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Characteristics of atrophic rhinitis in Thai patients at the Siriraj Hospital*

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SUMMARY

The common characteristics of primary atrophic rhinitis were studied in 46 Thai patients. From history and demographic data the female to male ratio was found to be 5.6 to 1. The significance of environmental factors was supported by the findings that 69.6% were people from rural areas and 43.5% were industrial workers but a hereditary factor has not been confirmed. The results of the blood tests did not elucidate iron deficiency anemia or nutritional deficiency as the cause of primary atrophic rhinitis. However, all nasal swab cultures yielded pathogenic organisms where Klebsiella species especially, K. ozaena, were the most common bacteria isolated which were 100% susceptible to cephalosporins. This finding together with the evidence of sinusitis seen in 58.7% of either plain x-rays or CT scans, was suggestive of the important role of infection in atrophic rhinitis. Atrophic change of the mucosa and bone with widening of the nasal cavity were constant findings in the CT scans but the developmental anomaly of the maxillary antrum was found in only 15.2%. The histological study showed characteristic changes especially squamous metaplasia and 80% of the cases were compatible with the Type II histopathological classification, i.e vasodilatation of the capillaries. The mucociliary function was proven to be impaired in accordance with the loss of cilia. The evidence of Type I allergy demonstrated by skin testing, which was obvious in 85%, is highly suggestive of allergic/immunologic disorders. Although many factors have been cited previously as the possible cause of primary atrophic rhinitis, the common characteristics found in our patients indicate that only bacterial infection, environmental factors and allergic/immunologic disorders could be one or more of its multifactorial etiology and should be further investigated.

Key words: allergic/immunologic factor, bacterial infections, environmental factor, klebsiella, ozaena, primary atrophic rhinitis

INTRODUCTION

Atrophic rhinitis is a well known and quite common disease in Thailand and other developing countries. It has been recognized nearly 4000 years ago but the exact etiology has not been established yet. The history and details of this disease has recently been reviewed by Shehata (1996).

Atrophic rhinitis is generally divided into two types, i.e. a primary or idiopathic type where the etiology is not known and a secondary atrophic rhinitis where the disease developed after certain diseases such as chronic granulomatous infections (e.g. leprosy, syphilis, tuberculosis, sarcoidosis) or following chronic rhinosinusitis or post extensive nasal/septal surgery, trauma and after radiation. Although the etiology of primary atrophic rhinitis has not been established yet, many possibilities have been implicated, for instance: nutritional deficiency, hormonal imbalance, hereditary, developmental disorders or environmental factors (Shehata, 1996; Zohar, 1990).

Atrophic rhinitis is common in Thailand but there is no published report from our country in the world literature yet, therefore a prospective study was performed to reveal specific characteristics of our primary atrophic rhinitis patients which may be related to its etiology.

MATERIALS AND METHODS

From November 1993 to May 1997, all new patients attending the ENT outpatient clinic at the Siriraj Hospital, Bangkok, Thai-

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land, who had symptoms and signs compatible with atrophic rhinitis were included in the study. The complete history and physical findings were recorded. The nasal smear and stain for acid fast bacilli (mainly tubercle and lepromatous bacilli) and serological test for syphilis (VDRL) were performed to exclude patients with secondary atrophic rhinitis. Patients after radiation therapy were also excluded, however, we did not see any patient who developed atrophic changes after nasal or septal surgery.
Then the following investigations were performed:

- Complete blood count to look for iron deficiency anemia.
- Serum cholesterol and total protein to check for nutrition condition.
- Bacterial culture from nasal crust or discharge in the middle meatus to confirm the presence of Klebsiella species and other pathogenic bacteria and test for their susceptibility to commonly used antimicrobial agents.
- Plain radiography and computerized tomography of the nose and paranasal sinuses to study the radiological images of atrophic rhinitis and to record concomitant sinus infection.
- Histological study from biopsy of the middle turbinate to reveal the type of histologic findings.
- Routine allergy skin test to common aeroallergens to identify Type I allergy.

In addition, a mucociliary transport test using saccharin and charcoal powder was performed in order to confirm the impaired mucociliary function claimed to be the characteristic of this disease.

