Journal of Asthma and Allergy Dovepress

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Clinical Relevance of Elevated Serum Carcinoembryonic Antigen in Allergic Bronchopulmonary Aspergillosis/Mycosis: A Multicenter Retrospective Study

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Background: Allergic bronchopulmonary aspergillosis/mycosis (ABPA/M) is a complex non-infectious pulmonary benign disease characterized by an immune response against aspergillus/fungus. Carcinoembryonic antigen (CEA), typically recognized as a tumor marker, also elevated in certain benign diseases. Few studies on ABPA/M cases presenting with elevated serum CEA levels have been reported.

Patients and Methods: A cohort of 115 patients diagnosed as ABPA/M were divided into two groups (CEA normal and CEA elevated). The characteristics of ABPA/M patients in terms of its demographic profile, clinical symptoms, pertinent clinical laboratory examinations were analyzed. Levels of cytokines (IL-4, IL-5, GM-CSF, IFN-γ) were analyzed by enzyme-linked immunosorbent assay. Comparative evaluation included pre-therapy and post-treatment eosinophil count and total IgE level, to evaluate therapeutic disparities between the two groups.

Results: Among 115 cases of ABPA/M, 32 exhibited elevated serum CEA levels above baseline and 83 were normal. ABPA/M patients with elevated serum CEA tended to be younger (50, IQR [43–56] years vs 59, IQR [47–68] years; $P < 0.05$) with superior pulmonary function (FEV1/FVC ratio, 65.1% (44.2, 79.6) vs 79.1% (65.2, 84.2), $P < 0.05$), and showed marginally higher baseline levels of the total IgE ($P < 0.05$), blood eosinophils counts and ratios ($P < 0.01$) compared to those with normal CEA. Higher serum levels of IL-4, IL-5, GM-CSF and IFN-γ in ABPA/M patients with elevated serum CEA levels were observed ($P < 0.0001$). After treatment (at 12w), compared to ABPA/M patients with normal serum CEA, the decrease in eosinophil count and total IgE levels was less pronounced in ABPA/M patients with elevated serum CEA eosinophil count, 523±481.66 vs 267±200.68, $P < 0.05$; total IgE, 619 ±680.47 vs 263±400.90, $P < 0.05$), which indicates a poor response to treatment.

Conclusion: Monitoring serum CEA levels may serve as a supplementary tool in the clinical management of ABPA/M patients.

Keywords: allergic bronchopulmonary aspergillosis/mycosis, carcinoembryonic antigen, IgE, eosinophils

Received: 11 October 2024
Accepted: 17 December 2024
Published: 25 December 2024

Introduction

Allergic bronchopulmonary aspergillosis (ABPA) is a complicated disorder due to immune response to *Aspergillus fumigatus* (*A. fumigatus*) adhering to the airway, characterized by central bronchiectasis and recurrent pulmonary infiltrations.[1] Cases caused by fungi included *A. fumigatus* are referred to allergic bronchopulmonary mycosis (ABPM). The classic pathological characteristics of ABPA/M include mucoid impaction, eosinophilic pneumonia, bronchiolitis obliterans, granulomatous bronchiolitis and pulmonary fibrosis.[2,3] The patients with ABPA often present with wheezing, cough, bronchial hyperreactivity, or hemoptysis.[4] ABPA/M is often underdiagnosed, and the average time from symptom onset to diagnosis may be as long as 10 years.[5] Chest computed tomography (CT) is a necessary examination for ABPA/M, the radiological presentation classification includes five classes: serologic ABPA/M (ABPA/M-S), ABPA/M with bronchiectasis (ABPA/M-B), ABPA/M with mucus plugging (ABPA/M-MP), ABPA/M with high attenuation mucus (ABPA-HAM), and ABPA/M with chronic pleuropulmonary fibrosis (ABPA/M-CPF).[6] Non-fixed infiltrative lesions and bronchial mucous plugging are typical radiological features of ABPA/M. However, lung tumors can also show similar typical findings, making it challenging to differentiate them from ABPA/M.[7,8] The goal of ABPA/M treatment is to control symptoms, prevent acute exacerbations, preserve lung function, and prevent irreversible damage to bronchopulmonary structures. Early identification and treatment of ABPA/M recurrence are crucial for improving the prognosis of patients. Therefore, long-term follow-up and monitoring of ABPA/M patients are vital. Serum total IgE is currently the primary indicator for monitoring the progression of ABPA.[9,10] This means that novel indicators would need to be proposed for clinical monitoring.

It is widely recognized that carcinoembryonic antigen (CEA) is a broad-spectrum tumor marker, which usually elevated in a wild variety of tumors such as colorectal cancer, breast cancer and lung cancer.[11] An increased levels of CEA can be acquired by a blood test, which commonly used for diagnosis, recurrence or progression of malignant diseases.[12] In addition to malignant conditions, a few benign diseases such as viral hepatitis, cirrhosis, pancreatitis and ulcerative colitis have also reported elevated serum CEA levels.[13,14] A few studies have identified ABPA/M cases with elevated serum CEA levels.[15–17] However, the significance of these elevated CEA levels remains largely unexplored due to the scarcity of cases available for analysis.

