

Evaluation of Serum Levels of Carcinoembryonic Antigen in Allergic Bronchopulmonary Aspergillosis

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Abstract

Background: The serum level of carcinoembryonic antigen (CEA) is a marker of malignant disease but can also be increased in benign diseases. Patients with allergic bronchopulmonary aspergillosis (ABPA) have bronchial asthma showing a wide variety of radiological findings. We measured serum CEA levels in patients with ABPA and evaluated the relationships of serum CEA levels with peripheral blood eosinophil counts, total blood levels of immunoglobulin (Ig) E, and findings of computed tomography (CT) in ABPA.

Methods: The subjects were 13 patients (6 men and 7 women aged 34 to 76 years) who had been treated for ABPA at our hospital. Serum levels of CEA, peripheral blood eosinophil counts, total blood IgE levels, and CT findings were examined before and after treatment with prednisolone.

Results: Before the start of the treatment 7 of 13 patients had serum CEA levels higher than the upper limit of normal. The serum CEA level was not correlated with eosinophil counts or total IgE values. Serum CEA levels were examined after treatment in 9 patients and were found to have significantly decreased as pulmonary consolidation improved. Furthermore, serum CEA levels before treatment in patients with pulmonary consolidation were significantly higher than those in patients without consolidation.

Conclusion: Serum CEA levels are elevated in some patients with ABPA; these elevations might be associated with consolidation in the lung. Elevated serum CEA levels decrease as the consolidation decreases after treatment. The elevation of serum CEA might be attributed to the presence of local inflammation in the lung.

(J Nippon Med Sch 2013; 80: 404–409)

Key words: carcinoembryonic antigen, allergic bronchopulmonary aspergillosis, computed tomography, consolidation on chest radiographs

Introduction

The serum level of carcinoembryonic antigen

(CEA) is a marker of malignant diseases and can also be elevated in benign diseases, such as idiopathic lung fibrosis¹ and bronchial asthma with mucoid impaction^{2,3}. Allergic bronchopulmonary

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Journal Website (<http://www.nms.ac.jp/jnms/>)

Table 1 Characteristics of 13 patients treated as allergic bronchopulmonary aspergillosis

Case	Age (years) Sex	Smoking status (Brinkman Index)	Serum CEA (ng/mL)		Blood Eosinophil count (/ μ L)	Blood total IgE value (IU/mL)	Computed Tomography Findings			Diagnosis	
			before treatment	after treatment			Central Bronchiectasis	Consolidations ≥ 1 segment < 1 segment	Others		
1	67 M	former (840)	41.8	7.2	1,154	795	+	+	-	small nodules	definite
2	37 M	former (170)	16.6	2.4	697	7,868	+	+	-		definite
3*	69 M	former (400)	13.4	11.2	608	387	+	-	+	cystic changes, ground-glass opacity, pleural effusion	definite
4	61 M	current (246)	10.3	7.0	4,228	10,669	+	+	-	small nodules, pleural effusion	definite
5	66 F	never	10.0	1.6	2,944	1,037	+	-	+	cystic changes	definite
6	66 F	never	9.1	5.6	8,308	589	+	+	-	ground-glass opacity	definite
7	69 F	never	6.8	5.3	1,024	793	+	+	-	small nodules	probable
8	67 F	never	6.0	not done	1,376	6,199	+	+	+		definite
9	49 F	never	5.9	2.4	1,596	9,680	+	+	+	small nodules, large nodule	definite
10	53 F	never	5.4	3.4	403	646	+	+	-		definite
11	37 F	never	4.9	not done	1,161	1,913	+		-	small nodules, large nodule	probable
12	34 F	never	3.2	not done	862	1,824	+		-	globe- or club-like shadows	definite
13	76 M	never	2.2	not done	1,053	206	+		-	club-like shadows	probable

*Gastric cancer was diagnosed 1 year after the start of treatment with prednisolone.

aspergillosis (ABPA) shows bronchial asthma with a wide variety of radiological findings, including mucoid impaction⁴. We have observed high serum levels of CEA in some patients with ABPA but not in others. Cases of ABPA with abnormal findings on chest radiography and high serum levels of CEA can be difficult to differentiate from lung cancer. Therefore, in the present study we examined serum CEA levels in patients with ABPA and evaluated the relationships of serum CEA levels with peripheral blood eosinophil counts, total blood immunoglobulin (Ig) E levels, and findings of computed tomography (CT) in patients with ABPA.