RESULTS

Altogether 48 new patients with the diagnosis of atrophic rhinitis were examined. Two patients were later excluded because one was proven to have intranasal leprosy (Vitavasiri et al., 1994) and another one had positive anti HIV test. Therefore, only 46 patients with primary or idiopathic atrophic rhinitis were studied.
Thirty nine patients were females and seven were males so the female to male ratio was 5.6:1. The mean age was 31 years (30.98±10.13) with the age ranging from 17-59 years (Figure 1). The earliest age at onset was 5 years old and the latest was 53 years old (Figure 2). Duration of the symptoms was from 6 months to more than 20 years with the most common duration between one to 10 years.
Twenty three patients are now living in the Bangkok metropolis, the capital city of Thailand, but 32 of the total population (69.6%) were born and lived in rural area for a long time and developed the disease symptoms before they moved to live in Bangkok.
Therefore these patients could be considered as rural people. Concerning the occupation, 20 patients (43.5%) work in factories or in places where they were exposed to chemicals or other irritants for more than one year.
The chief complaints included crust, purulent discharge, foul smell and nasal obstruction. The details of the presenting symptoms are listed in Table 1. Associated diseases were found in 4 patients, two had hypertension, one had asthma and another

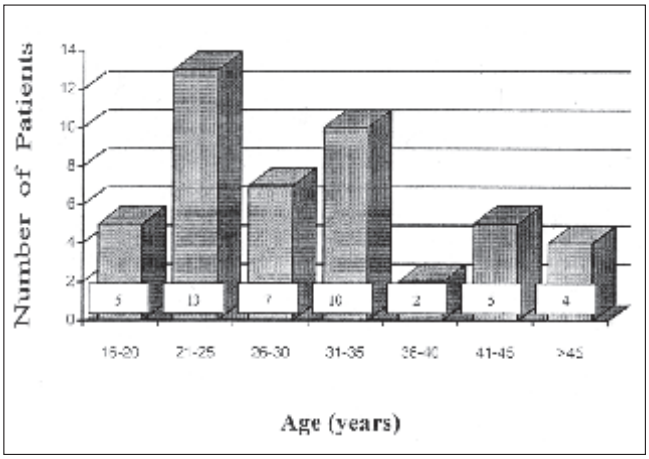


Figure 1. Age distribution of 46 atrophic rhinitis patients. The mean age was 30.98±10.13 with the range from 17-59 years.

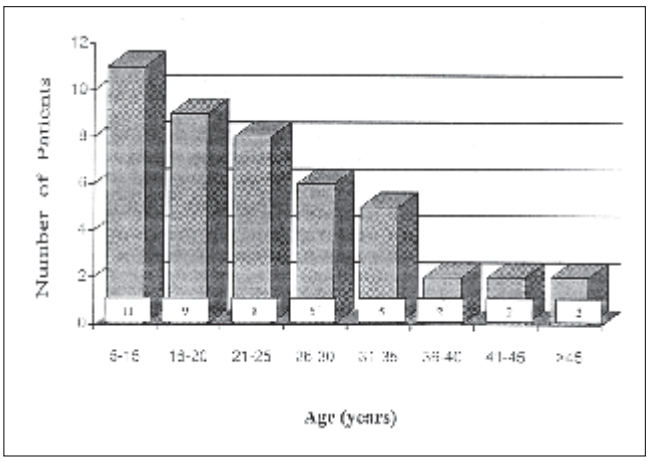


Figure 2. Age at onset of primary atrophic rhinitis. The earliest onset was 5 years old and the latest was 53 years old.

Table 1. Presenting symptoms of 46 atrophic rhinitis patients, listing in decreasing order.