In this retrospective study, we collected the clinical data of 115 ABPA/M patients including 83 patients with normal serum CEA levels and 32 with elevated serum CEA levels. Their clinical features, laboratory test results, imaging findings, inflammatory status and therapeutic effect were explored. We determined the relationship between serum CEA and clinical manifestations of the disease severity. Furthermore, we have also conducted a longitudinal survey on a number of ABPA/M patients to evaluate the role of serum CEA for monitoring the response to treatment.

Materials and Methods

Study Subjects and Patients

This program is a multicenter retrospective study conducted in Xiangya Hospital of Central South University, the first Hospital of Changsha, Jiangxi Provincial People's Hospital and Zhongnan Hospital of Wuhan University. From the database of all the hospitals, we filtered out a total of 115 ABPA/M patients between January 2018 and April 2024. Patients with malignant tumors and benign diseases mentioned above were excluded. Patient data collected encompassed demographic information such as age and gender, as well as comprehensive medical assessments including blood routine, pulmonary function, imaging, bronchoscopy, total serum immunoglobulin E (IgE), molds (including *A. fumigatus*)/filamentous fungi specific IgE (sIgE), molds (including *A. fumigatus*)/filamentous fungi specific IgG (sIgG), serum CEA concentrations, erythrocyte sedimentation rate (ESR) and clinical and medication records. The normal range for CEA in an adult is defined as <5 ng/mL. Serum levels of cytokines (Interleukin-4 (IL-4), Interleukin-5 (IL-5), Interferon-gamma (IFN-γ) and Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF)) were assessed during the ABPA/M episode by enzyme-linked immunosorbent assay (ELISA) according to the manufacturer's instruction (Neobioscience), the standard curve was constructed by using the standards provided in ELISA kit.

According to the clinical records, the moment when patients were first diagnosed with ABPA at our hospital was defined as the baseline period. All patients were treated with glucocorticoids with or without an antifungal agent

(itraconazole/voriconazole). The initial dose of prednisone was 0.5mg/kg/d, then gradually decreased. Patients who took a visit after treatment for 12W were considered as after treatment.

Diagnosis Criteria

The diagnosis of ABPA/M were based on Asano et al in 2021:[18] (1) current or previous history of asthma or asthmatic symptoms, (2) peripheral blood eosinophilia (≥500 cells/mm3), (3) elevated total serum IgE levels (≥417 IU/mL), (4) immediate cutaneous hypersensitivity or presence of specific IgE for *A. fumigatus*; (5) presence of precipitins or specific IgG for *A. fumigatus*; (6) positive culture of *A. fumigatus* or other Aspergillus spp. in sputum or bronchial lavage fluid, (7) fungal hyphae in bronchial mucus plugs, (8) central bronchiectasis on CT, (9) presence of mucus plugs in central bronchi, based on the history of expectoration/CT/bronchoscopy; (10) HAM in the bronchi on CT. Patients who fulfilled five and six or more items were diagnosed with probable and definite ABPA, respectively. The diagnosis of asthma was based on the Global Initiative for Asthma (GINA) guidelines.

Statistical Analysis

Categorical variables are presented as counts and percentages (%), while continuous variables are described as the median and interquartile range (IQR). The Mann–Whitney *U*-test was utilized to compare the differences for continuous variables, and the Chi-square test was employed for categorical variables. To assess the differences of serum CEA levels, serum total IgE levels and peripheral blood eosinophil counts pre-therapy and post-treatment, Wilcoxon matched-pairs test was employed. Differences among multiple groups were assessed by one -way analysis of variance (ANOVA) with Tukey's multiple comparisons tests. The statistical analysis was performed using SPSS version 26.0 for Windows (IBM SPSS Inc, Armonk NY) and GRAPHPAD PRISM 8.0 software (GraphPad Software Inc, La Jolla, California). The significance levels were set at $P < 0.05$.

Results

Study Population

As shown in Table 1, a total of 115 participants were enrolled in the study, of whom 63 (55%) were males and 52 (45%) were females, with a median age of 55 years [IQR 47–67] at diagnosis. The majority of patients have symptoms of wheezing, coughing, and expectoration, while a smaller proportion of patients present with chest tightness and hemoptysis. Ventilatory dysfunction was observed in most cases based on lung function assessments. The median serum total IgE levels in patients were 1127 IU/mL [IQR, 607–1662], the median number of peripheral blood eosinophils was 570/ul [IQR, 200–970]. The sIgE expression was positive in all patients, while only some patients had positive sIgG expression. The fungal culture in sputum or bronchial samples revealed the presence of *A. fumigatus* or other aspergillus genera in a proportion of patients. The study population had extensive bronchiectasis on CT chest, with mucus plugs observed in 37% of the study population. Sputum jammed was found on bronchoscopy in 26% of patients.

