Eosinophilic Mucin Rhinosinusitis : Terminology and Clinicopathological Presentation

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Abstract

Many terms related to allergic fungal rhinosinusitis (AFRS) such as eosinophilic mucin rhinosinusitis (EMRS), eosinophilic fungal rhinosinusitis (EFRS), and AFRS-like syndrome have been proposed. The authors define EMRS as patients with rhinosinusitis who demonstrate eosinophilic mucin on histopathological examination. EMRS patients who demonstrate fungal hyphae within the mucin are diagnosed as having EFRS and those who cannot demonstrate fungal hyphae within the mucin are diagnosed as having EFRS-like syndrome. EFRS patients who demonstrate an allergic response to the fungi are diagnosed as having AFRS and those who cannot demonstrate any allergic responses to the fungi are diagnosed as having non-allergic fungal rhinosinusitis (NAFRS). In the United States, the prevalence of AFRS in chronic rhinosinusitis patients who require surgery is 5-10 per cent. However, the prevalence of AFRS in Thailand is not known because AFRS has never been reported and studied in Thailand. This study shows the clinical and pathological entities of patients with EMRS in King Chulalongkorn Memorial Hospital from July 2001 to July 2002. From a total of two hundred and fourteen rhinosinusitis patients who required surgery, six were diagnosed as having EMRS. Two of six EMRS patients were diagnosed as having EFRS (both of them were also diagnosed as having AFRS) and four patients were diagnosed as having EFRS-like syndrome. In this study, the prevalence of AFRS is much less than in the United States because of the limited understanding of this disease, the lack of commercially available antigens for dematiaceous fungi, and the lack of awareness and knowledge of pathologists to diagnose eosinophilic mucin and fungi within the mucin. The terms related to AFRS are also discussed in this study.

Key word : Allergic Fungal Rhinosinusitis, Eosinophilic Mucin Rhinosinusitis, Eosinophilic Fungal Rhinositins, Allergic Fungal Rhinosinusitis Like Syndrome

AEUMJATURAPAT S, SAENGPANICH S, ISIPRADIT P, KEELAWAT S
J Med Assoc Thai 2003; 86: 420-424

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Since allergic fungal rhinosinusitis (AFRS) was recognized by Millar et al[1] in 1981 and Katzenstein et al[2] in 1983, many terms related to this disease such as eosinophilic mucin rhinosinusitis (EMRS), eosinophilic fungal rhinosinusitis (EFRS), and AFRS-like syndrome have been proposed[3-5]. Controversies in definition and diagnostic criteria of each terminology still exist. The authors define EMRS as patients with rhinosinusitis who demonstrate eosinophilic mucin (allergic) on histopathological examination regardless of the presence of fungal hyphae within the mucin or evidence of an allergic response to the fungi. The goal of this study was to show the clinical and pathological entities of patients with EMRS in King Chulalongkorn Memorial Hospital from July 2001 to July 2002. The terms related to AFRS are also discussed.

PATIENTS AND METHOD

All patients who were diagnosed as EMRS since July 2001 were included in the study. EMRS patients were studied for the following information: age; sex; asthma; aspirin sensitivity; eosinophil count; skin prick test to fungi; presence of polyps; characteristic CT; bony erosion; unilateral *versus* bilateral disease; and fungi within the mucin. Characteristic CT is defined as having central areas of hyperattenuation within the sinus cavity. Histopathological examination of the secretion was studied with hematoxylin-eosin stain and further evaluated with Gomori methenamine-silver stain to try and identify fungal organisms. Eosinophilic mucin is defined as having clumps of necrotic eosinophils and other cellular debris, free eosinophilic granules within a background of tenacious-appearing pale, eosinophilic to basophilic amorphous mucin.

RESULTS

From July 2001 to July 2002, two hundred and fourteen patients were operated on for rhinosinusitis. Of these, six patients were diagnosed as EMRS. Data of each patient are shown in Table 1.

Eosinophilic mucin had to be demonstrated in all patients. Eosinophilia, polyps, characteristic CT, bony erosion, fungi within mucin, and skin prick test to fungi were not noted in every patient. They were noted in 3/6, 4/6, 3/6, 1/6, 2/6, and 2/6 patients, respectively. Five patients had bilateral disease and one patient had unilateral disease.

DISCUSSION

Fungal rhinosinusitis can be seen in five distinct forms: acute invasive, chronic invasive, fungus ball, saprophytic colonization, and allergic fungal rhinosinusitis. Allergic fungal rhinosinusitis (AFRS) is the final recognized type and it is believed to be the most common type of fungal sinus infection in most areas of the United States[6]. It was recognized about twenty years ago, initially by Millar et al[1] and subsequently by Katzenstein et al[2]. The disease was originally termed "allergic aspergillus sinusitis" due to the similarity of histopathology to allergic bronchopulmonary aspergillosis (ABPA). A subsequent study

Table 1. Features of patients with EMRS.

