

LATE MORPHOLOGICAL CHARACTERISTICS OF THE PAROTID SALIVARY
GLANDS IN MONKEYS AFTER MUMPS

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The tendency for the frequency of chronic non-neoplastic diseases of the salivary glands to increase is still continuing. The most important of these diseases are the metabolic sialoses, characterized by a progressive lesion of the acinar cells, leading to sclerosis, and lymphoepithelial benign lesions of the salivary glands [1, 11]. Numerous investigations have demonstrated the multifactorial nature of salivary gland diseases, and among the various exogenous and endogenous factors, a viral nature of salivary gland diseases has been stipulated [7]. Natural immunologic tolerance may be disturbed by viruses, which, on insinuating themselves into the cell genome, modify the process of recognition of "own" and "foreign" cells [10]. This may be the case also with mumps, recurrences of which are found in elderly persons, with characteristic disturbances in the immunoglobulin-forming system [9]. The role of mumps in the pathogenesis of chronic non-neoplastic diseases of the parotid glands still remains in dispute. Some workers consider that these diseases are interconnected [3], whereas others reject any such connection [2, 4-6]. However, none of the investigators cited has obtained any convincing proof in support of his own point of view.

The aim of this investigation was to determine the morphological characteristics of the parotid salivary glands infected with mumps virus, at different times after the beginning of the disease in monkeys.

EXPERIMENTAL METHOD

Experiments were carried out on three male crab-eating macaques (*Macaca irus*), with average body weight of 3.5 kg and aged 2-3 years. Mumps was produced by injecting 1 ml of culture fluid containing mumps virus in a titer of $10^{5.75}$ - 10^6 TCD₅₀/ml, into the main efferent duct of the parotid salivary gland. The virus was obtained from the virus museum of the Research Institute of Virology, Academy of Medical Sciences of the USSR. The experimental animals were kept in the same cage and were fed together. Culture fluid with virus was injected into the gland of monkey No. 1 bilaterally. The animals developed a clinical picture of bilateral mumps 8 days after infection. A clinical picture of right-sided mumps was observed in monkey No. 2, 2 days after the beginning of the illness in monkey No. 1; infection took place by contact. Signs of mumps were not observed in monkey No. 3, and she was accordingly given an injection of 1 ml of culture fluid with virus into each duct; 8 days later she also had a marked picture of the disease. Serologic and the principle clinical blood parameters corresponded to those of mumps. Excision biopsy of both parotid salivary glands of monkeys Nos. 1, 2, and 3 was carried out 3 months and 1 year after the beginning of the disease, under general anesthesia (Callipsol, 0.2 mg/kg body weight). Material was taken from all the animals from the lower pole of the gland. Pieces of parotid gland tissue thus obtained were fixed in 80° ethanol and embedded in paraffin wax; sections were stained with hematoxylin and eosin and with eosin-azure. The area of infiltration of connective and adipose tissue, the dimensions of the acini, and the number of salivary tubules were determined by means of an ocular grid.

