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Experience with Administration of BioBran in Patients with Chronic Rheumatism

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Abstract

The functional food, rice bran arabinoxylan derivative (BioBran), was administered for a long period to patients with chronic rheumatism given mainly symptomatic treatments with steroids, to evaluate its supplementary effect with representative treatments for rheumatism, such as steroids, analgesics, and thermotherapy. Steroids are essential for treatment of rheumatism, but it is desirable to minimize the dose, because they may cause adverse reactions. In recent years, there have been many reports on the functions of food ingredients, including superoxide scavenging and biophylaxis improving actions. This study evaluated the efficacy of BioBran, a functional food material. BioBran has been reported to have the effects of activating natural killer cells (NK cells) and inhibiting inflammation. The author confirmed and reported that it relieved cold symptoms in the elderly. The present study, where 8 patients with chronic rheumatism were given BioBran for 6 to 12 months, demonstrated the improvements of symptoms and QOL, suggesting its effectiveness.

Key words: Rice bran arabinoxylan derivative, rheumatism, supplementary treatment, and inhibition of inflammation

Introduction

Chronic rheumatism is a kind of autoimmune disease, where the IgG-type autoantibody, rheumatoid factor, and IgM in response to IgG are produced in synovial fluid and recognize each other to form an IgM-IgG complex, which induces inflammatory reactions. The immune complex activates complements, which promotes tissue destruction by attracting polymorphonuclear leukocytes and simultaneously activates basophils and platelets, stimulates release of histamine and serotonin, and increases vascular permeability, leading to further increase in immune complex deposition. Corticosteroids and nonsteroidal anti-inflammatory drugs are generally used in treatment of rheumatism. Immunosuppresants are also sometimes combined to inhibit the production of autoantibodies. Thus, patients are likely to experience adverse reactions. In this study, the rice bran arabinoxylan derivative (BioBran), a functional food with immunomodulatory and anti-inflammatory effects, was

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administered to evaluate its supplementary effect in drug treatment with steroids and analgesics.

Study method and clinical courses

BioBran, a derivative of hemicellulose contained in the rice coat, is a biological response modifier (BRM) that mainly consists of polysaccharide composed of arabinose and xylose[1]. Eight patients with chronic rheumatism were administered BioBran for 6-12 months to observe changes in their subjective symptoms and CRP and improvement in QOL. Five of 8 patients were on steroids and analgesics and the others on analgesics, Chinese medicines, and thermotherapy.

The clinical courses of 3 patients who responded well to BioBran will be reported below.

Case 1

Symptoms and treatments

A 78-year-old woman received regular treatment for osteolytic rheumatism from March 1998. The disease was classified as Stage IV in Class III by the Stein-Blocker classification.

The patient was orally given Predonine at 10 mg and Bucillamine at 200 mg/day as a symptomatic therapy. She had a severe pain and walking difficulty, and bone destruction was progressive. Artificial joint replacement was recommended, but postponed on her wish. After obtaining her consent, BioBran was administered from April 17. She had severe pain in both hands and knees and the joints, slept poorly, and was almost bedridden. Serological test results were ++ for RA test, 65 IU/ml for RF, and 2.0 mg/dl for CRP. The dose of BioBran was 1 g/day during the 1st week, 2 g/day for the next 3 weeks, and 3 g/day after that.

Clinical course

Pain in the hands and feet were relieved at 1 week of BioBran intake, and she was able to sleep well and walk using a walker. She had reduced pain in the knee and foot joints at 2 weeks and could walk with a cane at 1 month. In the serological test on October 5, the RA test result was +, RF 34 IU/ml, and CRP 0.6 mg/dl, and the steroid and DMARD were withdrawn. On January 4, 1999, the RA test was -, RF 14 IU/ml, and CRP 0.6 mg/dl, and the disease followed a good course (the normal range for RF was ≤20 IU/ml) (Figure 1).

