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An Examination of Supplement Dose Dependence and Safety in Integrative Medicine for Cancer: Based on the Experience of Tabebuia avellanedae, a South American Medicinal Plant Commonly Known as Taheebo

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Abstract:

Clinical research of NQ801 extracted from Taheebo was tested for anti-tumor effects, dose dependence and safety of cancer patients. 4 advanced cancer patients were given daily NQ801 by oral ingestion during 3 months, and afterwards 3 times dose NQ801 were taken during more 3 months. As a result, NQ801 made to reduce the tumor in 3 patients in 4. In addition dose dependence effect of NQ801 was seen. And also no negative side effects were seen in this clinical examination.

The "NQ801" is suggested from above that it is the anti-tumor effects, dose dependence and safety of cancer patients.

Keywords: Integrative medicine for cancer, sapliments, NQ801, Dose dependence, safety of cancer patient

Introduction

Supplements have various roles in integrative treatment of cancer, such as improving effects on the body's internal environment (improvement of the gut environment, antioxidant effect, detoxifying effect, nutrient supplementation, and enhancement of the metabolism), and also immunostimulatory effect, inhibition of neovascularization, induction of cancer cell apoptosis, analgesic effect, etc. Various basic studies have been carried out on the effects of such supplements, and the results of clinical studies have also been reported from many medical institutions.

NQ801 is extracted from the inner bark of the tree *Tabebuia avellanedae* (common name taheebo), a medicinal plant native to South America that grows naturally in certain regions. NQ801 is the code name for the effective component, 5–hydroxy–2–(1–hydroxyethyl)–naphtho[2,3–*b*]furan–4,9–dione[1], which has a chemical structure that gives strong biological activity, and was isolated by a Kyoto university research group. The anticancer activity of NQ801 has been studied. It is reported to have (1) direct effects[2),3)] (selective toxicity, induction of apoptosis, inhibition of neovascularization, and suppression of metastasis and infiltration), (2) indirect effect[2),3)] (immunostimulation), and (3) auxiliary effects (antioxidant effect[4)], analgesic and sedative effect, and anti-inflammatory effect), on cancer cells[5),6),7)].

In the present study, we examined the anticancer effect of NQ801 clinically in cancer patients. We also carried out clinical investigations on the dose dependence of NQ801's effect, and its safety, using the newly developed product X6. X6 is a fortified taheebo extract powder prepared by adding a group of fractionated and extracted components that includes NQ801, called "NQ801 fraction", at six times (1.8 mg) the standard dose (0.3 mg) of NQ801 so far used in clinical studies.

Ⅰ. Methods

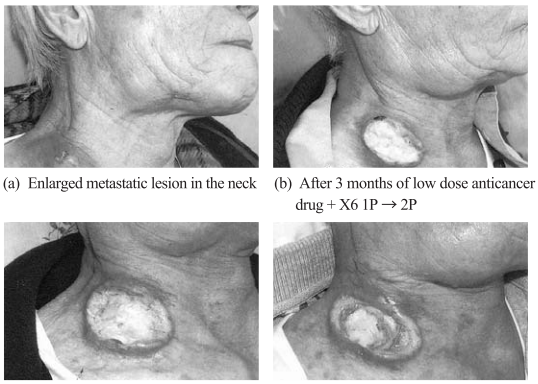
Four terminal cancer patients (Case 1: Cancer of the tongue metastasized into the neck, Case 2: Cancer of the upper jaw and buccal mucosa, Case 3: Cancer of the upper jaw, and Case 4: Rectal cancer), who had been informed by other hospitals that all their treatment options had been exhausted, were treated by giving 1.8 mg (1P)/day of X6 (NQ801-fortified taheebo extract powder) for three months, after explaining the treatment to them and obtaining written consent. During the next three months, the dose was raised to 3P (5.4 mg) /day, and the anticancer effect, effect on QOL and safety of the X6 supplement were evaluated clinically. Low doses of anticancer drugs, etc that the patients were taking before the start of the X6 treatment were continued so that the patients would not be deprived of the benefits of the integrative treatment. But, no additional supplements, which the patients were not taking earlier, were given. One patient (Case 3), as desired by him, continued the high dose vitamin C drip that he was receiving before the X6 treatment.

Ⅱ. Results

【Case 1】Tongue cancer metastasized into the neck (80-year-old male)

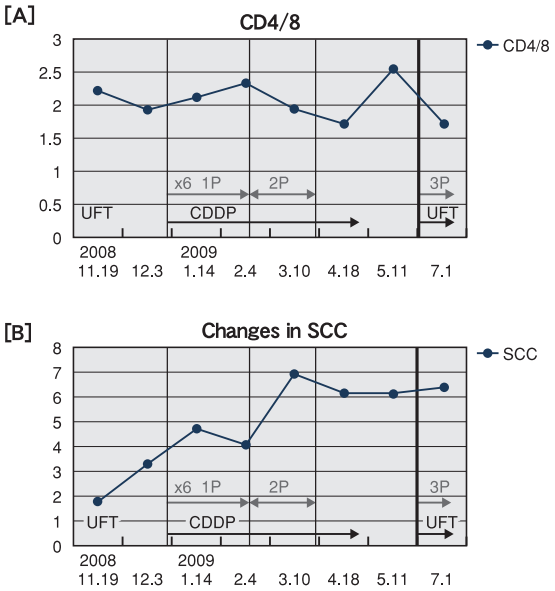
The patient had T2N2 cancer of the tongue in the year X, and had severe tongue pain and eating disorder. He underwent only partial resection of the tongue cancer because of his advanced age and his alcoholic hepatitis. He was taking only UFT 400 mg orally for the metastatic foci in the neck lymph nodes, and he was under observation. However, in the year X+1, the metastatic foci in the neck started to increase in size (Fig. 1-a). Therefore, low dose of anticancer drug (CDDP 5 mg/body, iv drip, once a week) treatment concurrently with 1P/day of X6 was given for two months. But, as the metastatic foci in the neck continued to enlarge, the dose of X6 was increased to