Presenting symptoms.	n	%
Crust	25	54.3
Purulent discharge	20	43.5
Foul smell	19	41.3
Nasal obstruction	17	37.0
Frequent colds	9	19.6
Anosmia	5	10.9
Pain (nose and glabella)	4	8.7
Bloody nasal discharge	1	2.2

one had diabetes mellitus which was controlled by oral antidiabetic drugs. Regarding family history, 6 patients (13%) informed that other members in their families also had similar symptoms, but we did not have a chance to examine them so evidence of hereditary factors could not be confirmed.
On examination, the severity of the disease was classified into 3 stages according to the findings in the nasal cavity as recommended by Ssali (1973) i.e. early stage, advanced and late advan-

ced stages. This classification and the number of patients in each stage are shown in Table 2. The majority or 39 patients (84.8%) were in the advanced stage. It should be noted that in patients with markedly deviated nasal septum, crust was found only in the wider side of the nasal cavity. Table 3 shows the average values of hemoglobin, hematocrit, serum cholesterol and total protein in this group of patients. The statistics were calculated by the SPSS (Statistical Packages for the Social Sciences) program and the frequency of variables indicated the number and percentage of patients whose laboratory values were outside the normal range. There were 2 patients who had an abnormally low value of hemoglobin and hematocrit and 4 patients had borderline value. One patient who had a hemoglobin value of only 7.7 gm/dL had hypertension and was admitted in the hospital twice due to moderately severe epistaxis before inclusion in this study. Hence the results of her hemoglobin and hematocrit values were not added to the group.

The mean value of serum cholesterol and total protein in our atrophic rhinitis patients were all within normal or above the normal range. So there was no evidence of poor nutrition.

The result of the nasal swab culture is shown in Table 4. Klebsiella was recovered from the first swab in 78.3% of the patients and if the result of the second and third swabs were included, 97.8% yielded Klebsiella species. The most common type of Klebsiella found was *K. ozaena* (67.4%), *K. rhinoscleromatis* was found in 30.4% while *K. oxytoca* was found from only one patient. *Pseudomonas aeruginosa* was the second most common organism found in 34.8%, *Pr. mirabilis* 10.9% and *S. aureus* 6.5%.

Since *K. ozaena* was the most common bacteria isolated from nasal swabs of our atrophic rhinitis patients, its susceptibility to oral antimicrobial agents familiar to Otolaryngologists in our country was studied and the results are presented in Table 5.

Table 2. Severity of disease found in 46 atrophic rhinitis patients according to the classification recommended by Ssali[4].

	Staging		
	Early	Advanced	Late - advanced
Crust	- minimal	- lots	- extensive
Odour	- mild foetor	- foul	- foul
Atrophy	- only at turbinates	- generalized, including bones.	- ulceration/bleeding, very large nasal cavities.
N	3	39	4
%	6.5	84.8	8.7

K. ozaena isolated from this series of patients were 100% susceptible to first and second generation cephalosporins while amoxycillin plus clavulanic acid and ciprofloxacin were also more than 90% effective for this organism.

Ciprofloxacin has been recommended for the treatment of atrophic rhinitis or ozaena since 1993 (Borgstein et al., 1993; Nielsen et al., 1995), however in this report cephalosporin seems to be better.

The evaluation of the nose and paranasal sinuses from plain x.rays and computerized tomography is shown in Table 6. Evidence of sinusitis was seen in 20 patients or 58.7%. Using the level system to describe the degree of sinus involvement in CT scan by Van der Veken et al. (1990), CT scan staging was classified from Grade 0 = no change to Grade IV = total opacity, there were 13 patients or 28.3% showing Grade I change, 3 patients or 6.5% showing Grade II, 6 patients or 13% = Grade III and 5 patients or 10.9% = Grade IV. The most commonly affected sinus was the maxillary (41.3%), the ethmoid sinuses were involved in 28.3%, sphenoid sinuses in 8.7% and frontal sinus in 6.5% of the patients, respectively.

The typical CT changes of atrophic rhinitis as reported by Pace-Balzan et al. (1991) e.g. atrophic change of the mucosa and bone and widening of the nasal cavity were constantly observed (Figure 3) and correlated well with the severity of atrophic rhinitis seen clinically. However the developmental anomaly of the maxillary antrum was not common in our patients.