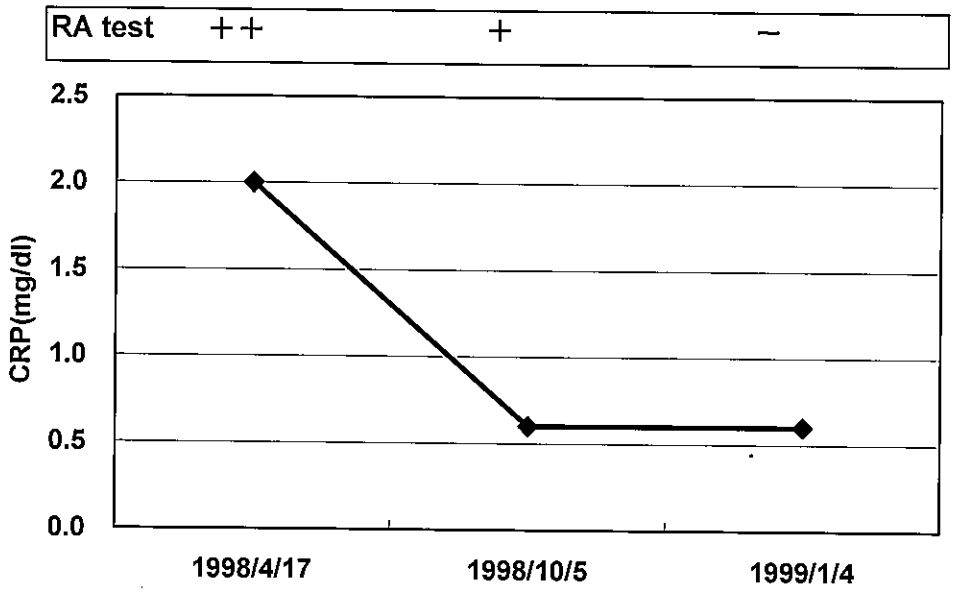

Figure 1 Changes in CRP and RA test

Case 2

Symptoms and treatment

A 77-year-old woman visited our clinic in March 2003. She had severe pains in the hand and foot joints, sleeplessness, and markedly reduced physical strength because of decreased appetite. The disease was classified as Stage IV in Class III. The RA test result was +++, RF 500 IU/ml, and CRP 1.8 mg/dl. She was diagnosed as having typical rheumatism. The steroid Predonine at 10 mg and a DMARD were given combined with thermotherapy, but pain persisted without any effect. Administration of BioBran at 3 g/day was started on June 20, 2000, and continued for 1 year, and then the dose was decreased to 2 g/day. She receives the therapy now.

Clinical course

Pain in the hands and feet were reduced at 3 days of administration of BioBran, and the patient was able to sleep and had increased appetite. At 3 months, pain in the hand and foot joints were further reduced, and she gained 2 kg. In late December at 6 months, the pain became endurable and test values improved: the RA test was ++, RF 62 IU/ml, and CRP 1.0 mg/dl. The steroid was withdrawn and only the DMARD was given. In June 2001, she still took BioBran at 2 g/day and symptoms were stable.

Case 3

Symptoms and treatment

A 39-year-old woman visited our clinic on June 10, 2000. A diagnosis of rheumatism was made and she was given steroid Predonine at 15 mg, an analgesic, Chinese medicine, and thermotherapy. BioBran was

administered from October 5. The dose was 1 g/day during the 1st week, 2 g/day for the next 1 month, and 3 g/day after that. The RA test result was ++, RF 320 IU/ml, and CRP 1.6 mg/dl.

Clinical course

Coldness in her hands and feet was reduced at 3 days of administration of BioBran, and the frequency of pain decreased. The pain was further reduced at 1 week, and the analgesic was withdrawn. Facial and hand swelling were reduced in early November at 1 month. At 3 months, she had almost no pain and could sleep well. The RA test result was +, RF 92 IU/ml, and CRP 1.0 mg/dl. The dose of the steroid was decreased to half the previous level. She had no pain and could bend both middle fingers freely in April 2001 at 6 months.