Comparison Between ABPA/M with Normal Serum CEA and ABPA/M with Elevated Serum CEA

Among 115 patients, 32 of them had significant elevated serum CEA levels above baseline and 83 had normal levels (Table 1, Figure 1A). As we can see, the median age at diagnosis of ABPA/M among patients with elevated serum CEA (50, IQR [43–56] years) was notably lower than that of patients with normal CEA levels (59, IQR [47–68] years) (Table 1, Figure 1B). There was no significant difference in smoking exposure between the two groups ($P > 0.05$). Patients with elevated CEA level have better lung function than those with normal CEA ($P < 0.05$). 56(49%) patients have a history of asthma (serum CEA normal: 38(46%); serum CEA elevated: 18(56%), $P>0.05$). As for immunological findings, the ABPA/M patients with elevated CEA showed significantly higher total IgE levels than the patients with normal CEA (1082, IQR [550, 1582] IU/mL vs 1389, IQR [960, 2098] IU/mL) (Table 1, Figure 1C). Similarly, among ABPA/M patients with elevated CEA levels, eosinophil counts (500, IQR [200,

Table 1 Demographics and Clinical Characteristics of ABPA/ABPM Patients

	All	Serum CEA Normal	Serum CEA Elevated	*P* value
No. of patients	115 (100)	83 (72)	32 (28)	
Sex				
Male (n, %)	63 (55)	45 (54)	18 (56)	0.84
Female (n, %)	52 (45)	38 (46)	14 (44)	
Age at diagnosis (IQR, y)	55 (47, 67)	59 (47, 68)	50 (43, 56)	<0.05
Smoking (n, %)	29 (25)	21 (25)	8 (25)	0.97
A history of asthma, n (%)	56 (49)	38 (46)	18 (56)	0.314
Clinical symptoms				
Wheeze (n, %)	56 (49)	42 (51)	14 (44)	0.51
Chest distress (n, %)	24 (21)	18 (22)	6 (19)	0.73
Cough (n, %)	105 (91)	74 (89)	31 (97)	0.19
Expectoration (n, %)	81 (70)	61 (73)	20 (63)	0.25
Hemoptysis (n, %)	5 (4)	4 (5)	1 (3)	0.69
Spirometry				
FVC (% pred)[a]	77.8 (66.0, 90.4)	77.4 (65.3, 90.5)	78.7 (68.0, 88.0)	0.65
FEV1 (% pred)[a]	59.0 (39.1, 80.1)	59.0 (32.0, 78.6)	61.0 (47.4, 80.3)	0.36
FEV1/FVC ratio (%)[a]	67.0 (51.3, 83.0)	65.1 (44.2, 79.6)	79.1 (65.2, 84.2)	<0.05
Immunological findings				
Total eosinophil count (cells/ul)[a]	570 (200, 970)	500 (200, 900)	955 (400, 1570)	<0.01
Eosinophil ratio (%)[a]	8.2 (3.3, 14.5)	7.1 (2.7, 12.9)	14.5 (5.4, 19.1)	<0.01
Total IgE levels (IU/mL)[a]	1127 (607, 1662)	1082 (550, 1582)	1389 (960, 2098)	<0.05
Fungus-specific IgE positive (n, %)	115 (100)	83 (100)	32 (100)	-
Fungus-specific IgG positive (n, %)	28 (24)	16 (19)	12 (38)	<0.05
ESR (mm/h)[a]	31 (12, 51)	26 (11, 51)	33 (20, 92)	0.21
CEA (ng/mL)[a]	3.2 (1.8, 6.1)	2.3 (1.6, 3.4)	9.8 (6.8, 20.6)	<0.001
Fungal culture in sputum or bronchial samples				
A. fumigatus (n, %)	24 (21)	18 (22)	6 (19)	0.73
Any Aspergillus spp. (n, %)	9 (8)	6 (7)	3 (9)	0.70
Radiological findings				
Central bronchiectasis (n, %)	76 (66)	51 (61)	25 (78)	0.09
Fleeting infiltration (n, %)	59 (51)	38 (46)	21 (67)	0.06
Mucous plugs (n, %)	42 (37)	27 (33)	15 (47)	0.15
Bronchoscopy				
Suppurative inflammation (n, %)	37 (32)	22 (27)	15 (47)	<0.05
Sputum jammed (n, %)	30 (26)	16 (19)	14 (44)	<0.01

Notes: [a]Data were given as medians with interquartile range (IQR).
Abbreviations: ABPA, allergic bronchopulmonary aspergillosis; ABPM, allergic bronchopulmonary mycosis; CEA, Carcinoembryonic antigen; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; A. fumigatus, Aspergillus fumigatus; IgE, immunoglobulin E; ESR, Erythrocyte sedimentation rate.

900] /ul vs 955, IQR [400, 1570] /ul, P < 0.05) and ratios (7.1, IQR [2.7, 12.9] % vs 14.5, IQR [5.4, 19.1] %, P < 0.01) were higher than those in ABPA/M patients with normal CEA levels (Table 1, Figure 1D and E). No differences were found in ESR. Furthermore, there were also no discernible differences between the two groups in terms of fungal culture in airway samples and imaging changes. During bronchoscopy, ABPA/M patients with elevated CEA showed obvious manifestations of airway inflammation, such as purulent inflammation and mucus embolism (Table 1). In our subsequent analysis, we investigated serum CEA levels based on radiological classification. We observed that CEA levels were elevated in ABPA/M-MP/HAM patients than in ABPA/M-S and ABPA/M-CB patients (Figure 1F). Additionally, serum CEA levels at the start of treatment were positively correlated with peripheral eosinophil counts (r = 0.2423, p = 0.0091) or total IgE levels (r = 0.3711, p = 0.0001) (Figure 2A and B).