2P/day and the concurrent treatment continued for another month. But, the metastatic foci in the neck continued to grow (Fig. 1-b) and the tumor marker SCC increased (Fig. 2 [B]) during that time. However, the QOL did not decline and the patient could go on family trips to Guam and Okinawa from Hokkaido. Despite the increase in size of the metastatic foci, the CD4/8 ratio was maintained, which suggested that there was no decrease in immunocompetence (Fig. 2 [A]), and the QOL was maintained with improved liver function. No X6 was given during the next four months, and only the low dose treatment with the anticancer drug was continued. The metastatic foci increased in size (Fig. 1-c), and the CD4/8 ratio (immunocompetence) also worsened. Therefore, the low dose treatment with the anticancer drug (CDDP 5 mg/body, iv drip, once a week) was stopped. Instead, oral administration of UFT 400 mg concurrently with the increased dose of 3P/day of X6 was started. After two months of this treatment, the tumor in the neck was localized, as shown in Fig. 1-d, and the QOL during this period remained good.



(a) Enlarged metastatic lesion in the neck
(b) After 3 months of low dose anticancer drug + X6 1P → 2P
(c) After treatment with low dose anticancer drug alone
(d) After 2 months of oral UFT + X6 3P

(Fig.1) Case 1: Neck lymph node metastasis of tongue cancer.

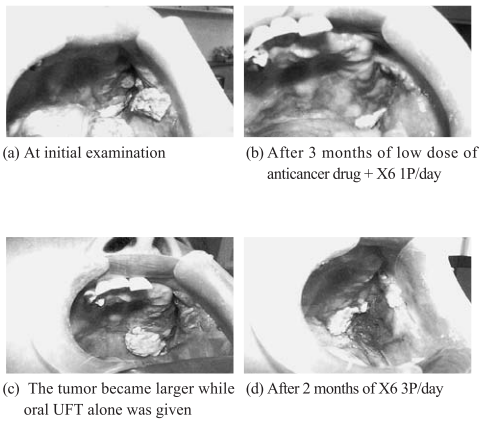


(Fig.2) Case 1: Changes in immunocompetence (CD4/8 ratio) and tumor marker (SCC) in the course of changing the dose of X6 (NQ801-fortified taheebo extract powder), 1P→ 3P.

【Case 2】Cancer of the left upper jaw and buccal mucosa (60-year-old female)

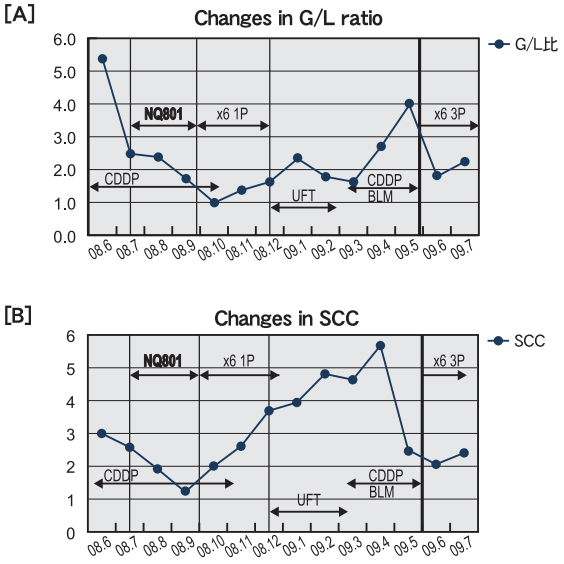
The patient was first given a low dose of anticancer drug (CDDP 5 mg/body, iv drip, once a week) for the cancer (Fig. 3-a). After that, concurrently with the anticancer drug, the standard dose of NQ801 was given for two months, and then X6 was given at 1P/day for three months (Fig. 4). This improved the granulocyte/lymphocyte (G/L) ratio (parasympathetic dominant state) (Fig. 4 [A]). Along with this change, the tumor also shrank (Fig. 3-b). She was coming for hospital visits in Sapporo from a far away location. As it was winter, the visits were temporarily halted and she was put on oral UFT 400 mg (Fig. 4). Three months later she returned to the hospital with an enlarged tumor (Fig. 3-c). She was put on low doses of anticancer drugs (CDDP 5 mg/body, once a week, plus BLM 5 mg/body, iv drip, once a week) for two months (Fig. 4). The SCC decreased once but the G/L ratio increased as the lymphocyte count decreased, and the tumor increased in size. Even though the anticancer drugs were being given at low doses, she lost appetite and therefore the anticancer drugs (CDDP and BLM, iv drip) were discontinued. Instead, X6 3P/day was started (Fig. 4).

Two months after the start of the X6 3P/day treatment, the tumor did not show rapid increase in size though there was no shrinkage either (Fig. 3-d). The G/L ratio improved again (Fig. 4 [A]), and the QOL did not worsen during this period.



(a) At initial examination
(b) After 3 months of low dose of anticancer drug + X6 1P/day
(c) The tumor became larger while oral UFT alone was given
(d) After 2 months of X6 3P/day

(Fig.3) Case 2: Cancer of the upper jaw and buccal mucosa.

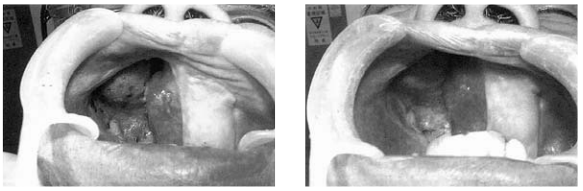


(Fig.4) Case 2: CDDP 5 mg/day + NQ801 (2 months) → X6 (NQ801-fortified taheebo extract powder) 1P (3 months) → 3P.

