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Histological examination of the lacrimal gland after experimental administration of Cladribine

Cladribine is a new promising antileukemic and immunosuppressive agent (6). 2-chloro-2'-deoxyadenosine is a potent drug against hairy cell leukemia and other lymphomas (5, 8, 9). 2-CDA has recently been reported to favourably alter the clinical course of chronic progressive multiple sclerosis (10, 11).

The purpose of the research was to estimate the structure of the lacrimal gland after the application of Cladribine to experimental animals.

MATERIAL AND METHODS

The experiment was carried out on 30 rabbits of New Zealand breed weighing about 3 kg. The rabbits received water and standard granulated fodder *ad libitum*. The animals were divided into three groups: one control and two experimental groups. The control group included animals receiving 0.9% NaCl (subcutaneously). The experimental group I included rabbits receiving Cladribine in the dose corresponding to the schema of experimental treatment in the hairy cell leukemia and the experimental group II the dose corresponding to the schema of experimental treatment in multiple sclerosis. After 24 hrs from the last dose of 0.9% NaCl in the control group and the last dose of Cladribine in the experimental groups the rabbits were sacrificed and specimens of the lacrimal gland were collected for histological examinations. The obtained tissue material was fixed in 10% neutral formalin, dehydrated in ethyl alcohol, cleared in xylene and embedded in paraffin. Then we performed the routine staining with hematoxylin and eosin, the staining with azan for the visualization of connective tissue fibers and PAS reaction for the detection of neutral polysaccharides on paraffin 5 μm thick sections. The staining procedures were performed simultaneously on the

material of both experimental and control groups. The slides were observed and the photos were taken in the light microscope Janamed with the photo-camera (Carl Zeiss, Jena). We performed the histological analysis of the lacrimal gland.

RESULTS AND DISCUSSION

We observed the nuclei of the cells of the lacrimal gland from the experimental group I (Fig. 1). They had of an oval shape and were smaller in comparison with the control group. The basic membranes of the lacrimal gland had an irregular shape. The connective tissue forming the stroma of the gland was reduced. The aforementioned changes could have been caused by the administration of the medicine. The morphological changes were not discovered in the lacrimal gland in animals of the experimental group II in slides stained with hematoxylin and eosin (Fig. 2).

The available literature does not present papers concerning the influence of Cladribine on the lacrimal gland. However, the toxic influence of many cytostatic and immunosuppressive medicines on the lacrimal gland has been observed. Ahmadi and Esmaeli observed canalicular stenosis secondary to weekly treatment with docetaxel (1). Esmaeli et al. described epiphora, which is a newly recognized side effect of

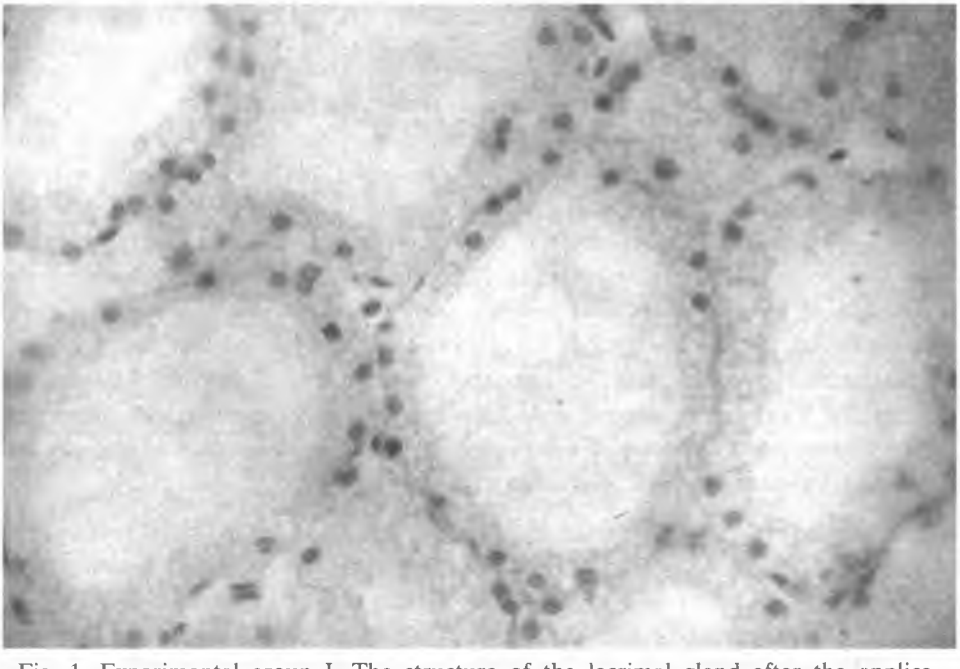

Fig. 1. Experimental group I. The structure of the lacrimal gland after the application of Cladribine – H+E staining. Magn. approx. 800x