Materials and Methods

Patients

The subjects were 13 patients (6 men and 7 women aged 34 to 76 years; 9 never smokers, 3 ex-smokers, and 1 current smoker) who had been treated for confirmed or suspected cases of ABPA at our hospital from 2003 through 2009 (**Table 1**). When these 13 patients had abnormal findings on chest radiography before the diagnosis of ABPA, malignant diseases were also suspected, and serum CEA levels were measured. Diagnoses of ABPA had been made according to the criteria of Rosenberg and Patterson⁵. Bronchiectasis was considered to be "central" when confined to the medial half of the

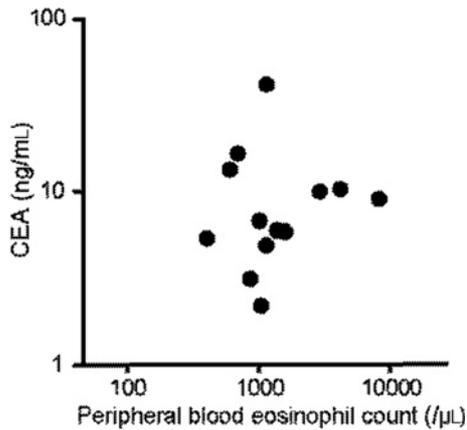


Fig. 1 The relationship between serum CEA levels and peripheral eosinophil counts. Serum CEA values at the start of treatment for ABPA were not correlated with peripheral eosinophil counts ($r=-0.038$, $p=0.902$). The vertical axis shows a logarithm of the serum CEA level, and the horizontal axis shows a logarithm of the peripheral eosinophil count.

lung, at a point midway between the hilum and the chest wall. Instead of assessing immediate skin reactivity to aspergillus, we measured levels of IgE specific for aspergillus.

CEA and CT Evaluation

Levels of CEA were measured with an immunoenzymometric assay (ST AIA-PACK CEA, Tosoh Corp., Tokyo, Japan). For serum CEA levels the upper limit of normal in our hospital is 6.7 ng/mL. All patients underwent spiral CT. The CT images were evaluated by 3 of the authors (TN, KY, and KU). Peripheral blood eosinophil counts and total blood IgE levels were compared with findings of CT and serum CEA levels.

Treatment for ABPA

The treatment for ABPA was started with prednisolone at a dose of 30 mg per day, which was then tapered. The total duration of treatment was 4 months to several years.

Statistics

Statistical analysis was performed with the statistical software package SPSS 13.0J (SPSS Inc., Chicago, IL, USA). Data were compared by means of

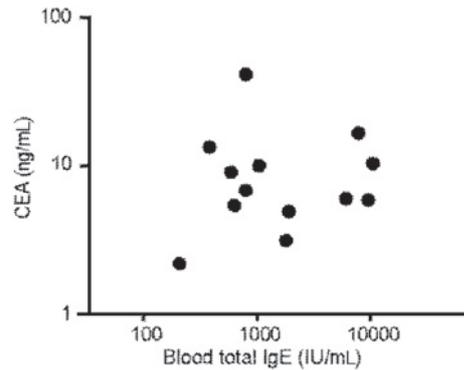


Fig. 2 The relationship between serum CEA and total blood IgE levels.

Serum CEA levels at the start of treatment for ABPA were not correlated with total blood IgE levels ($r=-0.065$, $p=0.833$). The vertical axis shows a logarithm of the serum CEA level, and the horizontal axis shows a logarithm of the total blood IgE level.

the Mann-Whitney U test. Correlations were evaluated by means of Pearson's correlation coefficients. Statistical significance was assumed at $p < 0.05$.

Results

The serum CEA values of the 13 patients at the start of treatment for ABPA ranged from 2.2 to 41.8 ng/mL (**Table 1**). Of these patients, 7 had CEA levels greater than the upper limit of normal (6.7 ng/mL). Serum CEA values at the start of treatment were not correlated with peripheral eosinophil counts ($r=-0.038$, $p=0.902$) (**Fig. 1**) or total blood IgE levels ($r=-0.065$, $p=0.833$) (**Fig. 2**).

The findings of CT were central bronchiectasis in all 13 patients, multiple cystic changes in 2 patients, consolidation in 1 or more segments in 8 patients (**Fig. 3A**), consolidation in an area less than 1 segment in 4 patients, pleural effusion in 2 patients, scattered small nodules in 5 patients, large lung nodules in 2 patients, ground-glass opacity in 2 patients, globe- or club-like shadows (**Fig. 4A**) in 2 patients, and strip-like shadows in 2 patients (**Table 1**).