【Case 3】Recurrence after surgery for cancer of the upper jaw (70-year-old male)

The patient had recurrence of cancer after the surgery and was told in the year X that he would live only for another 6 months, and all treatments were stopped. Since then, the patient received no anticancer treatment or radiotherapy, and volunteered to have Gerson's diet therapy along with yoga therapy and hot spring therapy. After that, he also had high dose vitamin C drips once or twice a week. The progression of the tumor became very slow, and the patient visited our hospital for the first time in the year X + 3. However, the tumor continued to advance, and the patient started taking X6 1P/day concurrently (Fig. 5-a) from the year X+3. Three months from the start of the X6 treatment, MRI showed that the tumor had not increased in size form the previous observation, and thus the cessation of tumor enlargement could be confirmed for the first time through imaging. After that, X6 was continued at the increased dose of 3P/day, and concurrently, the diet therapy and high concentration vitamin C drip once or twice a week were also continued.

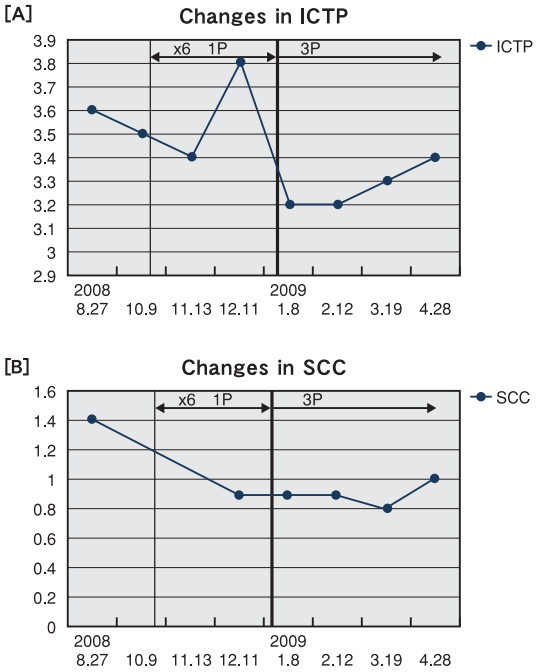
After one month on X6 3P/day, MRI showed shrinkage of the tumor (Fig. 6) for the first time. The MRI finding (Fig. 7) after two months on X6 3P/day led to the comment, "Staining of the tumor by gadolinium has clearly decreased, which suggested decreased tumor activity or decreased blood flow, intravenous injection of gadolinium was smooth, and there was no leakage of the contrast agent". During this period, the tumor marker ICTP increased once and then decreased sharply, whereas SCC decreased continuously (Fig. 5 Bottom). Intraoral observations also showed that the tumor that had been advancing slowly had shrunk (Fig. 5 Top) three months after the dose of X6 was increased form 1P to 3P/day.



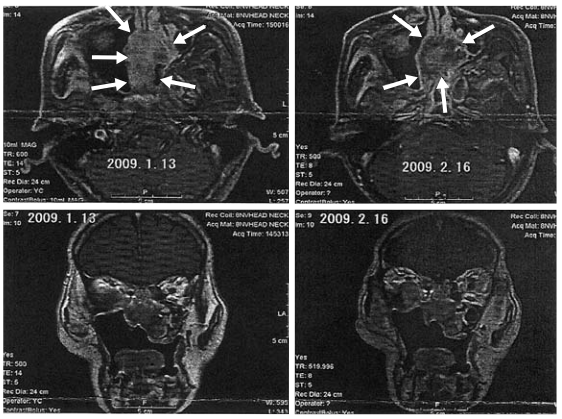
(a) Immediately before the start of the X6 oral treatment

(b)) After X6 1P (3 months) and 3P (3 months)

Changes in tumor markers during X6 (NQ801-fortified taheebo extract powder) oral treatment 1P → 3P



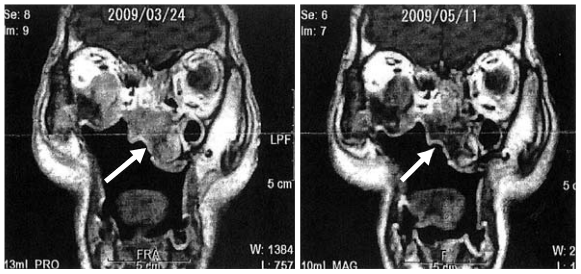
(Fig.5) Case 3: Cancer of the upper jaw.



【Imaging findings】
In a comparison of MRI of February 16, 2009 with that of January 13, 2009, the residual tumors in the nasal septum, the right orbit, etc appeared to have shrunk slightly.
The post imagining staining intensity also appeared to be slightly less in February.

【Impression】
The residual tumors in the nasal septum, ethmoid sinus, right orbit, etc appeared to have shrunk, though only slightly.

(Fig.6) Case 3: MRI findings one month after the start of the X6 3P treatment.



【Imaging findings】
In a comparison of MRI of May 11, 2009 with that of March 24, 2009, there was little change in the size of the tumors known to be present. However, the intensity of gadolinium staining of the tumors was clearly less in May. The possible reasons for this are a decrease in tumor activity and a decrease in blood flow.

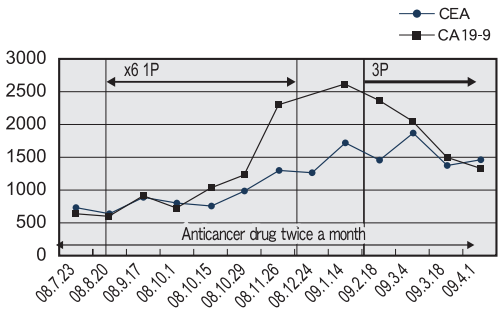
【Impression】
There was little change in the size of the tumors known to be present in the nasal cavity and the right orbit. However, the intensity of gadolinium staining of the tumors was clearly less in May.

Note：The intravenous injection of gadolinium was smooth, and there was no leakage of the contrast agent.

(Fig.7) Case 3: MRI findings three months after the start of the X6 3P treatment.