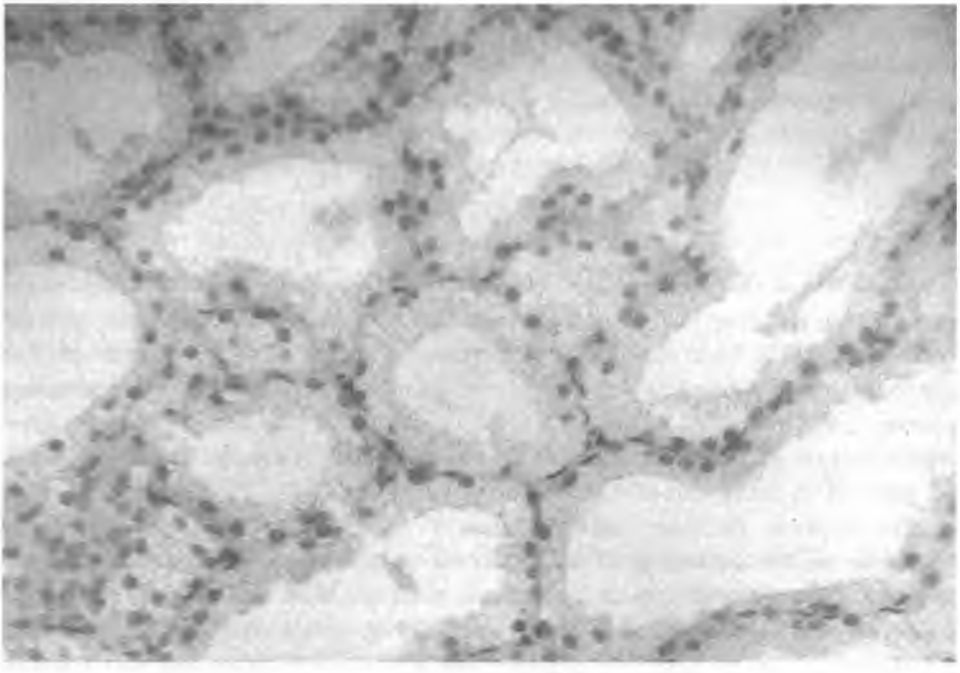

Fig. 2. Experimental group II. The structure of the lacrimal gland after the application of Cladribine – H+E staining. Magn. approx. 800x

docetaxel and may occur more frequently with weekly cycles of this drug. The mechanism for epiphora seems to be punctal and canalicular stenosis. This side effect, in advanced cases, is not reversible with discontinuation of the drug (3). Hassan et al. suggest that the prevalence of tearing and canalicular fibrosis in patients receiving systemic 5-fluorouracil therapy as palliative treatment is related to the total dose and duration of treatment. The epiphora is often reversible on stopping therapy if canalicular fibrosis has not yet developed (4). "Documenta Ophthalmologica" described the obstruction of the tear ducts after systemic therapy with fluorouracil, due to punctal and canalicular stenosis and fibrosis (2). Prasad et al. observed that severe stenosis of puncta and canaliculi may be associated with prolonged systemic 5-fluorouracil therapy (7). Tsai et al. suggest good long-term results for probing with adjunctive, topical Mitomycin–C for cases of adult epiphora caused by obstruction of the nasolacrimal duct followed by repeat procedure (12).

CONCLUSIONS

1. The administration of Cladribine in the doses corresponding to the therapeutic doses used in the therapy of hairy cell leukemia causes mor-

phological changes in the lacrimal gland on the level of the light microscope.

2. Cladribine administered in therapeutic doses in the therapy of multiple sclerosis does not cause morphological changes in the structure of the lacrimal gland.

3. Regular ophthalmological examinations are indicated during Cladribine treatment.

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SUMMARY

The experiment was carried out on female rabbits of New Zealand breed weighing about 3 kg. The rabbits from experimental group I received Cladribine in the dose corresponding to the schema of treatment in the hairy cell leukemia and the animals from the experimental group II the dose corresponding to the experimental treatment in multiple sclerosis.

The lacrimal glands were collected for histological examinations in the light microscope. It was observed that administration of Cladribine in the dose corresponding to the therapeutic dose used in the therapy of hairy cell leukemia could have caused morphological changes in the lacrimal gland, but the medicine administered in therapeutic doses in experimental therapy of multiple sclerosis does not cause morphological changes in the structure of the lacrimal gland on the level of the light microscope.

Histologiczna ocena gruczołu łzowego po eksperymentalnym podaniu Kladrybiny

Badania wykonano na królikach, samicach rasy nowozelandzkiej o masie ciała ok. 3 kg. Królikom grupy doświadczalnej I podano Kladrybinę według schematu leczenia białaczki włochatokomórkowej, a zwierzętom grupy doświadczalnej II według schematu eksperymentalnego leczenia stwardnienia rozsianego.

Do oceny histologicznej w mikroskopie świetlnym pobierano gruczoły łzowe. Zaobserwowano, że podawanie Kladrybiny w ilości odpowiadającej dawce leczniczej stosowanej u człowieka w terapii białaczki włochatokomórkowej może powodować zmiany morfologiczne w obrębie gruczołu łzowego, natomiast lek stosowany w terapeutycznych dawkach w eksperymentalnej terapii stwardnienia rozsianego nie powoduje widocznych zmian morfologicznych w strukturze gruczołu łzowego, stwierdzanych w badaniach przy użyciu mikroskopu świetlnego.