Table 5. Antimicrobial susceptibility of *K. ozaena* isolated from

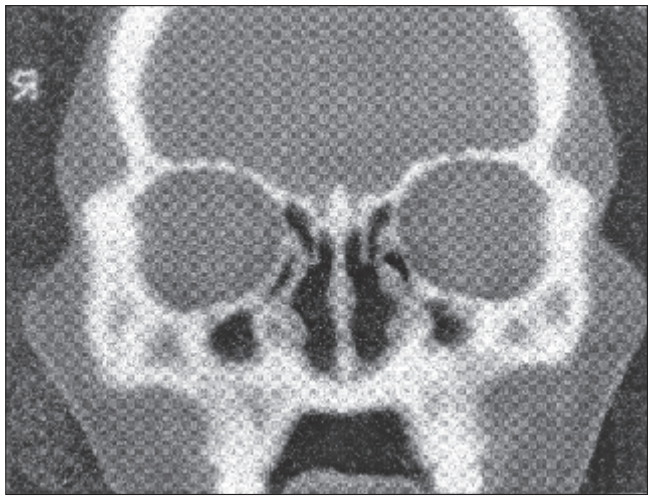
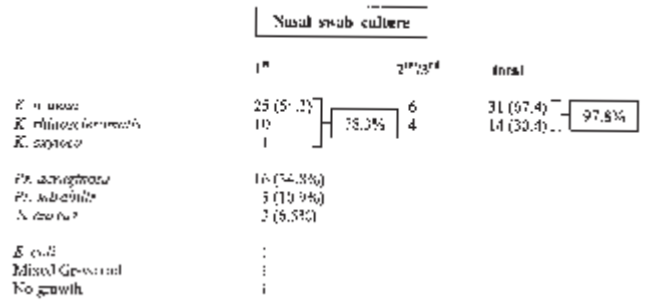


Figure 3. Computerized tomography of the nose and sinuses (coronal view) showing typical findings in atrophic rhinitis i.e, atrophic change of the nasal mucosa and turbinate bone and widening of the nasal cavity. In this case, hypoplasia of maxillary antrum was also observed.

Table 3. Hemoglobin, hematocrit, serum cholesterol and total protein in atrophic rhinitis Thais.

	Normal Thais Range	Atrophic Rhinitis Range	Atrophic Rhinitis Mean + SD	Frequency of Variables	%
Hemoglobin (n=40)	12-18 g/dL	10.7-17.0	13.42±1.15	4	9.5
Hematocrit (n=39)	37-52 %	34.0-49.5	41.26±3.41	7	16.7
Cholesterol (n=37)	100-200 mg/dL	125-259	196.89±35.85	16	37.2
Total protein (n=33)	6.5-8.5 g/dL	6.7-9.3	8.20±0.57	7	16.3

Table 4. Organisms found in the culture from nasal swab.



atrophic rhinitis patients (only oral form).

	+/n	% sensitive
Betalactam Antibiotics		
Ampi/Amoxycillin	10/25	40
BL/BI : Amoxy./Clavulanate	23/24	95.8
: Ampi./Sulbactam	16/18	88.9
Cefaclor	16/16	100
Cefuroxime	7/7	100
Co-trimoxazole	17/25	68
Chloramphenicol	17/25	68
Quinolones		
Ofloxacin	20/23	87
Ciprofloxacin	11/12	92
Pefloxacin	10/12	83.3

Histological findings of atrophic rhinitis were classified into two types as pointed out by Weir (1987), i.e. Type I: characterized by endarteritis and periarteritis of the terminal arterioles and Type II characterized by vasodilatation of the capillaries. From the nasal biopsy of 30 patients, apart from squamous metaplasia, gland atrophy and inflammatory cells which were constant findings, we found that 24 cases or 80% could be classified into Type II. The details of the histological findings in this series of patients will be reported in a separate paper.

Common aeroallergens which were routinely tested at our center are divided into 4 groups i.e. group I: pollen of grass and weeds, group II: house dust mite and other danders, group III: household insects e.g. cockroach, mosquito and housefly, group IV: common moulds. The results of the intracutaneous test to these aeroallergens were divided into a 0–4^{+} scale according to the criteria recommended by Vanselow (1967). We further classified the positive reactions into 4 grades and the results observed in 33 atrophic rhinitis patients tested are shown in Table 7. If we excluded patients who gave negative Grade I reaction, nearly 85% could be considered to have rather definite evidence of Type I allergy.