【Case 4】Rectal cancer metastasized into the lung (46-year-old male)

The patient was under treatment at another hospital with anticancer drugs for Stage IV rectal cancer metastasized into the lung. He was then given concurrent treatment of X6 1P/day for four months. There was no sign of tumor shrinkage, and the level of the tumor marker also increased (Fig. 8). However, the QOL was maintained during this period, and the treatment with anticancer drugs was continued. In the following four-month period, when he did not take X6, the tumor further enlarged and the tumor marker also increased. Therefore, X6 was resumed at the higher dose of 3P/day concurrently with the ongoing treatment with anticancer drugs. One month later, the tumor marker decreased, the tumor was seen to have shrunk, and the QOL improved sufficiently for him to return to work.



The tumor marker levels decreased only when the dose of X6 was increased to 3P.

(Fig.8) Case 4: Lung metastasis of Stage IV rectal cancer (46-year-old patient)
Anticancer drug → X6 (NQ801-fortified taheebo extract powder) 1P → 3P
(The patient received anticancer drug treatment from the Department of Gastrointestinal Medicine of another hospital, and that hospital provided the data).

Ⅲ. Conclusion

Ueda, Tokuda and coworkers[8),9)] had reported that NQ801 inhibited proliferation of 21 types of cancer cells *in vitro*, including lung cancer cells, and had selective toxicity, with little effect on normal cells at a dose that was effective against cancer cells. Ebina[2),3)] had reported that *T. avellanedae* extract, which contains NQ801, showed inhibitory effects on metastasis and infiltration of cancer cells, induced their apoptosis, and had an inhibitory effect on neovascularization.

Therefore, in the present study, we undertook clinical investigations on the anticancer effect of NQ801 in cancer patients. We also investigated the dose dependence of the anticancer effect of NQ801, and its safety, using the newly developed product X6 (NQ801-fortified taheebo extract powder), which contains six times the standard dose of NQ801 so far used in clinical studies. The following conclusions were reached.

【Conclusions from Case 1】

X6 showed anticancer effect, as the tumor became localized in the eighth week after the dose of X6 was increased to 3P/day (Fig. 1), although the disease remained as PD when the dose was 1P/day.

The immunocompetence (CD4/8 ratio) was maintained while the patient was taking X6, and showed maximum decrease when the X6 treatment was withheld (Fig. 2 [A]). Along with this decrease, the metastatic foci in the neck also showed the maximum enlargement. The tumor marker SCC showed a temporary decrease when he was under combination therapy of CDDP 5 mg/body and X6 1P/day, and also under combination therapy with 2P/day of X6. But, overall it increased (Fig. 2 [B]). Nevertheless, his QOL was maintained during this period, and he could travel from Hokkaido to far away places without incident.

Based on the above results, it was concluded that the X6 form of NQ801 had an immunostimulatory effect, an indirect anticancer effect, apart from its direct anticancer effects. The direct anticancer effects, in particular, showed dose dependence, and blood samples tested during the study did not reveal any biochemical abnormalities. But, there was a gradual increase in anemia with the advancement of the cancer.

After the study, the cancer worsened, the patient was hospitalized for palliative care, X6 was discontinued, and he died in the third week of hospitalization.

Thus, in spite of the terminal cancer, the patient's QOL was maintained while he was taking X6, and the period spent in hospital for palliative care was short.

【Conclusions from Case 2】

Concurrent use of X6 1P/day with low dose of the anticancer drug for three months lowered the G/L ratio (parasympathetic dominant state) and there was no adverse reaction or loss of appetite even while she was on the anticancer drug. The X6 1P/day treatment, especially with the concurrent use of the anticancer drug, increased lymphocytes and improved parasympathetic dominance (decreased the G/L ratio; Fig. 4 [A]), and the QOL was maintained.

During this period, however, no clear improvement in immunocompetence (CD4/8 ratio) could be detected hematologically (data not shown). When we take the clinical findings (Fig. 3) and changes in SCC (Fig. 4 [B]) into account, we can see that X6 did not show anticancer effect (Fig. 5-a) during the treatment with X6 1P/day alone for three months following the drip administration of the anticancer drug, and also during the treatment with X6 3P/day alone for three months, as the SCC increased in both these periods.

The tumor shrunk only when NQ801 was given concurrently with the low dose anticancer drug for two months.

After the study period, the treatment with X6 3P/day concurrently with the low dose of anticancer drug was started and is continuing until now, but the tumor is showing signs of enlargement, although the QOL is maintained.

【Conclusions from Case 3】

The tumor markers ICTP and SCC decreased after the X6 treatment started (Fig. 5 Bottom, ICTP decreased after increasing once) and clinically also the tumor was seen to have shrunk, for the first time. After three months on X6 3P/day, the MRI showed a clear decrease in uptake of the contrast agent, which suggested lowered activity of the tumor (Fig. 7). The X6 3P/day treatment changed into parasympathetic dominance favorably (decreased the G/L ratio) (data not shown). Besides this, the patient showed no biochemical or clinical abnormality during the X6 treatment.

The results of this case also suggested dose dependence of the effect of NQ801 and its safety.

The patient continues to be on X6 3P/day concurrently with diet therapy and high dose vitamin C drip, and the tumor is shrinking and has reached about half its former size.

【Conclusions from Case 4】

Treatment with X6 1P/day for four months did not improve the tumor marker level. But, the tumor marker decreased, and the QOL improved, after increasing the dose to 3P/day.

This case also suggested the dose dependence of NQ801's effect, and its safety.

Afterwards, as his physical condition improved, the patient was treated with a not yet approved anticancer drug in another hospital. He died three months later from adverse reactions to the anticancer drug.

As discussed above, NQ801 showed anticancer effect in cases 1, 3, and 4. Suppression of cancer proliferation was noticed when patients received 3P/day of X6, which showed the dose dependence of the effect of NQ801. Besides this, NQ801 showed better anticancer effect when used in combination with an anticancer drug than when used singly. This effect was particularly clear in Case 2.