Consolidation, globe- or club-like shadows, and large nodules improved after treatment with prednisolone (**Fig. 3B, 4B**). Serum CEA levels were

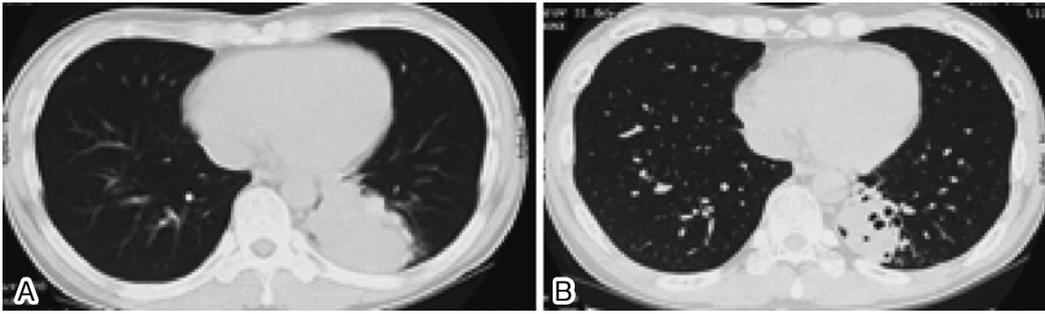


Fig. 3 Computed tomography showed consolidation in S9 and S10 of the left lower lobe (A). The serum CEA level was 16.6 ng/mL (the upper limit of normal in our hospital is 6.7 ng/mL). After treatment with prednisolone, the consolidation was absorbed (B), and the serum CEA level decreased to 2.4 ng/mL.

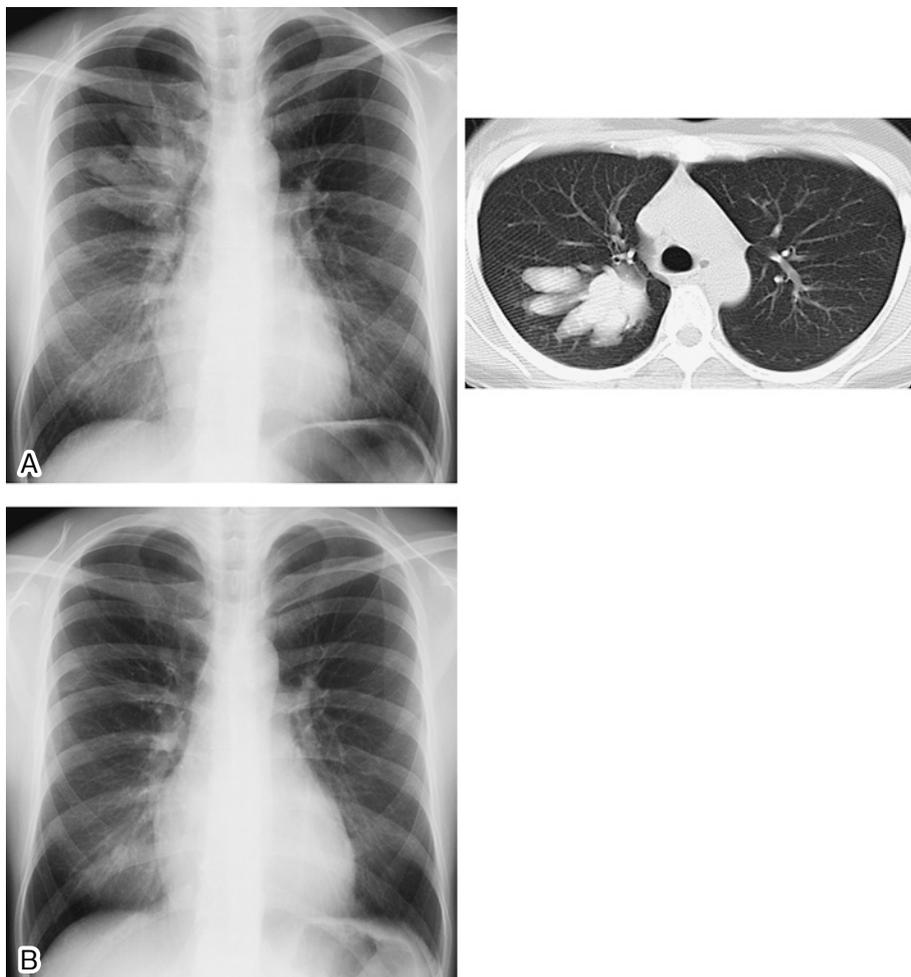


Fig. 4 A chest X-ray film and computed tomography showed globe- or club-like shadows of the upper lobe of the right lung (A). The CEA level was 4.9 ng/mL. After treatment with prednisolone, the globe- or club-like shadows disappeared (B).

examined after treatment with prednisolone in 9 cases and were found to have decreased significantly as consolidation improved in all 9 cases

(Fig. 5).