Table 7. Grading of the degree of positive skin test and the result in 33 atrophic rhinitis patients.

Grading	n	%	
- Positive			
Grade 4 = ++++ to Ag in 3-4 groups	6	18.2	84.39%
Grade 3 = ++++ to Ag in 2-3 groups	6	18.2	
Grade 2 = +++ to Ag in 2-4 groups	16	48.5	
Grade 1 = less than +++ to Ag in 1-2 groups	1	3.0	
- Negative	4	12.1	

Ag = common aeroallergens tested.

The mucociliary function was tested in 23 patients using both saccharin and charcoal powder (Sakakura et al., 1983; Passali et al., 1984). When compared to normal subjects (Table 8) there was an obvious, statistically significant delay of the mucociliary transport time in atrophic rhinitis patients.

Table 8. Comparison of mucociliary transport time between normal Thais* and atrophic rhinitis patients.

		Mucociliary Transport Time (min)		
		Normal Control*	Atrophic Rhinitis	P-value
Total number		**60**	**23**	
Saccharin	- Mean ± SD	7.15±2.33	30.78±24.95	0.044652
	- Range	3.18-17.10	3-60^{+}	
Charcoal	- Mean ± SD	6.51±2.35	36.96±21.60	0.016447
	- Range	2.46-12.0	4–60^{+}	

(> 60 minutes = 9 cases)

* Vannavart N. Mucociliary transport time in normal Thai subjects. Dissertation. Department of Otolaryngology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, 1996:21.

Table 6. Radiological findings from plain x-rays and CT scan of the nose and paranasal sinuses in atrophic rhinitis.

Sinusitis	n	%	Sinus involved	n	%	other findings	n	%
Grade 0	19	41.3	maxillary	19	41.3	- atrophy of bone and mucosa	24	52.2
Grade I	13	28.3	ethmoid	13	28.3			
Grade II	3	6.5	sphenoid	4	8.7	- atrophy of mucosa	6	13.0
Grade III	6	13.0	frontal	3	6.5			
Grade IV	5	10.9				- hypoplasia of max. sinus	7	15.2

Nine cases did not experience sweet taste or showed no charcoal particles on their posterior pharyngeal wall after 60 minutes which was the maximum observation period for this test. This finding simply reflects the degree of squamous change of the nasal ciliated epithelium which is very important for the mucociliary function of the nose and later was proven to be due to *K. ozaena's* ciliostatic effects (Ferguson, 1990).

DISCUSSION

From our study in Thai patients, we have confirmed the fact that primary atrophic rhinitis is more common in women than in men, by the ratio of 5.6 to 1. The age of onset is widely distributed before puberty and during child-bearing period suggesting a possible hormonal influence. Regarding a chronic exposure to irritants in the environment, nearly 70% of our patients used to live in rural areas where open-type stoves using burning wood is widely used for everyday cooking, therefore the SO_2 concentration in their living environment must be high and may have contributed to the etiology (Lu et al., 1995). Another piece of evidence for the environmental factor is that 43.5% of our atrophic rhinitis patients are industrial workers. The study in workers exposed to phosphorite and apatite dust by Mickiewicz et al. (1993) already supported this factor. Although we did not know exactly what kind of chemicals or irritants the industrial workers have been exposed to we believe that any kind of irritants are toxic to the nasal mucosa. If the duration of the exposure is long enough, they are capable of causing squamous metaplasia of the respiratory epithelium.

Nutritional deficiency has been marked as one of the etiologic factors of atrophic rhinitis by many authors including Hiranandani (1976). Vitamin A deficiency and iron deficiency have also been reported as possible causes (Bernat, 1968; Zakrzwski et al., 1975; Han-Sen, 1982; Zakrzewski, 1993; Wiatr et al., 1993). However, a study from Norway which reported about a high incidence of iron deficiency anemia without a relatively high incidence of atrophic rhinitis (Barkve and Djupesland, 1968). The study in our patients also did not confirm the significance of a nutritional factor.