Patient number	1	2	3	4	5	6
Age (years)	32	41	47	45	60	63
Sex	M	F	F	M	F	F
Asthma	-	+	-	-	-	-
Aspirin sensitivity	-	+	-	-	-	-
Eosinophil count (%)	6.1	3.5	6.8	9.7	1.45	2.4
Skin prick test to fungi*	+	+	-	-	-	-
Polyps	+	+	+	+	-	-
Characteristic CT	+	+	-	+	-	-
Bony erosion	+	-	-	-	-	-
Unilateral or bilateral	bil	bil	bil	unil	bil	bil
Eosinophilic mucin	+	+	+	+	+	+
Fungi within mucin	+	+	-	-	-	-

* *Alternaria tennis, Aspergillus niger, Helminthosporium sativum, Hormodendrum bordei, Penicillium notatum, Curvularia spicifera, Fusarium moniliforme, Mucor plumbeus, Pullularia pullulans, Rhizopus nigricans*

showed that AFRS was caused by non-aspergillus species[7]. This disease is now appropriately called AFRS.

AFRS is defined as patients with an allergy to the fungus who demonstrate an allergic mucinous response to the fungi[6]. A review by Bent and Kuhn [8] in 1994 identified five consistently seen characteristics in their patients with AFRS. They proposed the following criteria for diagnosis of AFRS: 1) type I hypersensitivity confirmed by history, skin tests, or serology; 2) nasal polyposis; 3) characteristic CT signs; 4) eosinophilic mucin without fungal invasion into sinus tissue; 5) positive fungal stain of sinus contents removed during surgery.

Polyps occur because of persistent inflammation. Central areas of hyperattenuation within the sinus cavity on CT scan represent the proteinaceous allergic mucin. Difficulty of fungal culture may cause a negative fungal culture and a positive culture may represent a saprophytic growth of fungi. The atopic patient who does not have polyps, a characteristic CT, or positive fungal culture, but has the characteristic histopathology of allergic mucin with hyphal elements, is still diagnosed as having AFRS[9].

In 1994, Cody et al[3] defined patients who have allergic mucin without documentation of the presence of fungi (fungal hyphae within the allergic mucin or positive results of cultures for fungi) were identified as having AFRS-like syndrome.

In 1999, Ponikau et al[4] have reported that allergic mucin was found in 97 (96%) of 101 consecutive surgical cases of chronic rhinosinusitis and fungal elements (hyphae, destroyed hyphae, conidae, and spores) were found in 82 histologic specimens (81%), but only 42 per cent of their patients had evidence of allergy. Based on histologic findings and culture results, the diagnosis of AFRS was made in 94 (93%) of 101 consecutive surgical cases of chronic rhinosinusitis. They proposed a change in terminology from AFRS to EFRS since the presence of eosinophils in the allergic mucin, not a type I hypersensitivity, was likely the common denominator in the pathophysiology of AFRS.

In 2000, Ferguson[5] termed the disease that has histology similar to AFRS except for the presence of fungus as EMRS. She proposed that EMRS represents a heterogenous group of pathophysiological mechanisms all associated with eosinophilia, but in which the driving pathological mechanism is not a hypersensitivity to fungus antigen, but rather a systemic dysregulation associated with upper and lower airway eosinophilia.

As mentioned above, there is controversy in the terminology related to AFRS. The authors' suggestions about the terminology and diagnostic criteria related to AFRS are:

1. Eosinophilic mucin is a better descriptive term than allergic mucin.

2. EMRS is defined as patients with rhinosinusitis who demonstrate eosinophilic mucin on histological examination.

3. EMRS patients who demonstrate fungal hyphae within the mucin are diagnosed as having EFRS and those who cannot demonstrate fungal hyphae within the mucin are diagnosed as having an EFRS-like syndrome (similar to the previous term "AFRS-like syndrome"). The authors do not include fungal culture in the diagnostic criteria because a positive culture may represent a saprophytic growth of fungi as in the study of Ponikau et al[4] that 100 per cent of normal volunteers showed culture positive for fungi.

4. EFRS patients who demonstrate an allergic response to the fungi are diagnosed as having AFRS and those who cannot demonstrate any allergic responses to the fungi are diagnosed as having non-allergic fungal rhinosinusitis (NAFRS).