In spite of all the patients having advanced cancer, treatment with NQ801 improved parasympathetic dominance, and also immunocompetence. The QOL as either maintained or improved in all the cases of advanced cancer studied here. It is expected that treatment with NQ801 would improve or maintain QOL in advanced cancer patients for whom all other treatments have been given up, and in patients on palliative care. There were no abnormal clinical or biochemical findings when patients are given X6, which has six times the normal dose of NQ801, even at the high dose of 3P/ day.

Ⅳ. Areas for future studies

Clinical investigations of the present study have suggested that the anticancer effect of NQ801 is dose dependent, and confirmed the safety of NQ801 up to 5.4 mg/day. In the future, it is necessary to investigate the dose requirement of NQ801, when used in combination with anticancer drugs in specific cases, by using it on a larger number of patients in integrative treatment of cancer.

Literature

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がん統合医療におけるサプリメントのDose dependenceとその安全性の考察

―南米薬用植物タベブイア・アベラネダエ（通称タヒボ）の使用経験から―

平田　章二

平田口腔顎顔面外科 腫瘍内科 がんヴィレッジ札幌

（要旨）

南米薬用植物である天然木タベブイア・アベラネダエ（通称タヒボ）から抽出された「NQ801」は、抗がん作用として、がん細胞に対する①直接作用②間接作用そして③補助作用が研究・報告されている。そこで「NQ801」のがん患者に対する抗腫瘍効果とそのDose dependence性、さらに安全性について臨床的に検討した。

進行がん患者4例に、「NQ801」強化エキス末2g/dayを3ヵ月間、その後3倍量（6g/day）を3ヵ月間飲用してもらった。

4例中3例において「NQ801」の摂取量を3倍にすることにより、より抗腫瘍効果がみられた。しかし副作用は見られなかった。また抗がん剤を使用していた3例は、副作用を軽減しながら長期間抗がん剤治療が可能であった（腫瘍との共存）。

今回の臨床研究により、がん統合医療においてNQ801の抗腫瘍効果が確認され、さらにDose dependence性があることが示唆された。また臨床的にNQ801（6g/day）の安全性も確認された。

キーワード：がん統合医療、サプリメント、NQ801、用量依存性、安全性

はじめに

がん統合医療におけるサプリメントの役割として、体内環境改善作用（腸内環境改善、抗酸化作用、デトックス作用、栄養補給、代謝改善など）、さらに免疫賦活作用、新生血管抑制作用、がん細胞アポトーシス作用、鎮痛作用など、数多く基礎研究が行われ、さらに臨床研究結果も多くの施設から報告されている。

中でも南米薬用植物である天然木タベブイア・アベラネダエ（通称タヒボ）から抽出された「NQ801」（京都大学の研究者らのグループが、生理活性の強い化学構造式の有効成分5–hydroxy–2–(1–hydroxyethy1)–naphtho[2,3–*b*]furan–4,9–dione[1]（成分コードネームNQ801）を特定地域に自生するTA（通称タヒボ）の内部樹皮部より単離した。「NQ801」は、抗がん作用として、がん細胞に対する①直接作用[2),3)]（選択毒性、アポトーシス誘導、血管新生阻害、転移・浸潤能抑制）②間接作用[2),3)]（免疫賦活）、そして③補助作用（抗酸化作用[4)]、鎮痛・鎮静作用、抗炎症作用）が研究・報告[5)-7)]されている。

そこで今回、「NQ801」のがん患者に対する抗腫瘍効果について臨床的検討を行った。またNQ801のDose dependence性を考え、「NQ801」を含む成分群（「NQ801」フラクション）を分画、抽出し、それをこれまで臨床報告で一般に用いられていた量(0.3mg)の6倍増量添加（1.8mg）した「x6」（NQ801通常量×6の強化エッセンス末）が開発されたので、今回さらに、「NQ801」のがんに対するDose dependence性とそのときのがん患者への安全性についても臨床的に検討を行った。

Ⅰ. 方法

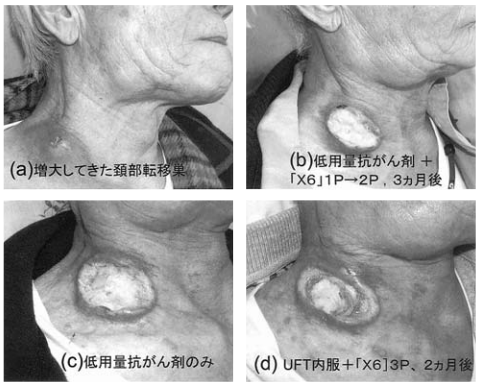
他院からすでに治療手段がないと宣告された進行末期がん患者4例（舌がん頚部転移、上顎・頬粘膜がん、上顎がん、直腸がん）に対し、充分な説明と同意のもと、「x6」（NQ801強化エッセンス末）1P/日（1.8mg/day）を3ヵ月間、その後3倍量3P/日（5.4mg/day）を3ヵ月間飲用してもらい、そのときの効果（抗腫瘍効果とQOLに関して）と安全性を臨床的に検討した。その間統合医療として患者の不利益にならないよう、低用量抗がん剤など、「x6」飲用前から行っていた治療は継続した。しかしその他のサプリメントはもともと使用していなかったため、特に追加併用はしなかった。1例（症例3：上顎がん）で「x6」の飲用前から高濃度ビタミンC（VC）点滴療法を受けていたため、患者の希望によりそのまま併用した。

