Influenza Virus Infection as a Possible Cause of Elevated Squamous Cell Carcinoma Antigen

Kazuki Fujioka, Tatsuya Kawasaki, Satoshi Kaimoto, Yoshiaki Akakabe, Michiyoshi Yamano, Sigeyuki Miki, Tadaaki Kamitani and Hiroki Sugihara

Department of Cardiology, Matsushita Memorial Hospital

Abstract: We report the case of a 54-year-old man who had the complaint of general fatigue with a marked increase of serum SCC antigen. Rapid influenza diagnostic kit demonstrated influenza B virus infection, but any other examinations did not show tumorous findings. Thus, oseltamivir therapy was administered for influenza virus infection. Three weeks later, SCC antigen turned out to decrease to <1.0 ng/mL, and remained normal 6 weeks later. This case suggests that influenza virus infection can cause an elevation of SCC antigen.

Key words: Squamous cell carcinoma (SCC) antigen, Influenza

Introduction

Squamous cell carcinoma (SCC) antigen, which is a glycoprotein with a molecular weight of about 48,000 daltons, was reported in 1977 by Kato and Torigoe as a tumor marker in cervical SCC. Thereafter, SCC antigen has been rapidly introduced into routine clinical practice for assessment of various SCC, e.g., esophagus, lung, and cervix uteri. We report a patient with transiently elevated serum SCC antigen accompanied by influenza B virus infection.

Case Report

A 54-year-old previously healthy man consulted our hospital with a complaint of general fatigue. He had a temperature of 38°C, a pulse of 82 beats per minute, and blood pressure of 120/70 mmHg. Physical examinations, 12-lead electrocardiography, routine blood examination, and chest X-ray were unremarkable. Tumor markers including carbohydrate antigen 19-9, carcinoembryonic antigen, and alpha-fetoprotein were normal, but serum SCC antigen was markedly elevated with a value of 14.4 ng/mL. The next day, he was diagnosed as having influenza B virus infection using a rapid influenza diagnostic kit (POCTEM Influenza A/B, Sysmex Corporation, Kobe, Japan). Treatment with 75 mg of oseltamivir twice daily was continued for 5 days, and symptoms were improved. Thereafter, the patient underwent whole body examinations due to the elevated SCC antigen, but no significant lesions were detected on chest and abdominal computed tomography, upper and lower endoscopy, gallium-67 citrate scintigraphy, brain magnetic resonance imaging. Three weeks later, SCC antigen turned out to
decrease to <1.0 ng/mL, and remained normal 6 weeks later. The patient has remained well without any disease for over 2 years.

**Discussion**

SCC antigen is potentially high in non neoplastic diseases. Possible causes for elevated SCC antigen include atopic dermatitis\(^5\), bronchial asthma\(^4\), pemphigus\(^3\), tuberculosis\(^6\), sarcoidosis\(^7\), or chronic renal failure\(^8\), spondylitis\(^9\), none of which were detected in the present case. These findings suggest the association of elevated SCC antigen with influenza B virus infection. To our knowledge, this is the first case to report such a finding.

The mechanism for elevated SCC antigen in influenza virus infection remains unclear, but immune reactions may play an important role. Influenza virus infection provokes the expression of tumor necrosis factor alpha\(^10\), leading to SCC antigen production in squamous epithelium tissue\(^11\). Furthermore, anti-inflammatory cytokine interleukin–4 and interleukin–13 seem to be promoters of SCC antigen in cultured airway epithelial cells\(^12\).

Schneider et al\(^13\) found in 1995 that SCC antigen is encoded by two highly homologous genes, SCC antigen 1 and SCC antigen 2. The expression of SCC antigen 2 messenger ribonucleic acid is reported to be higher in SCC than in normal tissues, while that of SCC antigen 1 does not significantly differ between SCC and normal tissues\(^14\). Some investigators showed that the ratio of SCC antigen 1 to SCC antigen 2 expression might be a reliable marker for the detection of SCC\(^15,16\). Therefore, independent measurement of SCC antigen 1 and SCC antigen 2 might elucidate the occult elevation of SCC antigen in influenza virus infection. However, neither SCC antigen 1 nor SCC antigen 2 was measured in the present case. On the other hand, expression of SCC antigen 1 and SCC antigen 2 did not differ between SCC and normal tissues in another study\(^17\). Thus, the disease specificity between SCC antigen 1 and 2 is controversial, and further examination is needed.

In conclusion, the present case suggests an association of elevated SCC antigen with influenza virus infection. Attention may be paid for assessment of SCC antigen in patients with influenza virus infection.

**References**


7 ) Bando M, Tani K, Kohrai F, et al. A case of sarcoidosis with elevated SCC antigen in the serum and bronchoalveolar lavage fluid which was difficult


Squamous cell carcinoma抗原値の一過性上昇を伴った
B型インフルエンザウイルス感染の1例

藤岡数記、川崎春也、階元 聡、赤壁佳樹、
山野倫代、三木茂行、神谷匡昭、杉原洋樹

松下記念病院 循環器科

Squamous cell carcinoma（SCC）抗原は扁平上皮由来の悪性疾患に関連して上昇する腫瘍マーカーである。今回、インフルエンザウイルスの感染時にSCC抗原値が一過性に上昇した1例を経験した。症例は54歳の男性で、全身倦怠感を主訴に来院した。スクリーニング目的で測定されたSCC抗原が14.4ng/mLと上昇していた。翌日、B型インフルエンザウイルス感染と診断され、オセルタミビルが投与された。その後に施行された全身検査でSCC抗原の上昇の原因となる悪性疾患は検出されなかった。インフルエンザ治療3週間後および6週間後に再検されたSCC抗原値は、ともに1.5ng/mL以下と正常化していた。その後、2年以上にわたり経過観察しているが悪性疾患の兆候を認めていない。

キーワード：Squamous cell carcinoma（SCC）抗原、インフルエンザ

Editor’s Comment

SCC抗原は扁平上皮癌の腫瘍マーカーとして臨床で重用されているが、論文にてもあるように皮膚疾患を初めとして、様々な疾患において非特異的に上昇することが知られている。本論文はインフルエンザ感染に伴ってSCC値の上昇を認め、その改善により正常化したことを初めて報告した。臨床においてSCC抗原を測定するに当たっては患者の状態などで考慮すべきことであるが同時に、SCC抗原の上昇がどのような機序によってもたらされるかについて示唆を与えてくれる貴重な論文と考える。