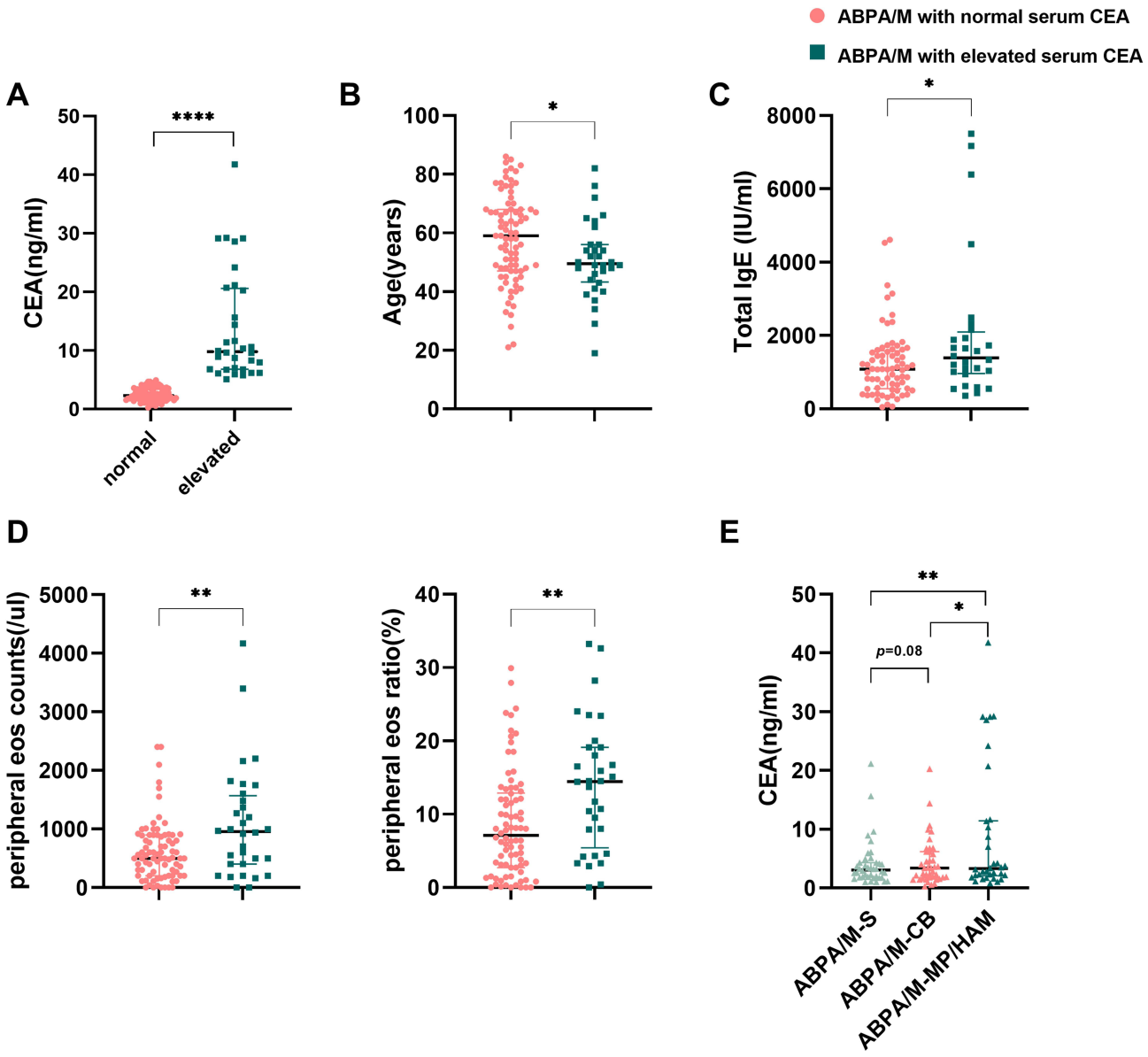

Figure 1 Clinical and immunological data of ABPA/M patients (two groups: CEA normal (n=83) and CEA elevated (n=32)). Baseline levels of serum CEA (**A**), Age (**B**), serum total IgE (**C**), peripheral eosinophil counts and ratios (**D**) in ABPA/M patients. Serum CEA levels in ABPA/ABPM patients according to mucus plugs (**E**). *P <0.05, **P <0.01, ****P < 0.0001.

Abbreviations: ABPA, allergic bronchopulmonary aspergillosis; ABPM, allergic bronchopulmonary mycosis; CEA, carcinoembryonic antigen.

Cytokine Levels

We gathered serum samples from the ABPA/M patients, asthma patients and healthy controls (HC), and assessed the levels of cytokines. Our analysis revealed that production of IL-4 and IL-5 were significantly higher in ABPA/M patients and asthma patients than in HC. Furthermore, ABPA/M patients with elevated serum CEA exhibited heightened production of IL-4 and IL-5 compared to ABPA/ABPM patients with normal serum CEA. Additionally, expression of IFN-γ and GM-CSF displayed a similar trend in all groups (Figure 3A–D).