Results and discussion

BioBran had a very good effect on 3 of the 8 patients. Subjective symptoms, especially pain, improved, and the RA index and CRP level decreased. The steroid was completely withdrawn in 2 patients, and the dose was decreased in the remaining 1. Two other patients, in whom no very good effect was observed, had improved subjective symptoms. As a result, their QOL improved. The 3 remaining patients had no improvement or exacerbation in the 6-month administration period. Although symptoms were expected to worsen temporarily because of the immune-enhancing effect of BioBran, gradual increase of the dose caused no adverse reactions in any patient.

There are many reports on the actions of BioBran: NK-cell activation (Ghoneum et al.)[2], anti-inflammatory effect on a rat asthma model (Endo et al.)[3], survival improvement in an LPS-induced sepsis model (Kubo et al.)[4], intestinal-membrane protection against anticancer drugs in mice (Jacoby et al.)[5], protection against anticancer drugs in mice (Endo et al.)[6] and resistance to drug-related hepatic impairment (Sanada et al.)[7]. From these, BioBran could be estimated to be a functional food that enhances immunity and exerts a prophylactic effect based on the anti-inflammatory action. The authors conducted a double blind clinical study to evaluate the preventative effect of BioBran on the common cold syndrome in elderly people who stayed in the author-managed care institution and confirmed the effect of symptom relief[8]. BioBran showed the effect in a relatively short time in the patients of this study. These good results may have been because it exerted an anti-inflammatory effect on rheumatism and at the same time, enhanced immunity in the patients: it was reported that patients with rheumatism are generally immunocompromised because of decreased lymphocyte counts[9].

Conclusion

These results suggested the efficacy of BioBran as a supplement therapy. The main mechanism of the action is considered relief of immunological inflammation. We will try this therapy further, because it caused no adverse reactions.

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慢性関節リウマチに対するバイオブランの投与経験

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要　約

ステロイド剤を用いた対症療法を主とする慢性関節リウマチの患者に対して，機能性食品米ぬかアラビノキシラン誘導体（バイオブラン）を長期間投与し，ステロイド剤，鎮痛剤，温熱療法等のリウマチの通常療法に対する補完効果を検討した。リウマチの治療においてステロイド剤の投与は欠かすことができないが，副作用を考慮すると可能な限り投与量を減少させることが望ましい。近年，食品成分の機能については多くの報告があり，スーパーオキサイドの消去をはじめ，生体防御能を高める働きも報告されている。そこで，機能性食品素材の一つであるバイオブランに着目し，その有効性を検討した。バイオブランはナチュラルキラー細胞（NK細胞）の活性化作用と抗炎症作用を有していると報告されており，著者も高齢者のかぜ症状緩和作用を確認し，報告している。この度8名の慢性関節リウマチ患者にバイオブランを6ヶ月～12ヶ月間投与し，症状の改善とQOLの改善効果等の有効性を示唆する結果が得られたので報告する。

キーワード：米ぬかアラビノキシラン誘導体，リウマチ，補完療法，炎症防止

はじめに

慢性関節リウマチは自己免疫疾患の一種であり，IgGに対するIgMおよびIgG型の自己抗体いわゆるリウマチ因子が関節滑液中に産生され，互いに互いを認識しあう型で，IgM-IgG免疫複合体を関節滑液中に生成し炎症反応を誘起する。免疫複合体は補体を活性化し，多形核白血球を引き寄せて組織の破壊を促進すると同時に好塩

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基球や血小板を活性化し，ヒスタミンやセロトニンの放出を促し，血管透過性を高めて免疫複合体の沈着をさらに促進する。通常，関節リウマチの治療は副腎皮質ホルモン(certicosteroid)剤や非ステロイド系抗炎症剤が用いられる。また自己抗体産生を抑制する目的で，免疫抑制剤が併用される場合もある。いずれにしても副作用を避けることは困難である。そこで免疫調節作用と抗炎症作用を有する機能性食品素材，米ぬかアラビノキシラン誘導体(バイオブラン)を用いてステロイド剤や鎮痛剤等の薬剤治療の補完療法を検討した。