Ⅱ. 結果

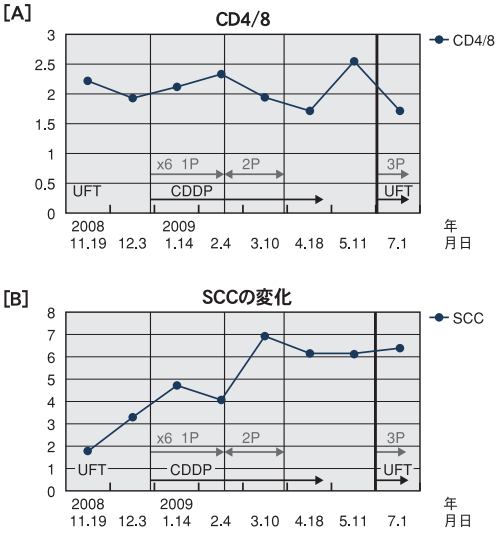
【症例1】舌がん頚部転移（80歳）

X年、舌がんT2N2のため、舌疼痛と摂食障害が強かった。そこで年齢的にも、またアルコール性肝炎もあったため、舌がん部分切除手術のみ施行。頚部リンパ節転移巣に対しては、その後UFT 400mg内服のみで経過見ていたが、X＋1年、頚部転移巣は増大してきた（Fig.1a）。頚部転移

巣に対しては、低用量抗がん剤（CDDP 5mg/bodyを1回/週Div）と同時に「x6」1P/日を2か月間併用開始したが、頚部転移巣は増大傾向にあり、「x6」2P/日に増量してさらに1ヶ月間併用した。しかし頚部転移巣は増大（Fig.1b）。その間腫瘍マーカーSCCは増加した（Fig.2[B]）。しかし、QOLは維持され、家族とグアム旅行、沖縄旅行へ行くことができた。転移巣の増加にもかかわらず、その間CD4/8は維持され、免疫能の低下は見られず（Fig.2[A]）、QOLが維持された（肝機能も改善）。その後4ヶ月間「x6」は中断し低用量抗がん剤のみの治療で経過を過ごした。転移巣は増大（Fig.1c）。CD4/8比（免疫能）も悪化したため低用量抗がん剤（CDDP 5mg/bodyを1回/週Div）は中止とした。その後はUFT 400mg内服に「x6」を3P/日に増量して併用した。「x6」を3P/日併用2ヶ月後、頚部腫瘍はFig.1dのごとく、限局化した。その間のQOLは良好であった。



(Fig.1) 症例1. 舌がん頚部リンパ節転移

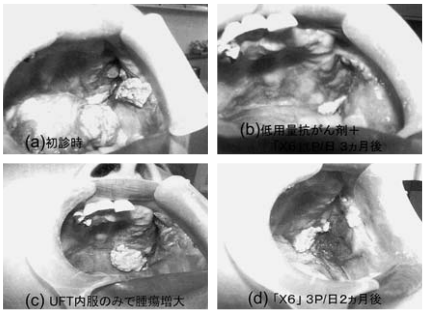


(Fig.2) 症例1.「x6」（NQ801強化エッセンス末）1P→3Pの免疫能（CD4/8）と腫瘍マーカーSCCの変化

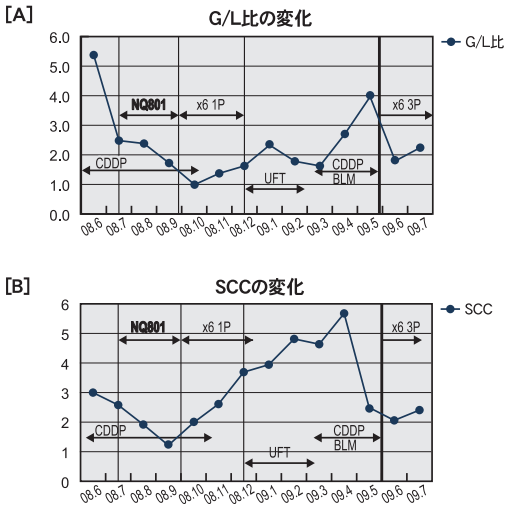
【症例2】左上顎・頬粘膜がん（60歳）

左上顎・頬粘膜がん（Fig.3a）に対し、低用量抗がん剤（CDDP 5mg/bodyを1回/週Div）先行後、通常量の「NQ801」を2ヶ月間、その後「x6」1P/日を3か月間併用（Fig.4）したところ、G/L比は低下した（副交感神経優位状態に改善）（Fig.4[A]）。それに伴い腫瘍は縮小した（Fig.3b）。その後札幌へは遠方から通院していたため、冬季間患者の希望により一時通院中断し、UFT 400mg内服のみとした（Fig.4）。3ヵ月後、腫瘍が増大してきた、と再来（Fig.3c）。再度低用量抗がん剤（CDDP 5mg/bodyを1回/週＋BLM 5mg/body 1回/週をDiv）を開始（2ヶ月間）（Fig.4）。いったんSCCは低下したが、リンパ球数の減少に伴いG/L（顆粒球/リンパ球）比は増加し、腫瘍は増大した。低用量抗がん剤でも食欲がなくなったため抗がん剤（CDDP, BLMのDiv）は中止した。その後「x6」3P/日を開始した（Fig.4）。

「x6」3P/日2ヶ月後、腫瘍の縮小は確認できなかったが、急激な増殖はみられなかった（Fig.3d）。しかし再びG/L比は改善し（Fig.4[A]）、その間QOLは保たれた。