Longitudinal Follow-Up

In this study, the majority of patients were treated with oral corticosteroids, either alone or in combination with antifungal medication (itraconazole and voriconazole). Of the 115 patients who underwent a baseline assessment,

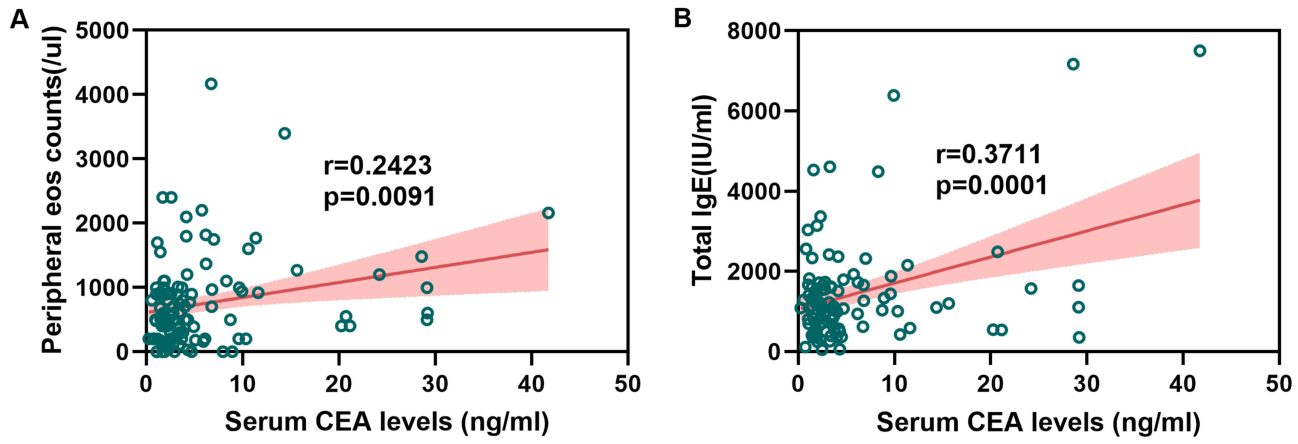

Figure 2 The correlation of serum CEA levels with peripheral eosinophil counts (**A**) or total IgE levels (**B**) at the start of treatment.
Abbreviation: CEA, carcinoembryonic antigen.

