoxamine 独特のことなのか、判然としない。

吃音症治療に於いてベンゾジアゼピン系抗不安薬は用いない、という意見が強い4)。これはベンゾジアゼピン系抗不安薬の依存性を強く嫌う欧米医学界の考えと、パニック障害に頻用される alprazolam などが逆に一時的ながら吃音症を重症化させる6)ことが大きく影響していると思われる。

meprobamate が１８症例のうち１４症例に奏功するという報告が１９５８年に成されている17)。meprobamate による吃音症軽症化の報告は少なくとも４つ存在する。

現在は非ベンゾジアゼピン系選択的ＧＡＢＡ受容体アゴニストでパニック障害に効果があるとされる pagoclone が話題であったが、評価は芳しくない8,14)。

少なくともベンゾジアゼピン系抗不安薬である alprazolam、flutoprazepam、flunitrazepam は吃音症を一時的ながら重症化させる。alprazolam については「三環系抗うつ薬と同じ作用すなわち抗コリン作用を持っている故に吃音症を重症化させる」6)と言及されている。これは carbamazepine も抗コリン作用を持っている故に症例１に於いて carbamazepine を服用すると吃音症が却って一時的ながら重症化したことと機序を同じくする。

しかし、bromazepam、cloxazolam、diazepam、etizolam というベンゾジアゼピン系抗不安薬が吃音症に一時的ながらも奏功することは多い。これらのベンゾジアゼピン系抗不安薬が奏功するのは緊張が非常に強い神経症的な症例と考えられる。

本邦に於ける吃音症者の自助グループである「言友会」では減感作療法的発声練習つまり出席者全員の前に立ちスピーチを行う、また出席者全員で様々な討議をする。しかし「減感作療法的発声練習だけで何にもならなかった」と一度出席するのみに終わる吃音症者は多い。

また「言友会」は、吃音症故に“とじこもり”に陥っている児童や生徒などの存在を知ると、その家へ訪問し“とじこもり”から抜け出すよう話し合いを行う。

現在、「言友会」は薬物療法に対し否定的見解に立っている。その否定的見解は頑なであり、これは精神科への偏見故と考えられる。

【結論】

吃音症者の苦悩は想像以上に強い。軽症ならば言語療法で十分かもしれない。しかし重症ならば薬物などを用いないと社会的隠遁は避けられない。

薬物療法を否定し、頑なに言語療法などを強要または放置することは、人心の堕落激しく“いじめ”が蔓延する今日、吃音による社会的隠遁者を造り出すのみと筆者は確信する。

吃音症が盛んに研究されている欧米では、吃音症は脳機能障害という意見が強くなっており、薬を服用することが必要との意見に傾いてきている。

これからは重症の吃音症には「ＳＳＲＩｓの長期服用」などを積極的に取り入れてゆくべきと信じる。

----------多数の吃音症者に捧げる----------

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