The authors propose two new terms related to AFRS, which are a EFRS-like syndrome and NAFRS. Using the terminology and diagnostic criteria mentioned above, two of the six EMRS patients in the present study were diagnosed as having EFRS (both of them were also diagnosed as having AFRS) and four were diagnosed as having an EFRS-like syndrome. The features of all EMRS patients were shown in Table 1. In the present study the prevalence of AFRS in rhinosinusitis patients who required surgery was 0.93 per cent, whereas in the United States it was 5-10 per cent[9]. The prevalence is much less than in the United States because of the limited understanding of this disease, the lack of commercially available antigens for dematiaceous fungi, and the lack of awareness and knowledge of pathologists to diagnose eosinophilic mucin and fungi within the mucin or it may be because of the low incidence of AFRS itself.

(Received for publication on September 6, 2002)

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โพรงอากาศอักเสบจากอีโอสิโนฟิลิกมิวซิน : ศัพทวิทยาและการนำเสนอลักษณะทางพยาธิวิทยาคลินิก

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ได้มีการเสนอชื่อของโรคที่เกี่ยวข้องกับ allergic fungal rhinosinusitis (AFRS) หลายชื่อเช่นeosinophilic mucin rhinosinusitis (EMRS), eosinophilic fungal rhinosinusitis (EFRS), และ AFRS-like syndrome ซึ่งยังมีความสับสนในความหมายหรือคำจำกัดความของแต่ละชื่อโรคอยู่ คณะผู้เขียนได้ให้คำจำกัดความชื่อโรค EMRS ว่า หมายถึงผู้ป่วยโพรงอากาศอักเสบที่การตรวจทางพยาธิวิทยาพบ eosinophilic mucin ผู้ป่วย EMRS ที่การตรวจทางพยาธิวิทยาพบเชื้อราใน eosinophilic mucin ด้วย เรียกว่า EFRS ถ้าตรวจไม่พบ เรียกว่า EFRS-like syndrome ผู้ป่วย EFRS ที่มีปฏิกิริยาภูมิแพ้ชนิดที่ 1 ต่อเชื้อราด้วย เรียกว่า AFRS ถ้าไม่มีเรียกว่า non-allergic fungal rhinosinusitis (NAFRS) ในประเทศสหรัฐอเมริกา พบความชุกของโรค AFRS ในผู้ป่วยโพรงอากาศอักเสบเรื้อรังที่ต้องทำผ่าตัดเท่ากับร้อยละ 5-10 ส่วนในประเทศไทยยังไม่ทราบความชุกของโรคนี้ เนื่องจากยังไม่เคยมีรายงานโรคและรายงานการศึกษาโรคนี้มาก่อน ในรายงานฉบับนี้ได้ศึกษาโรค EMRS ในโรงพยาบาลจุฬาลงกรณ์ ตั้งแต่เดือนกรกฎาคม พ.ศ. 2544 ถึงเดือนกรกฎาคม พ.ศ. 2545 โดยในระยะเวลาดังกล่าวมีผู้ป่วยโพรงอากาศอักเสบที่ได้รับการผ่าตัดทั้งหมด 214 ราย ตรวจพบว่าเป็น EMRS 6 ราย ใน 6 รายนี้ 2 รายเป็น EFRS (ทั้งสองรายเป็น AFRS ด้วย) และ 4 รายเป็น EFRS-like syndrome จากการศึกษานี้พบว่าความชุกของโรค AFRS เท่ากับร้อยละ 0.93 ซึ่งต่ำกว่าในประเทศสหรัฐอเมริกามาก ซึ่งอาจจะเนื่องจากยังมีความรู้ความเข้าใจโรคนี้น้อยอยู่ การขาดน้ำยาในการทดสอบปฏิกิริยาภูมิแพ้ต่อเชื้อรา การที่พยาธิแพทย์ขาดความตระหนัก และความรู้ในการวินิจฉัย eosinophilic mucin และเชื้อราใน eosinophilic mucin หรืออาจเนื่องจากความชุกของโรคนี้น้อยจริง ๆ ในรายงานฉบับนี้ยังได้อภิปรายถึงชื่อที่เกี่ยวข้องกับ allergic fungal rhinosinusitis

คำสำคัญ : โพรงอากาศอักเสบจากการแพ้เชื้อรา, โพรงอากาศอักเสบจากอีโอสิโนฟิลิกมิวซิน, โพรงอากาศอักเสบแบบอีโอสิโน-ฟิลิกฟังกัล, กลุ่มโรคที่คล้ายโพรงอากาศอักเสบจากการแพ้เชื้อรา, โพรงอากาศอักเสบ, โพรงอากาศอักเสบจากเชื้อรา

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จดหมายเหตุทางแพทย์ ฯ 2546; 86: 420-424

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