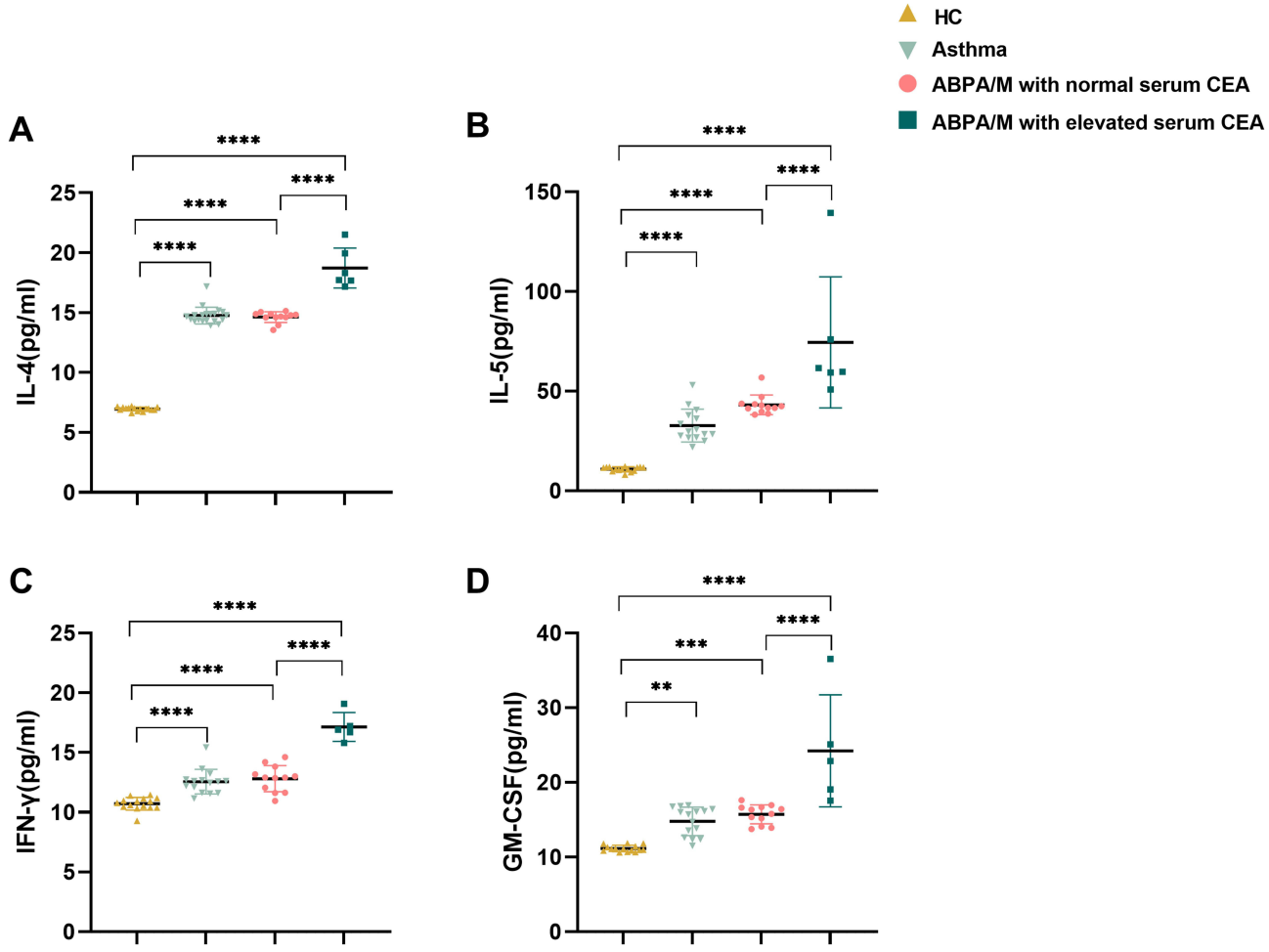

Figure 3 Serum levels of IL-4 (**A**), IL-5 (**B**), IFN-γ (**C**) and GM-CSF (**D**) in HC (n=15), asthma (n=15) and ABPA/M two groups: CEA normal (n=12) and CEA elevated (n=5). ***P* <0.01, ****P* <0.001, *****P* < 0.0001.
Abbreviations: HC, healthy controls; ABPA, allergic bronchopulmonary aspergillosis; ABPM, allergic bronchopulmonary mycosis; CEA, carcinoembryonic antigen.

Table 2 Demographics and Clinical Characteristics of ABPA/ABPM Patients After Treatment

	All	Serum CEA Normal	Serum CEA Elevated	*P* value
No. of patients	57	37 (65)	20 (35)	
Sex				
Male (n, %)	27 (47.4)	15 (40.5)	12 (60.0)	0.16
Female (n, %)	30 (52.6)	22 (59.5)	8 (40.0)	
Immunological findings				
Total eosinophil count (cells/ul)[a]	170 (20, 575)	90 (15, 265)	915 (180, 1328)	<0.001
Eosinophil ratio (%)[a]	2.6 (0.45, 5.8)	1.0 (0.2, 3.0)	7.3 (3.9, 15.4)	<0.001
Total IgE levels (IU/mL)[a]	725 (351, 1048)	487 (322, 988)	985 (740, 1627)	<0.01
Therapeutic effect				
Decline level of total eosinophil count (cells/ul)[b]	433±423.89	523±481.66	267±200.68	<0.05
Decline level of eosinophil ratio (%)[b]	7.3±7.02	7.4±6.08	7.1±8.49	0.55
Decline level of total IgE levels (IU/mL)[b]	511±631.20	619±680.47	263±400.90	<0.05

Notes: [a]Data were given as medians with interquartile range (IQR). [b]Data were given as Mean±standard deviation(SD).
Abbreviations: ABPA, allergic bronchopulmonary aspergillosis; ABPM, allergic bronchopulmonary mycosis; CEA, Carcinoembryonic antigen; IgE, immunoglobulin E.

about 50% (57) patients completed the required examinations in the follow-up assessment, of whom 37 (65%) were patients with normal serum CEA levels and 20 (35%) were patients with elevated serum CEA levels (Table 2). After 12 weeks of treatment, the elevated serum CEA levels decreased compared to baseline levels (Figure 4A). ABPA/M patients with elevated serum CEA still showed higher levels of the total IgE, blood eosinophils counts and ratios compared to those with normal CEA (Table 2). The levels of serum total IgE, peripheral blood eosinophil counts were both decreased in the two groups, while the degree of decline was more pronounces in the patients with normal serum CEA (Table 2, Figure 4B and C).