Furthermore, to examine whether serum CEA levels are higher in patients with ABPA and

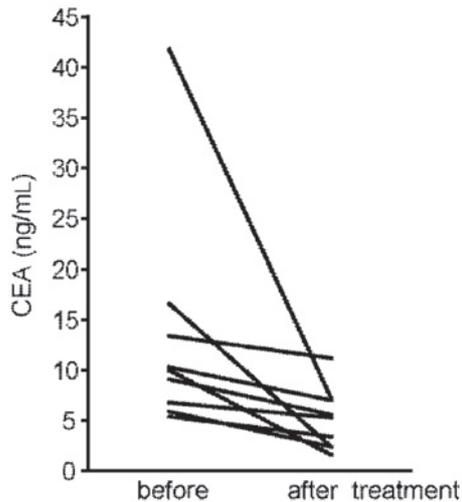


Fig. 5 Serum CEA levels were examined after treatment with prednisolone in 9 cases and were found to have decreased significantly as consolidation improved in all 9 cases.

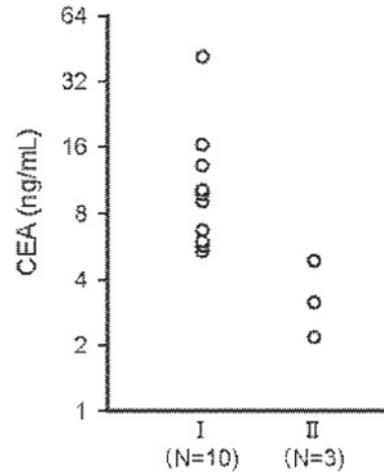


Fig. 6 Patients with consolidation (I) had higher serum CEA levels than did patients without consolidation (II) (Mann-Whitney U test; $p=0.011$). The vertical axis shows a logarithm of the serum CEA level.

pulmonary consolidation lesions, CT images and serum CEA values obtained before treatment for ABPA were compared in 13 patients. Serum CEA levels were found to be higher in the 10 patients with consolidation lesions (Fig. 3A) than in the 3 patients with globe- or club-like shadows (Fig. 4A) or large nodules without consolidation (Fig. 6) ($p=0.011$). Blood eosinophil counts and total IgE levels in patients with consolidation were not significantly higher than those in patients without consolidation.

One patient with consolidation showed decreased serum CEA levels after treatment with prednisolone, but 1 year after the start of treatment with prednisolone, gastric cancer was diagnosed (Case 3 in Table 1). The other patients with CEA levels greater than the upper limit of normal had no malignant disease after follow-up periods of 1 to 7 years.

Discussion

A wide variety of radiographic findings have been reported in patients with ABPA⁴. Occasionally, these radiographic findings suggest malignant diseases. Furthermore, CEA is a tumor marker, and patients with high serum CEA levels are also suspected to have malignant diseases. However, serum CEA levels are also high in bronchial asthma with mucoid

impaction²³. Some abnormal findings, such as mass-like lesions, atelectasis, and consolidation, in patients with ABPA and high serum CEA levels are difficult to differentiate from lung cancers. Therefore, we evaluated CEA in patients treated for ABPA who had new lesions on plain chest radiographs. We found that serum CEA levels at the start of the treatment were not correlated with eosinophil counts or total IgE levels. In addition, patients with pulmonary consolidation had higher serum CEA levels than did patients with globe- or club-like shadows or large nodules without consolidation.

The glycoprotein CEA is involved in cell adhesion; its production normally starts during fetal development but ceases shortly after birth, and only a very small amount can be detected in the serum of healthy persons¹. CEA can be produced in the epithelium of the mouth, stomach, intestines, bile ducts, and respiratory tract ranging from the trachea to the alveoli⁶. In the present study, serum CEA values were not correlated with peripheral blood eosinophil counts or total IgE values, but after treatment with prednisolone, the values of all 3 variables decreased together. This finding suggests that CEA is correlated with the inflammatory activity of ABPA. In areas of consolidation, bronchi and alveoli showed chronic inflammation and were activated, which might have induced the production

of CEA, and damage to the alveoli might have then caused CEA to be transferred into the vessels. In these areas of consolidation, mucus plugging may occur. However, when mucus plugging induced globe- or club-like shadows or large nodules in our patients with ABPA, CEA levels were not elevated. Although only 3 of our patients showed globe- or club-like shadows or large nodules without consolidation, this absence of elevated serum CEA levels might be attributed to the presence of less inflammation.

High serum CEA levels and the abnormal findings on chest radiographs improved after treatment with prednisolone in the present study. Serum CEA levels in patients with ABPA might be elevated in association with consolidation in the lung, and elevated CEA values decreased as consolidation decreased. We followed up all patients with elevated CEA over the upper limit for more than 1 year, and only 1 patient showed malignant disease. When patients with bronchial asthma have elevated serum CEA levels, peripheral eosinophil counts, total blood IgE levels and consolidation on chest radiographs, ABPA should be included in the differential diagnosis.

The elevation of serum CEA might be attributed to the presence of local inflammation in the lung. The role of CEA elevation remains unclear. Larger numbers of cases should be collected and evaluated.

Conflict of Interest: All authors declare that they have no conflict of interest.

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(Received, March 31, 2013)

(Accepted, May 15, 2013)