A CHEMICAL APPROACH TO CHRONIC SINUSITIS

Yoshihjsa Sasaki, Tokyo

In order to investigate chronic inflammation of the nose and paranasal sinus, it is necessary to study the fundamental metabolism of the nasal mucosa as well as the typical products of chronic inflammation such as fibro-edematous polypi. In this paper the author reports the experimental observation that the nasal mucosa has a special enzymatic action while nasal polypi, which are the secondary product of chronic inflammation of nose and sinus, have an anti-proteolytic action.

Only a limited part of the tissues of the human body is known to have fibrinolytic activity when tissue slices or an isotonic saline extract of the particular organ is added to a fibrin clot.

I have found that nasal mucosa is one of such tissues. This fibrinolytic activity was not observed in neighbouring tissue such as palatine tonsils, adenoids and also was not observed in the gastiric mucosa. That is to say we learned that nasal mucosa has a special proteolytic enzyme action distinctly different from the adjacent tissue.

Experiments:

1. Effect of the crude extract of maxillary mucous membrane on fibrin. Dissolution time of the fibrin clot was 25 minutes when the tissue substance was extracted in to 10 times normal saline solution of wet tissue weight. Solutions of two and four times the crude original extract of normal saline solution also have strong fibrinolytic activity.
2. Effect of the crude extract of inferior turbinate on fibrin. Dissolution time of fibrin by this extract dissolved in ten times its wet weight of isotonic saline solution was 15 minutes.
3. Effect of addition of cystein to the extract of mucous membrane of maxillary sinus on fibrinolysis.

Proteolytic enzyme is divided into two major groups. They are the trypsin-plasmin series and the cathepsin-papain group. It is known that enzymes such as cathepsin are activated by cystein which in turn inhibitis plasmin. Therefore I tried to analyze the fibrinolytic activity of normal saline extract of maxillary sinus mucosa by adding cystein. The dissolution time of fibrin clot by addition of cystein was markedly delayed and the optical density reading of the dissoluted fibrin clot was decreased; in other words the fibrinolytic activity was decreased considerably. This fact indicates that the fibrinolytic activity in nasal mucosa is different from cathepsin activity.

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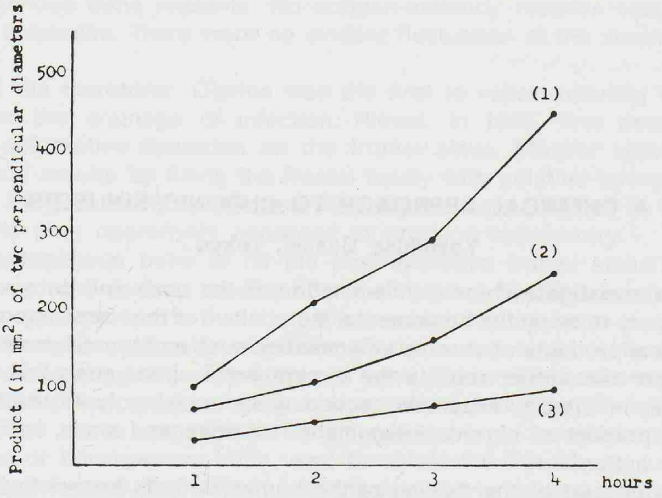

Figure 1. Action of the extract from the mucous membrane of inferior turminate (1), maxillary sinus (2) and nasal polyp (3) (extract from isotonic saline solution with 10 times weight of the wet original material).
Ordinate: Product (in mm^2) of two perpendicular diameters of the lysed zones (average of 3 single determinations).
Abscissa: Reaction time.

4. Effect on fibrinolysis of the addition of Σ-aminocaproic acid to the extract of mucous membrane of the maxillary sinus. It is known that Σ-aminocaproic acid is a plasmin inhibitor. Σ-aminocaproic acid inhibited completely the fibrinolytic activity of the extract of maxillary sinus mucosa.
The above experimental findings demonstrate that fibrinolytic action in nasal mucosa is caused by a plasmin like substance. Plasmin dissolves not only fibrin but also fibrinogen. But nasal mucosa extract does not have fibrinogenolytic action. This indicates that the proteolytic enzyme in nasal mucosa is slightly different from either plasmin or plasmin activator. Thus I have demonstrated that nasal mucosa has a proteolytic activity uniquely characteristic of this structure. This fibrinolytic activity was lost in heating the extract at 56°C for 30 minutes.
5. The distribution of fibrinolytic activity in the tissue extract and the blood serum. Agar electrophoresis of serum and extract of nasal mucosa was performed and compared. After electrophoresis the agar was sectioned into its separate parts and placed on a fibrin plate. The respective lyzed zones were measured after a certain number of hours. Patterns of distribution of fibrinolytic activity in the tissue extract and the serum were compared. The fibrinolytic activity in nasal mucosa was relatively localized in the β-globulin fraction. While the activity of streptokinase activated plasmin in the serum was broader in distribution than that of nasal mucosa.
6. Comparison of the fibrinolytic activities in the mucous membrane of maxillary sinus, inferior turbinate and nasal polypi. I compared the activity of the sinus mucosa affected by maxillary sinusitis, mucosa of the inferior turbinate and nasal polypi. The fibrinolytic activity of the inferior turbinate

mucosa was more potent than that of sinus mucosa. Although it is a typical form of chronic inflammation, extract of the nasal polyp was the least active in the fibrinolytic activity (fig. 1).

7. Antiproteolytic activity in nasal polypi. I have been following the metabolism of the nasal mucosa from the standpoint of proteolytic action. In the next step I investigated the metabolism of nasal mucosa from the standpoint of enzyme inhibition.

The presence of inhibitor of proteolytic enzyme in the normal saline extract of sinus mucosa, nasal polyp, palatine tonsil, adenoid and also blood serum was investigated using casein and trypsin.

After incubation of trypsin and these extracts for 5 minutes, casein solution was added. This mixture was incubated for another 15 minutes, then methyl alcohol with acetec acid was quietely added over these mixture. When these extracts have antiproteolytic action for trypsin, casein will not be dissolved and a white muddy precipitate will be formed at the border line between the solution mixture (extract, trypsin and casein) and methyl alcohol with acetic acid. By our arbitrary standard of measurement the antitryptic action of blood serum was found to be as high as 40 units, while that of nasal polyp was 6 units, and was not measurable in the tissue of sinus mucosa, palatine tonsil or adenoid. (table 1).

blood serum	40 units
nasal polyp	6 units
maxillary sinus mucosa	not observed
palatine tonsil	not observed
adenoid	not observed

Table 1. Antitryptic activity of the extracts of each tissues on caseinolysis

Conclusion:

My experimental findings indicate a characteristic proteolytic enzyme activity in the nasal mucosa with the weakest action in the nasal polyp. I found that in nasal polypi there is a certain inhibitor against proteolytic enzyme activity. These observations of mine may indicate that the fibrinolytic action in nasal mucosa is intimately related to the physiological function of the nasal mucosa. Furthermore inhibition against this proteolytic enzyme present in the nasal polyp may have a significant function in producing chronic pathologic changes in nasal and sinus mucosa. The source of this proteolytic inhibitor is still undetermined as to whether it is derived from blood serum or is produced locally.

It is my opinion that further investigation of this proteolytic action found in the nasal mucosa and the substance antagonistic to it in nasal polypi may lead to a new concept of the pathophysiology of chronic sinusitis.

Yoshihisa Sasaki,
Nihon University, School of Medicine,
Dept. Otorhinolaryngology, Tokyo, Japan.