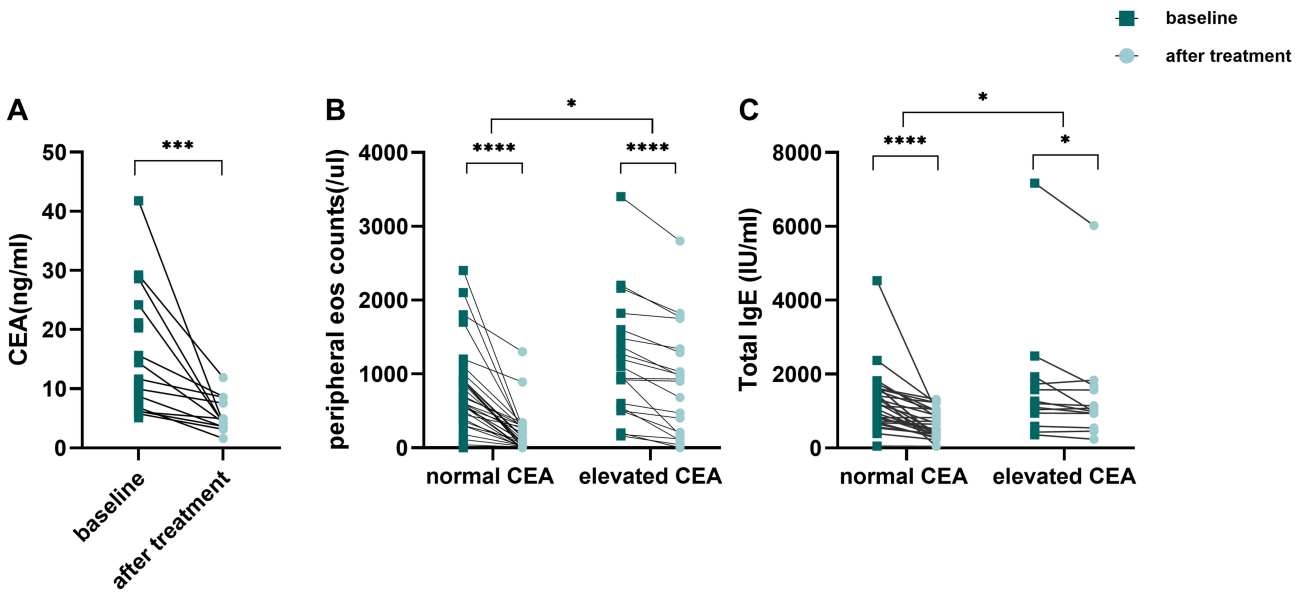

Figure 4 Longitudinally observation of serum levels of CEA (**A**), peripheral blood eosinophil counts (**B**) and serum total IgE levels (**C**) in patients with ABPA/M. **P* <0.05, ****P* <0.001, *****P* < 0.0001.
Abbreviations: ABPA, allergic bronchopulmonary aspergillosis; ABPM, allergic bronchopulmonary mycosis; CEA, carcinoembryonic antigen.

Discussion

ABPA was first reported in 1952 by Hinson et al.[19] Due to ABPA/M remains under recognized and under diagnosed, it is often misdiagnosed as asthma, tuberculosis, lung cancer and other diseases.[20–22] Clinically, serum CEA is frequently used as a key indicator to distinguish lung cancer from ABPA/M. CEA is a type of tumor marker, which serve as an important serologic indicator for clinical monitoring and diagnosis various tumors, including but not limited to lung cancer, breast cancer, gastric cancer. Studies have demonstrated that CEA is an important index to evaluate the diagnosis, therapy response and prognosis of lung cancer.[23,24] However, elevated levels of serum CEA can also be found in some benign lung conditions,[25] indicating a certain correlation with the occurrence and development of the disease. Ahmed Fahim et have demonstrated serum CEA correlates with disease severity in idiopathic pulmonary fibrosis (IPF).[26] Studies have reported that high CEA levels in serum and bronchoalveolar lavage fluid might connected with mucous embolism in asthma patients.[27,28] Our study indicates that bronchial mucus plugs were more prominent in the ABPA/M group with elevated CEA levels, but no significant difference in the proportion of patients with a history of asthma. Furthermore, Milene Caroline Koch al have shown that increase CEA levels associated with airway changes in rheumatoid arthritis patients such as bronchial wall thickening, bronchiectasis and nodules.[29] Our study indicated that over a quarter of ABPA/M patients (28%) exhibited elevated serum CEA levels, which were associated with disease severity and therapeutic response.

Sensitization to fungi is the initial step in pathogenesis of ABPA/M. Repeated exposure to fungi causes immune response such as IgE elevation, Th2 cytokines high expression, eosinophils infiltration and airway remodeling.[4] Therefore, typical laboratory investigations for clinical diagnosis of ABPA/M include increased serum total IgE levels, peripheral blood eosinophils, and HAM.[30] Studies have shown that the number of Th2 cells increased in peripheral blood and BALF in patients with ABPA/M, which reinforce the function of IL-4, further activate B cells and enhance IgE production, which promote disease activity and progression. The increase of IL-5 and GM-CSF will promote eosinophil recruitment, thus exacerbate airway damage.[31] In addition, Khosravi AR et al have found that airway epithelial cells exposed to aspergillus fumigatus spores produced more IFN-γ, which lead to brief periods of increased IFN-γ within the body to promote aspergillus clearance and play a defensive role.[32,33] In our study, ABPA/M patients with elevated serum CEA levels showed slightly higher baseline levels of total IgE, blood eosinophils counts and ratios and a higher level of Th2 cytokines (IL-4 and IL-5), GM-CSF and IFN-γ compared to those of patients with normal CEA. This indicates that ABPA/M patients with elevated CEA levels exhibited an intenser inflammatory response in their bodies. These findings contrast with a prior study which found no correlation between serum CEA levels and eosinophil counts or total IgE values.[15] However, it's worth noting that the previous study included only seven patients with elevated CEA levels. To our knowledge, the retrospective study we present represents the largest cohort of ABPA/M cases with elevated serum CEA levels reported in the literature to date. Recent studies have shown that the clinical characteristics and prognosis of ABPA/M are closely related to the presence of mucus plugs in central bronchiectasis.[34,35] In accordance with our study, we observe a higher frequency of mucus plugs in ABPA/M patients with elevated serum CEA levels bronchoscopy and serum CEA levels were elevated in ABPA/M-MP/HAM patients than in ABPA/M-S and ABPA/M-CB patients, which indicate that serum CEA levels may be related with the prognosis of ABPA/M.