試験内容と経過

バイオブランは米種皮のヘミセルロースの誘導体でアラビノースとキシロースを主な構成糖とするポリサッカライドが主成分のBRMである[1]。慢性関節リウマチ8例について6ヶ月間から12ヶ月間バイオブランの投与を行い，自覚症状，CRPの変動とQOL改善の経過を観察した。8例中5例はステロイド剤及び鎮痛剤を投与しており，他は鎮痛剤と漢方薬の投与および温熱療法を行なっていた。

以下，著効の認められた3例の治療経過を報告する。

症　例　1.

【患者の症状と治療内容】

患者は78歳の女性で1998年3月より骨破壊性関節リウマチで加療を続けていた。Stein-Blocker分類でClass Ⅲ・Stage Ⅳであった。

対症療法としてプレドニン10mg及びブシラミン200mg/日の経口投与を行っていた。痛みが強く，歩行困難で骨破壊が進行性であることから人工関節置換術を勧めていたが患者の意向により手術を延期していた。そこで患者の承諾を得て4月17日よりバイオブランの投与を試みた。投与開始時両手および両膝と両関節の痛みがひどく，睡眠が浅くほとんど寝たきりの状態であった。血清学的検査値はRAtest++，RF定量65IU/mlおよびCRP2.0mg/dlであった。バイオブランの投与量は投与開始1週間は1日1gとし，3週間は1日2g，その後は1日3gに増量した。

【治療経過】

バイオブラン摂取開始後1週間目に手足の痛みが緩和され，熟睡できるようになると同時に歩行器による荷重が可能となり，2週間後に膝と足関節の痛みは軽減し，1ヶ月後には一本杖の歩行も困難を感じなくなった。10月5日の検査値はRAtest+，RF定量34IU/ml，CRP0.6mg/dlであり，ステロイドおよびDMARD剤の投与を中止した。1999年1月4日RAtest−，RF定量14IU/ml，CRP0.6mg/dlとなり経過は良好である。(RF定量の正常値は20IU/ml以下)(**図1**)

症　例　2.

【患者の症状と治療内容】

患者は77歳女性で，2003年3月に来院。手足の関節に強い痛みがあり，不眠，食欲低下で体力の低下が顕著であった。Class Ⅲ・Stage Ⅳであった。RAtest+++，RF定量500IU/ml，CRP1.8mg/dlで典型的な関節リウマチであった。ステロイド剤プレドニン10mgおよびDMARD剤の投与に加え温熱療法を行なったが，効果が認められず痛みが継続した。2000年6月20日より1日3gバイオブランの投与を開始し，1年間継続して投与した。その後1日2gに減量し，現在も投与を継続中である。

【治療経過】

バイオブラン投与開始3日後より手足の痛みが軽減し，熟睡できるようになり，食欲も増進した。3ヶ月後，手足の関節痛がさらに軽減し体重が2kg増加した。6ヶ月後の12月後半には疼痛は自制内となり，RAtest++，RF定量62IU/ml，CRP1.0mg/dlと改善が認められステロイド剤の投与を中止，DMARD剤のみの投与となった。2001年6月現在，バイオブランは1日2g継続投与，症状は安定している。