Hereditary or familial tendency as cited by Barton and Silbert (1980) and Singh (1992) is not clearly confirmed in our patients as well as the developmental cause i.e. poor pneumatization of the maxillary sinus pointed out by Hagrass et al. (1992) was not a common finding either.

Bacterial infection of the nose and sinuses as shown by nasal swab cultures together with the high incidence of sinusitis from CT scans have confirmed the significance of chronic bacterial infection in atrophic rhinitis although the role of these infections as a cause of the disease remains controversial. If there is clear evidence that infection occured before atrophic changes develop this should be classified into secondary atrophic rhinitis.

The high incidence of *K. ozaena* recovered in our patients is surprisingly similar to a study done by Mangunkusumo and Marbun (1998) in 61 Indonesians with atrophic rhinitis i.e. 71.6% Klebsiella species, 32.8% *Ps. aeruginosa* and 22.9% *S. aureus* and deserve special attention. Klebsiella species and some other bacteria common to acute and chronic sinusitis do possess the ability to slow ciliary beating (ciliostasis) and disrupt normal coordinated ciliary activity, therefore the mucociliary clearance could be impaired causing persistent infection and probably injury to the ciliated epithelium (Ferguson et al. 1990). So, they are not just an opportunistic colonizer but could be considered as one of the multifactorial etiologies of atrophic rhinitis.

The antimicrobial susceptibility of these bacteria is dynamic and should be individually studied because long-term antibiotic use is still recommended as the mainstay of medical therapy for atrophic rhinitis (Chand and Mac Arthur, 1997). From our experience, apart from regular nasal cleaning, prescription of adequate and appropriate antimicrobial agents is very useful in relieving the patients annoying symptoms.

Vascular disorders of the nasal mucosa was mentioned as another possible cause of atrophic rhinitis, however, two studies of nasal mucosal blood flow which were available revealed different results (Bende, 1985; Liu et al., 1994). The histological study in our atrophic rhinitis patients showed vasodilatation of the capillaries in most cases. These Type II findings did not respond to estrogen therapy and this kind of treatment was not recommended anymore (Taylor and Young, 1961).

Immunological disorder is another factor suspected to play role in atrophic rhinitis patients but the studies of cellular immunity in patients with ozaena were also not conclusive (Fouad et al., 1980; Sipila and Hyrynkangas, 1984). However, Type I allergic reactions are commonly seen in our group of patients. Routine allergy skin test was performed because many patients claimed that they have symptoms typical of allergic rhinitis (e.g. itching, sneezing, rhinorrhea and eye symptoms) and it was surprising to obtain high incidence of positive skin test reactions. This high incidence cannot be just a coincidence. However, the nasal biopsy did not show many eosinophils which is recognized as the hallmarks of allergy. The most common cells found in the section were plasma cells which are capable of producing immunoglobulins, therefore further immunological studies are required. Unfortunately, the determination of serum level of IgE specific to common allergens is not a routine test in our country, because the test kit has to be imported and is very expensive.

It is also necessary to point out that the series of atrophic rhinitis patients in this study are mainly of moderate to severe degree because our center is for tertiary care and located in the capital city, therefore patients with a mild degree of disease are often managed by their local hospitals. However, medical treatment is still effective in controlling their offensive symptoms, only one patient had to undergo surgical treatment. Various surgical techniques to reduce the volume of the nasal fossae in atrophic rhinitis were comprehensively reviewed by Soetjipto (1998), including the latest method using triosite implants and fibrin glue (Bertrand, 1996).

Although secondary atrophic rhinitis from mycobacterial infection (TB, leprosy) is rare for some time, we still recommend our colleagues to be aware of this kind of infection when managing atrophic rhinitis patients. These acid fast bacilli are easily detected by nasal smear and biopsy as we have found and already

reported one case of lepromatous leprosy presented as atrophic rhinitis (Vitavasiri et al., 1994). We anticipate that with more AIDS patients, we will see tuberculosis as the cause of atrophic rhinitis again in the near future as well as syphilis.

In conclusion, the study in Thai patients suggested that certain bacterial infections, environmental factors and allergic or immunological disorders may contribute significantly to the etiology of primary atrophic rhinitis.

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