The Human Adenoidal Mast Cell. Suceptibility to Different Secretagogues and Secretion Inhibitors

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Abstract

Mast cells from adenoid tissues of man do not form a homogeneous population but differ in size and ultrastructure. They degranulate on stimulation with specific antigen, ionophore A 23187, Concanavalin A and, under certain conditions, antihuman IgE or acetylcholine. Compound 48/80, dextran, purified C3a or C5a are ineffective. Adenosine exerts either an enhancing or inhibiting effect on the stimulated histamine release, depending on the actual conditions of the mast cells. The study of a range of known mast cell degranulation inhibitors revealed important differences between human adenoidal mast cells and human basophils or animal mast cell systems. The efficacies of the drugs or drug combinations so far tested correspond well with the established therapeutic effects in man.

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Human adenoid tissues have been used as source of human mast cells for a number of years [6]. They offer the advantage to come from children with a clear case and drug history. The mast cells were isolated first employing enzymic tissue dissoziation with pronase [6] but later solely mechanical dispersion in Ca^{2+} - and Mg^{2+} -free medium. It was only recently recognized that the adenoidal mast cells are very susceptible to lack of Ca^{2+} ions and longer incubation periods [2, 3].

The highest yield of functionally intact mast cells was obtained using the following method: the adenoid tissues are placed into complete Hanks solution immediately after surgery and worked up as soon as possible. The tissues are washed, finely chopped on a McIlwain & Buddie tissue chopper and suspended in 5 volumes of ice-cold Hanks solution. The tissue suspension is then mechanically dispersed by pressure and suction using a plastic syringe, stored in an ice bath for 10 min and followed by a second mechanical dispersion and centrifugation (5 min, 50 g, 4°C). The sediment is resuspended in Hanks solution and filtered through Vyon filter (pore size about 100 μm), washed, and filtered again through the Vyon filter. After a final wash, the cells are stained with Alcian blue at pH 2.7, counted in a Neubauer chamber, made up with medium to the desired volume and are ready for further purification [5], experimental use or pharmacological or morphological analysis.

The morphology showed that adenoidal mast cells, in contrast to those obtained from nasal mucosa (turbinates) or mesentery, comprise several populations differing in size (fig. 1) and ultrastructure [1] and presumably also in function.

Until now adenoidal mast cells from more than 600 individuals have been prepared. Table I shows the susceptibility (significant histamine release) to various potential secretagogues and their relevant threshold concentrations.

Table I. Susceptibility of human adenoidal mast cells to different secretagogues (threshold concentrations for the induction of histamine release)

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Nasal mucosa (n = 410)

10-5 10-6 10-6

10-6

No inhibition

No(at > 10⁻⁵ release)

10-3

10-3

10-4

10-3

3 4 5
Cell diameter, μm

Fig. 1. Size distribution of human mast cells from nasal mucosa (turbinates), adenoid tissue and mesentery. The cells were isolated using the pronase method [6], fixed in glutaraldehyde (2.5%, pH 7.4), stained with toluidine blue (0.1%, pH 2.7) and smeared on slides and embedded in Eukitt (Kindler, Freiburg/Brsg.). All metachromatically staining cells/slide were measured using an equilibrated ocular micrometer (Leitz, Wetzlar).

Table II. Inhibitory effects of various drugs on the concanavalin A-induced histamine release from human adenoidal mast cells, M

Disodium Cromoglycate

Adrenaline

Reproterol, Procaterol

Azelastine

Ketotifen

Cyproheptadine

Verapamil/Gallopamil

Clozapepide

Xylometazoline

Inosine Pranobex

Table II shows the inhibitory effect of a range of potential degranulation inhibitors (significant inhibition of the histamine release induced by Concanavalin A 50 µg/ml.

It is noteworthy that adenoidal mast cells do not develop tachyphylaxis to DSCG [4]. The inhibitory effect of adrenaline was found to be less marked than expected. The same was the case with the calcium entry blocker verapamil and gallopamil. Ketotifen was found to be entirely ineffective. On the other hand, some imidazolines, e.g. xylometazoline, believed to act only as α -sympathomimetic agents in blood vessels of the mucosa, inhibited the histamine release at therapeutic concentrations. So did inosine pranobex, believed to be a specific immunostimulant. The effect of cloxazepide, a calmodulin inhibitor, is more complex.

The efficacy of these drugs corresponds rather well with their established antiallergic effects in man. Although important differences compared with animal mast cell systems or human basophils are obvious, human adenoidal mast cells seem to be a suitable model for the evaluation of drugs to be used therapeutically in man.

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