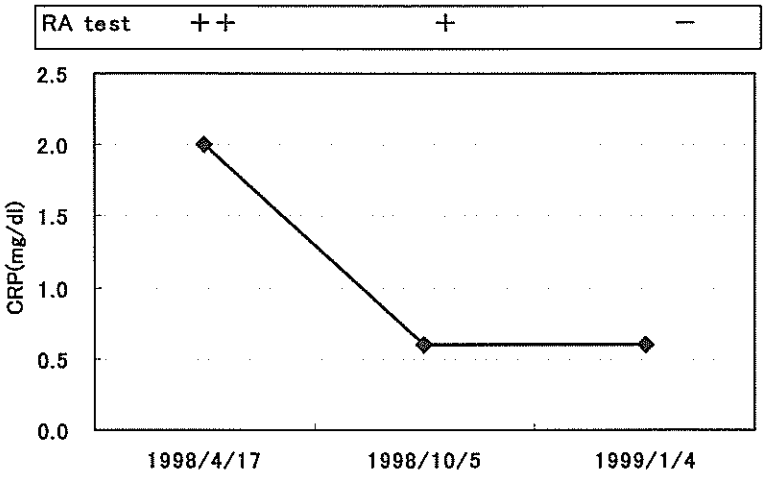

図1 CRPとRAtestの変動

症　例　3.

【患者の症状と治療内容】

患者は39歳の女性で2000年6月10日に来院。関節リウマチと判断しステロイド剤プレドニン15mg，鎮痛剤，漢方薬の投与と温熱療法の治療を行なっていた。10月5日よりバイオブランを投与した。投与量は最初の1週間は1日1g，1ヶ月間1日2g，その後は1日3gとした。バイオブラン投与開始時RAtest++，RF定量320IU/ml，CRP1.6mg/dlであった。

【治療経過】

バイオブラン投与開始後3日目に手足の冷えが軽減し，疼痛の発生頻度が減少した。1週間後に痛みがさらに軽減し鎮痛剤の投与を中止した。1ヶ月後の11月初旬には手足と顔のむくみが軽減した。3ヶ月後，痛みを殆ど感じなくなり熟睡できるようになった。この時点でRAtest+，RF定量92IU/ml，CRP1.0mg/dlとなり，ステロイド剤の投与量を2分の1に減量した。6ヶ月後の2001年4月に入り，痛みは全く感じなくなり，両手中指の屈伸が自由になった。

結果と考察

8例中3例にバイオブランの著効が観察された。痛みを主とする自覚症状の改善とRA指数とCRPの減少が認められた。2例はステロイド剤の完全離脱と1例は投与量の減量が可能となった。著効の認められなかった2例についても自覚症状の改善とそれに伴うQOLの改善が観察された。残る3例については6ヶ月間の投与期間に改善も増悪も観察されなかった。バイオブランの免疫強化作用による一時的な症状の増悪も懸念されたが，投与量を少量から漸増することにより，いずれの症例も副作用は観察されなかった。

バイオブランの作用についてはGhoneum等のNK細胞活性化[2]，Endo等のラット喘息モデルに対する抗炎症作用[3]，久保等のLPS惹起敗血症モデルの生存率の改善[4]，Jacoby等のラットの抗癌剤に対する腸粘膜保護作用[5]，Endo等のマウスの抗癌剤に対する防御作用[6]，真田等による薬物肝障害抵抗性[7]等が報告されており，免疫力強化と抗炎症作用を主とする生体防御作用の両面を有する機能性食品素材としての評価ができる。著者等も著者の経営する老人養護施設の入所者を対象にバイオブランのかぜ症候群の予防効果について二重盲検試験を行い，かぜ症状の緩和に有効性を確認している[8]。バイオブランの効果が比較的短期間で発現する傾向が認められたことは，慢性関節リウマチに対しては，抗炎症作用が主として働いており，さらにリウマチ患者は一般的にリンパ球数が減少して免疫抑制状態になっているという報告があることか

ら[9]，さらに免疫力の強化が相まって，良好な結果が得られたものと考える。

結　　論

バイオブランの投与は慢性関節リウマチ治療の補完療法として有効であることが示唆され，その主な作用は免疫性炎症の緩和作用と考える。副作用は認められなかったことから今後さらに症例を重ねる予定である。

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Key words : Rice bran arabinoxylan derivative, Rheumatism, Supplementary treatment, Inhibition of inflammation

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