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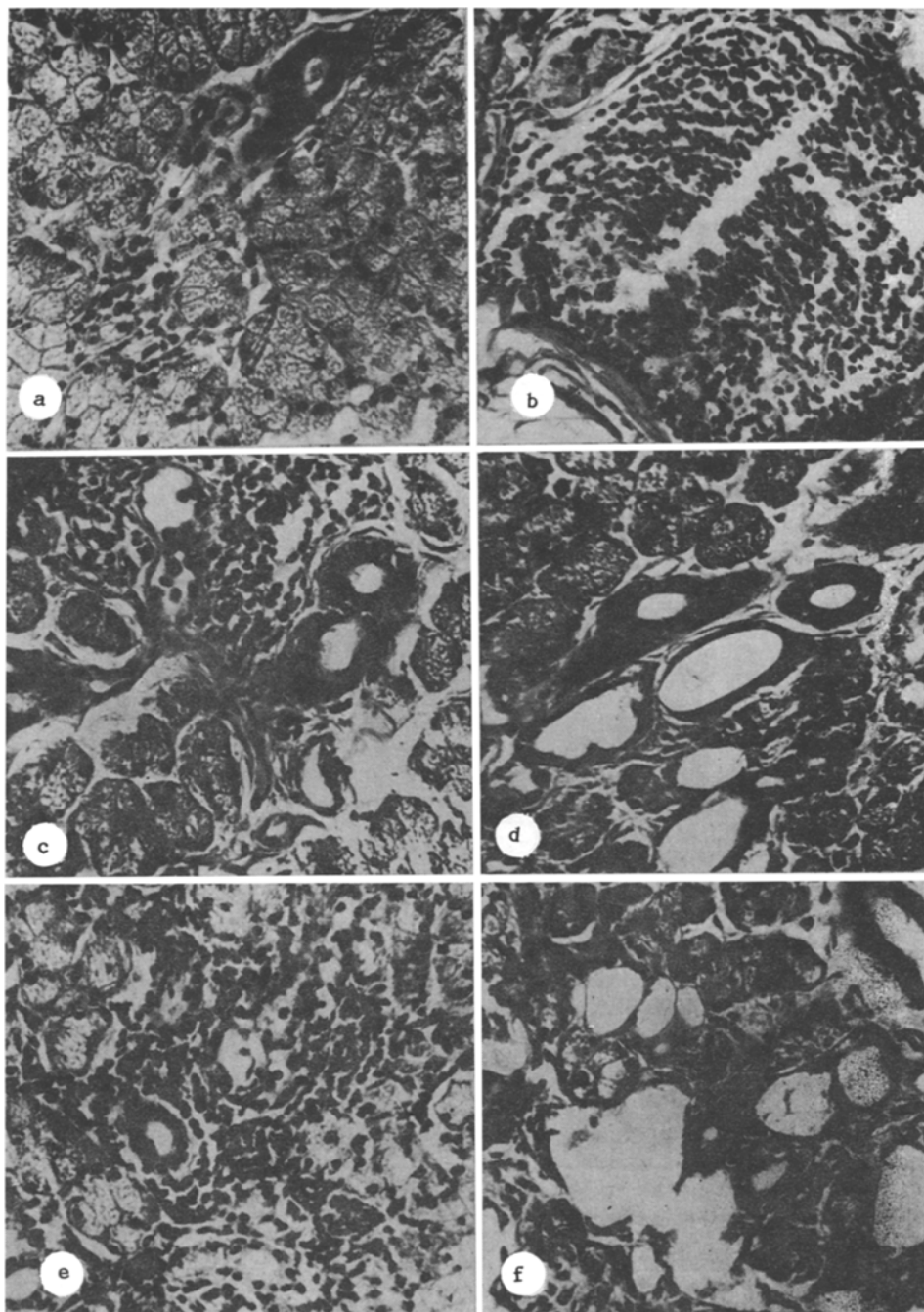


Fig. 1. Morphological characteristics of parotid salivary glands of monkeys 3 months (a, b, c) and 1 year (d, e, f) after mumps. 250 \times . a) Minimal infiltration around intralobular efferent ducts. Eosin-azure; b) focal infiltration into tissues of gland. Hematoxylin and eosin; c) cystic dilatation of efferent ducts of gland, accumulation of secretory granules in cytoplasm of acinar cells. Eosin-azure; d) diffuse infiltration of stroma and fibrosis of parotid salivary gland. Hematoxylin and eosin; e) lipomatosis of parotid salivary gland. Hematoxylin and eosin; f) periductal sclerosis, secretory stasis, focal infiltration of parotid salivary gland. Eosin-azure.

EXPERIMENTAL RESULTS

Morphological investigation of the parotid glands of the experimental animals 3 months after the beginning of the disease revealed stereotyped changes, except that the morphological picture of the left parotid gland of monkey No. 2 corresponded to the normal structure

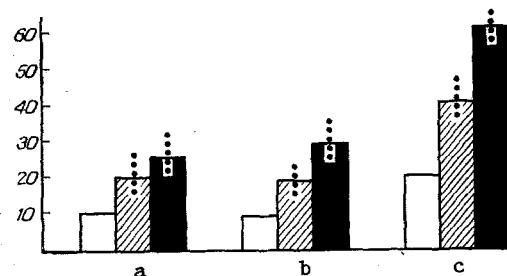


Fig. 2. Morphometric characteristics of parotid salivary glands of normal monkeys and in the late stages after mumps. Empty columns — normal, obliquely shaded — 3 months, shaded black — 1 year after mumps. a) Cellular infiltration, b) lipomatosis, c) connective tissue.

of the parotid salivary gland, and it was taken as the control group. The epithelium of the terminal secretory portions was characterized by a delicately vacuolated cytoplasm and the cell nuclei were located in the basal portion. In most lobules delicate fibrous connective tissue with solitary lymphocytes, macrophages, and plasma cells was identified around the intralobular efferent ducts (Fig. 1a). In some lobules focal infiltration by macrophages and lymphocytes, more especially the latter, was observed (Fig. 1b). The connective tissue was very poorly developed. Changes were most marked in the right parotid salivary gland of monkey No. 2 (contact infection). This was true in particular of the intralobular efferent ducts, which showed cystic dilatation; the epithelium lining them was greatly flattened (Fig. 1c). Distinct focal infiltration by lymphocytes, macrophages, plasma cells, and eosinophilic leukocytes was observed around the ducts and the terminal secretory portions. The cytoplasm of the acinar cells showed stronger basophilia and it stained unevenly. An increase in the quantity of adipose tissue, taking the place of the terminal secretory portions, also was noted.