(Fig.3) 症例2. 上顎・頬粘膜がん

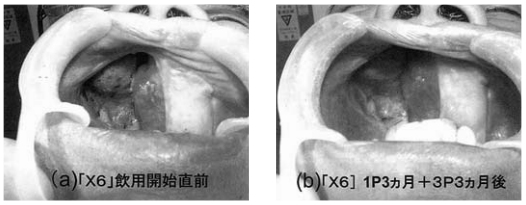


(Fig.4) 症例2. CDDP 5mg/day+NQ801（2ヶ月間）→「x6」（NQ801強化エッセンス末）1P（3ヶ月間）→3P

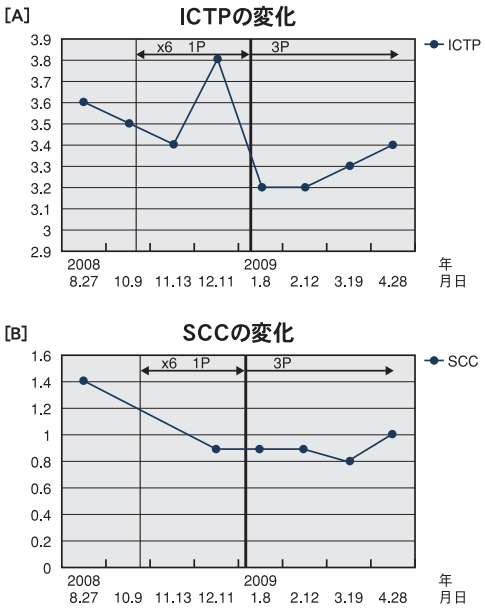
【症例3】上顎がん術後再発（70歳）

上顎がん術後再発に対し、X年に余命半年と宣告され、治療が打ち切られた。その後いっさいの抗がん剤治療、放射線治療は受けず、患者自身でゲルソン療法による食事療法を中心として、それにヨーガ療法、温泉療法、その後高濃度VC点滴療法を週1～2回施行。腫瘍の進展は非常にゆっくりとなり、X＋3年が経過し当院初診。しかし腫瘍は進行していった。X＋3年から「x6」1P/日飲用併用開始（Fig.5a）。「x6」1P/日飲用開始3ヵ月後のMRI検査で「腫瘍の大きさが前回と変化なし。」というコメントをもらい、はじめて腫瘍の増殖停止が画像的にも認められた。その後「x6」3P/日に増量し飲用継続。継続併用療法として、食事療法＋高濃度VC点滴療法を週1～2回。

「x6」3P/日1ヵ月後、MRI所見（Fig.6）にて、はじめて腫瘍の縮小が確認。



「x6」（NQ801強化エッセンス末）飲用（1P→3P）による腫瘍マーカーの変化

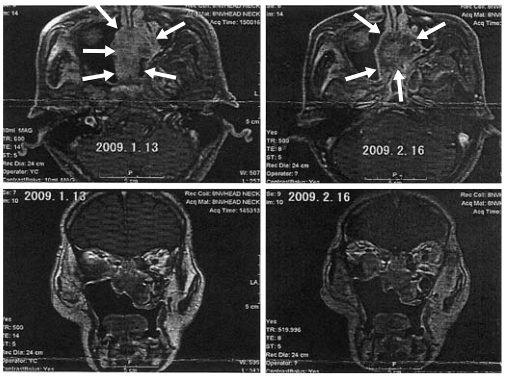


(Fig.5) 症例3. 上顎・頬粘膜がん

さらに「x6」3P/日2ヵ月後のMRI所見（Fig.7）にて、「腫瘤のガドリニウムによる染まりの程度は明らかに低下しており腫瘤の活動性の低下ないし血流の低下が考えられる。ガドリニウム静注はスムーズに行われ、造影剤の漏れはない。」とのコメント。

その間の腫瘍マーカーをみると（Fig.5下段）、ICTPは一旦増加してから、急激に減少した。SCCは継続的に低下していった。

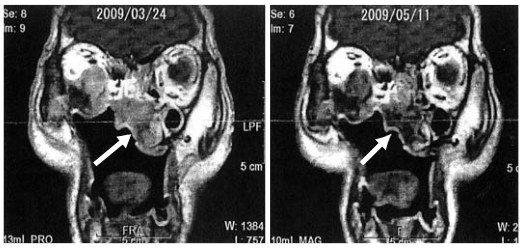
口腔内所見でも、ゆっくりながら進行していった腫瘍は、「x6」1Pから3P/日へ増量3ヵ月後、腫瘍の縮小が認められた（Fig.5上段）。



【画像所見】
2009 年 1 月 13 日の MRI と比較しました。
鼻中隔及び右眼窩等に認められた残存腫瘤は前回よりもやや小さくなっているように見えます。また造影後の染まりもやや薄くなったように見えます。

【Impression】
鼻中隔、篩骨洞、右眼窩などの残存腫瘤はごく軽度小さくなった印象を受けます。

(Fig.6) 症例3.「x6」3P開始1ヵ月後MRII所見



【画像所見】
2009 年 3 月 24 日の MRI と比較しました。
以前から知られている腫瘤の大きさに変わりはありません。しかしながら腫瘤ガドリニウムによる染まりの程度は今回明らかに低下しています。腫瘤の活動性の低下ないし血流の低下が考えられます。

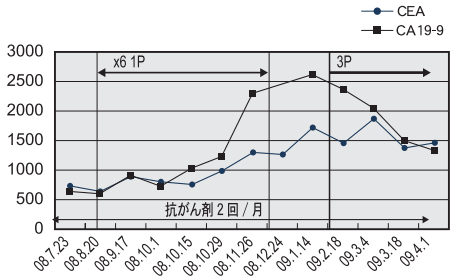
【Impression】
以前から知られている鼻腔及び右眼窩内腫瘤の大きさに変化はありません。
しかしながらガドリニウムよる腫瘤の染まりは前回よりも明らかに低下しています。

追伸：ガドリニウム静注はスムーズに行われた。造影剤の漏れはありませんでした。

(Fig.7) 症例3.「x6」3P開始3ヵ月後MRII所見

【症例4】直腸がん　肺転移（46歳）

直腸がん肺転移Stage Ⅳに対し、他病院にて抗がん剤継続治療を受けていた。そこに「x6」1P/日を4ヶ月間飲用併用開始。腫瘍の縮小傾向は見られず、腫瘍マーカーも増加していった（Fig.8）。しかしその間QOLは保たれ、抗がん剤は継続的に行われた。「x6」4ヵ月間中止中、さらに腫瘍は増大し、腫瘍マーカーも増加していった。その後継続的に行われている抗がん剤に、「x6」を3P/日に増量して併用した。その1ヵ月後より、はじめて腫瘍マーカーが低下し、腫瘍縮小が見られ、QOLも改善し、仕事に復帰した。