However, the cause of elevated serum CEA in some ABPA/M patients remains unclear. Early studies have identified a correlation between CEA levels with smoking and age,[36,37] with smokers and older individuals having higher CEA levels. In our study, however, ABPA/M patients with elevated CEA was younger than ABPA/M patients with normal CEA, and there was no significant difference in smoking prevalence between the two groups. Furthermore, a recent study found that elevated serum CEA levels were associated with eosinophils levels, using immunohistochemistry and immunofluorescence, they found that eosinophils in lung biopsies from ABPA patients could express CEA.[38] Additionally, multiple case reports suggest that eosinophils may be the primary source of elevated CEA production in benign pulmonary diseases.[39,40] Consistent with these findings, our study identified eosinophilia in ABPA/M patients with elevated CEA, which may be one reason for the high serum CEA level.

Currently, treatment efficacy of ABPA/M usually assessed by monitoring pulmonary imaging and serum total IgE levels. There should be improvements in radiographic lung changes and a reduction in total IgE levels.[10,41] Researchers

have found that serum CEA levels in ABPA patients could be reduced after treatment compared to baseline.[15] This reduction may be attributed to the corticosteroid's control and therapeutic effects on inflammation. In our study, corticosteroids were administered according to the dosage recommended by the guidelines. Our findings also indicated that high serum CEA levels were decreased following treatment, suggesting that serum CEA level correlated with the progress in treatment of the disease in ABPA/M patients with elevated serum CEA.

In summary, ABPA/M patients with elevated CEA levels exhibit a more severe inflammatory response and poor treatment response compared to ABPA/M patients with normal CEA levels. This indicates that CEA may serve as a novel serological indicator for the severity of ABPA/M. For ABPA/M patients with elevated serum CEA found in routine screening, excluding tumor diseases, actively monitoring CEA changes is an important approach to evaluate treatment response. Surely, our study had certain limitations. Firstly, continuous CEA monitoring data was lacked to better evaluate its role in monitoring therapeutic effects. Additionally, missing follow-up data of some patients were another drawback. Our findings provide valuable insights, but further studies are necessary to better understand the clinical characteristics associated with elevated serum CEA levels in ABPA/M patients. Moreover, the reason for the elevation of serum CEA levels in ABPA/M patients is also a problem worthy of further exploration.

Conclusion

Our study revealed that serum CEA levels are associated with the inflammatory status in ABPA/M patients. Moreover, ABPA/M patients with elevated serum CEA levels at the early stage of treatment tend to have a poorer therapeutic outcome. Therefore, monitoring serum CEA levels may serve as a supplementary tool in the clinical diagnosis and management of ABPA/M patients. This will provide additional meaningful metrics both for clinical assessment and scientific investigation.

Abbreviations

ABPA, Allergic bronchopulmonary aspergillosis; *A. fumigatus, Aspergillus fumigatus*; ABPM, Allergic bronchopulmonary mycosis; CEA, Carcinoembryonic antigen; sIgE, Molds (including *A. fumigatus*)/filamentous fungi specific IgE; sIgG, Molds (including *A. fumigatus*)/filamentous fungi specific IgG; ESR, Erythrocyte sedimentation rate; IL-4, Interleukin-4; IL-5, Interleukin-5; IFN-γ, Interferon-gamma; GM-CSF, Granulocyte-Macrophage Colony-Stimulating Factor; ELISA, Enzyme-linked immunosorbent assay; CT, Computed tomography; HAM, High-attenuation mucus; ABPA/M-S, serologic ABPA/M; ABPA/M-B, ABPA/M with bronchiectasis; ABPA/M-MP, ABPA/M with mucus plugging; ABPA-HAM, ABPA/M with high attenuation mucus; ABPA/M-CPF, ABPA/M with chronic pleuropulmonary fibrosis; IQR, Interquartile range.

Ethics Approval and Consent to Participate

This work has received approval from the Ethics Committee of Xiangya Hospital Central South University (approval number, 2023121128). Because this is a retrospective, observational study and all the samples used were leftover specimens from routine clinical examinations, the exemption of informed consent was approved by the Ethics Committee. This study complies with the guidelines of the Declaration of Helsinki.

Acknowledgments

We thank the members of our research group, especially Dr Feifei Yin, Dr Yuanyuan Jiang, Dr Lisha Luo, Dr Yingyu Zhang, Dr Daimo Zhang, Dr Yifei Yang for their support, helpful suggestions and stimulating discussions.

Part of the data presented in this paper is displayed in a preprint available at Researchsquare (https://www.researchsquare.com/article/rs-145782/v1).

Author Contributions

Huan Ge, Runjin Cai, Guotao Li, Bing Liu, and Jun Wang are co first authors. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of

the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This work was supported by the National Natural Science Foundation of China (82270033; 81873407) and Natural Science Foundation of Hunan province (2022JJ30924).

Disclosure

The authors declare that they have no competing interests.

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