Focal and diffuse infiltration still persisted in the parotid salivary glands of the experimental monkeys 1 year after the illness, both around the intralobular efferent ducts and also in the center of the lobules, with replacement of the parenchyma of the gland (Fig. 1d). The quantity of adipose tissue was considerably increased (Fig. 1e). The distribution of secretory granules was distinctly mosaic in character. Marked secretory stasis was observed in individual acinar cells. These cells were enlarged and their cytoplasm consisted of large basophilic secretory granules (Fig. 1f). These changes were most marked in the right parotid gland of monkey No. 1. The distinguishing feature of the right parotid gland of monkey No. 3 was considerable proliferation of coarse fibrous connective tissue around the ducts and blood vessels and between the lobules.

Thus 1 month after the illness not only were morphological changes still present in the salivary glands, but qualitative differences also appeared (Fig. 2): there was a clear tendency toward an increase in the area of infiltration not only around the intralobular efferent ducts, where normally there should be single lymphocytes, macrophages, and plasma cells [12], but also around the terminal secretory portions with foci of substitution of the latter. There was also an increase in the number of acini with evidence of secretory stasis, evidently depending on primary involvement of the duct system in mumps, followed by their dilatation, sclerosis, and increasing infiltration, which may interfere with the outflow of secretion. All the morphological changes in the parotid glands described above, moreover, were observed without any clinical signs of chronic non-neoplastic diseases.

It can accordingly be concluded that the morphological picture of the monkey parotid salivary glands found in the late stages after mumps corresponds to the early stages of autoimmune paratitis, i.e., Sjögren's disease [8, 13]. Increasing infiltration not only around the dilated efferent ducts, but also between the acinar cells, together with fibrosis and lipomatosis, reflect not only primary damage to the gland tissue by mumps virus, but also the onset of autoaggression. The increase in the number of gland cells with signs of secretory stasis — "lengthening of the duration of the phase of secretory granule preservation"

[14] - creates favorable conditions for their death and either their subsequent replacement by adipose tissue or the development of immunologic conflict, which lies at the basis of progression of Sjögren's disease. The present investigation shows that a virus disease of the salivary glands can play an important role in the triggering of autoimmune diseases of the salivary glands.

LITERATURE CITED

1. V. S. Kolesov, *Vrach. Delo*. No. 3, 96 (1983).
2. G. N. Maskalenko, *The Principal Stomatologic Diseases* [in Russian], Moscow (1981), pp. 153-156.
3. P. S. Polyanskii, *Mumps* [in Russian], Kiev (1979), p. 112.
4. I. F. Romacheva, L. A. Yudin, V. V. Afanas'ev, and A. N. Morozov, Moscow (1976).*
5. O. V. Rybalov, *Abstracts of Proceedings of a Scientific Conference of Stomatologists* [in Russian], Poltava (1981), p. 154.
6. O. V. Rybalov, *Stomatologia*, No. 6, 35 (1982).
7. M. G. Rybakova, *Arkh. Patol.*, No. 11, 85 (1979).
8. G. V. Savel'ev, Z. G. Aprosin, T. I. Lopatkina, and Z. N. Vavilova, *Arkh. Patol.*, No. 1, 44 (1978).
9. L. Sazama, *Diseases of the Salivary Glands* [in Russian], Prague (1971).
10. V. F. Semenov, *Arkh. Patol.*, No. 10, 77 (1973).
11. A. C. Thackray, *Histological Typing of Salivary Gland Tumours*, WHO, Geneva (1972).
12. C. Bimes, D. Barthe, and T. David, *Bull. Assoc. Anat. (Nancy)*, 59, 333 (1975).
13. K. Donath and G. Seifert, *Allergologie*, 4, 3 (1981).
14. G. Seifert and K. Donath, *Beitr. Pathol.*, 159, 1 (1976).

*As in Russian original; a search of "Ezhegodnye Knigi SSSR" (which lists all books published annually in the USSR) revealed nothing by these authors in 1972-82.

CHANGES IN RESPIRATORY ORGANS IN EXPERIMENTAL ADENOVIRUS INFECTION

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There have been few studies of the pathomorphology of adenovirus infection [1, 2]. The reason is evidently the difficulty of experimental reproduction of this infection [3-12].

The aim of this investigation was to reproduce adenovirus infection experimentally and to describe the structural changes in the respiratory organs.

EXPERIMENTAL METHOD

Experiments were carried out on six African green monkeys weighing 1.5-2 kg. Type AVL-4 adenoassociated virus, in combination with simian adenovirus S-15 (strain I-1) was instilled into the nasal passages and rubbed into the mucous membrane of the tonsils and conjunctiva of the eyes of these animals. Reinfection with the adenovirus was carried out on the 23rd and 40th days, and was preceded by administration of the immunodepressant cyclophosphamide. In another experiment 286 newborn cotton-tail rats were used and were infected intranasally, under superficial ether anesthesia, with adenoviruses of types 1 and 2. The respiratory organs were studied 6 h and 1-7, 10, 14, and 21 days after infection by histological,

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