「x6」3Pに増量して、はじめて腫瘍マーカーが低下した

(Fig.8) 症例4. 直腸がん肺転移（46歳）Stage Ⅳ
抗がん剤→「x6」（NQ801強化エッセンス末）1P→3P
（抗がん剤治療は他病院消化器科にて受け、データも提供）

Ⅲ.結論

上田・徳田らの研究[8),9)]によれば、NQ801が肺がんを始めとする21種のがん細胞の増殖を抑制し（*in vitro*）、がん細胞に効果がある投与量では正常細胞にほとんど影響を与えない選択毒性をもつと報告している。また海老名[2),3)]はNQ801を含むTAが、がん細胞に対し転移浸潤抑制、アポトーシス誘導、血管新生阻害作用をもつことを報告している。

そこで今回、「NQ801」のがん患者に対する抗腫瘍効果について臨床的に検討を行った。またNQ801の用量依存性を考え、それをこれまで臨床報告で一般に用いられていた量の6倍増量添加した「x6」（NQ801通常量×6の強化エッセンス末）が開発されたので、さらに、「NQ801」のがんに対するDose dependence性とそのときの安全性についても臨床的に検討を行った。

【症例1】の結論

抗腫瘍効果に関して、「x6」IP/日のときはPDであったが、「x6」3P/日に増量して8週目で、腫瘍が限局化し（Fig.1）、抗腫瘍効果がみられた。

免疫能（CD4/8）は、「x6」飲用中は維持されたが、「x6」中断中に、一番低下した（Fig.2-[A]）。それに伴い、頚部転移巣も一番増大した。腫瘍マーカーSCCは、CDDP 5mg/bodyに「x6」IP/日の時と、さらに「x6」2P/日を併用後に、一時的に減少したが、全体として増加した（Fig.2-[B]）。しかしその間、QOLは保たれ、無事に北海道から遠方へ旅行にも行くことも出来た。

以上より、「NQ801」の「x6」は、腫瘍に対しては、間接的抗腫瘍効果の免疫増強効果と直接的抗腫瘍効果がみられたと思われた。特に直接的抗腫瘍効果は、Dose dependence性がみられ、またそのときの採血で生化学的異常は認められなかった。しかしがんの進行につれ、貧血が徐々に進んだ。

その後、腫瘍は進行し、緩和ケア入院。「x6」も中止し、3週目で永眠。

末期がん状態にもかかわらず、「x6」飲用中はQOLも保たれ、緩和ケア入院期間も短かった。

【症例2】の結論

低用量抗がん剤に「x6」1P/日を3か月間併用したところ、G/L比は低下（副交感神経優位状態に改善）し抗がん剤を使用している間も、副作用や食欲不振は見られなかった。「x6」1P/日飲用中（特に低用量抗がん剤併用中）で、リンパ球が増加して副交感神経優位（G/L比の低下;Fig.4[A]）となり、QOLが維持された。

しかしその間、血液学的に免疫能（CD4/8)の明らかな改善は見られなかった（Figはなし）。

抗腫瘍効果は、臨床所見（Fig.3）とSCCの変化（Fig.4[B]）を照らし合せてみると、抗がん剤点滴先行後に「x6」を単独で1P/日（3ヶ月間），3P/日（2ヶ月間）飲用したが、両方ともSCCが増加し、抗腫瘍効果は認められなかった。（Fig.5a）

腫瘍が縮小したのは、「NQ801」を2ヶ月間、低用量抗がん剤と併用時であった。

その後現在、低用量抗がん剤と「x6」3P/日併用継続しているが、腫瘍は増大傾向にある。しかしQOLは維持されている。

【症例3】の結論

腫瘍マーカー(ICTP、SCC)は「x6」服用後低下し(Fig.5下段:ICTPは一旦増加後低下)、臨床的にもはじめて腫瘍は縮小した。「x6」3P/日3ヵ月間飲用後、MRI所見にて造影剤の取り込みが明らかに減少し、腫瘍の活動性の低下が示唆された(Fig.7)。「x6」3P/日で副交感神経優位(G/L比の低下)に転換した(Figはなし)。また、「x6」飲用中、生化学的や臨床的に異常所見は見られなかった。

本症例においても、NQ801のDose dependence性と安全性が示唆された。

その後現在も、食事療法+高濃度VC点滴療法に「x6」3P/日を併用継続しているが、腫瘍は、約半分に減少中。

【症例4】の結論

「x6」1P/日(4ヵ月間)飲用したときには、腫瘍マーカーは改善しなかったが、3P/日に増量してそれ以降は腫瘍マーカー値が低下し、QOLも改善した。

本症例においても、NQ801のDose dependence性と安全性が示唆された。

その後、体調がよくなったとのことで、他院にて未承認薬の抗がん剤を使ったところ、その副作用で3ヵ月後に永眠。

以上より、症例1、3、4で抗腫瘍効果が見られ、「x6」を3P/日飲用したときの方が、腫瘍の増殖抑制が見られ、NQ801のDos dependence性がみられた。また、NQ801単独飲用よりは、抗がん剤との併用の方が、抗腫瘍効果がみられた。症例2においては、特にそうであった。

さらに、進行がん患者にもかかわらず、NQ801飲用によって、副交感神経優位状態へ改善がみられ、また免疫能の改善がみられた。今回どの進行がん症例においてもQOLの維持・改善がみられた。治療が打ち切られた、あるいは緩和医療を受けている進行がん患者において、NQ801飲用は、QOL改善・維持が期待される。

そしてNQ801を通常飲用する6倍量添加した「x6」、さらにそれを3P/日飲用したときも、生化学的、臨床的に異常値や異常所見は観察されなかった。

Ⅳ.今後の研究課題

今回の臨床研究により、NQ801の抗腫瘍効果にはDose dependence性があることが示唆された。そしてNQ801(5.4mg/day)の安全性が確認された。今後は、がん統合医療におけるがん治療の中で、NQ801が抗がん剤などとの併用で、どのような症例に、どのくらいの用量が必要なのか、さらに症例を重ね、研究する必要がある。

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