Faculty of Veterinary Medicine, Department of Pathological Anatomy

SALIVARY GLAND VIRUS DISEASE IN GUINEA PIGS.

Hüseyin K. Urman*

A virus disease of man and animals characterized by intranuclear and intracytoplasmic inclusion bodies in greatly hypertrophied cells primarily in the salivary glands and several organs was described many years ago.

Strains of the virus are species-specific, although the similarity of the morphologic changes they produce suggests that they are biologically closely related.

It is now well recognized that there exist in man, monkey and seveal rodents closely related viruses called cytomegaloviruses, also salivary gland, submaxillary gland, and cytomegalic inclusion disease viruses which may lie dormant in the salivary glands, but are capable of causing fatal generalized infection in guinea pigs. A generalized blood dyscrasia, congenital defects such as microcephaly, cerebral calcification and hepatosplenomegaly has been noted in infants by a number of investigators [3, 12, 14]. Salivary gland disease in a 4-week-old dog with degeneration of the ductal epithelium of the submaxyllary gland and eosinophilic intranuclear inclusion bodies was reported by Haberman at all [4]. This is probbably the first recorded case of domesticated animals.

Avoiding confusion it has been proposed that the so-called "Sallivary gland virus (SGV)" or "Cytomegalic inclusion disease virus (CID)" viruses of man and anilmas be referred to as the "Cytomegalovirus" group [3].

In 1954 Margaret Smith [9] reported the succesful culture of the virus of salivary gland disease of mice. The culture of the virus of human cytomegalic inclusion disease was then reported by

* Dr. Med. Vet., Fuculty of Veterinary Medicine, Department of Pathological Anatomy. Ankara - Turkey.

Row and his associtates [7], by Margaret Smith [10], by Weller and his associates [14], and by Gear and le Roux [3].

The guniea pig salivary gland disease virus have been well characterized by Andrewes [1], and later by Hartley [5], More recently, strains of cytomegaloviruses were recoverd and cultivated from monkeys by Black in 1963 [2].

Studies have indicated that the behavior of the guinea pig cytomegalovirus in tissue culture is strikingly similar to that of the human cytomegalovirus [5, 7, 14]. The cytopathic effects of the agents are very similar, and are produced only in fibroblasts [5, 7]. The cytopathic changes in tissue culture are initially focal and are characterized by cytomegaly and intranuclear inclusions [5, 7, 10, 14].

Repeated attempts to infect tissue cultures of human celles with the guinea pig agent, and vice versa, were negative [5]. Similarly, non-human tissues inoculated with human cytomegalic virus gave also negative results [14]. However, Black and his associates [2] report on the ability of some monkey cytomegalovirus strains to multiply in both human and monkey tissue culture cells is the first exception to this specifity stated above.

The purpose of the present paper is to atract attention to lesions of guinea pigs when used for research on other viruses might be confused with those of cytomegalovirus.

Materials and methods

The present investigation is based on 15 animals which were randomly collected from the guinea pig collonies of the Veterinary-Bacteriology Department.

Immediately after the animals were killed the sallivary glands, liver, and kidneys were removed and immersed in buffered neutral formalin solution, Zenker's, and Susa's fluids. Paraffin sections were cut and stained with hematoxylin and eosin, Mallory's modified trippel stain, and periodic acid-Schiff recation (PAS).

Results

Eight of 15 guinea pigs revealed focal mononuclear cell infiltrations of the submaxillary glands with typical intranuclear and intracytoplasmic inclusions in the epithelial cells of the ducts. Altough the lesions were confined to the serous part of the glands, only in one case both serous and mucous glands were similary affected.

The disease was always accompanied by inflammatory changes such as a patchy interacinar and periductal accumulation of lymphocytes and plasma cells. Dilated and denuded ducts within such inflammatory foci were observed.. Intranuclear and cytoplasmic inclusions were prominent in epithelial cells of the ducts within or adjacent to the infiltrates described. In the much enlarged celles in which the inclusions were well developed, the nuclear chromatin was marginated, leaving a clear zone between the nuclear membrane and the inclusion. This inclusions were acidophilic and were quite granular in apperance. In the zone and on the inclusions body itself one or several dense basophilic granules suggesting chromatin could usually be found.

The cytoplasm of the affected cells projects into the lumen of the ducts. Many of these cells containing intranuclear inclusions, cytoplasmic inclusions were found as well. They appeared as round basophilic bodies and were located on the projecting pole of the cells, and some of them were surrounded by a halo. Occasionaly, large numbers of these cytoplasmic inclusions lay free in the lumen of the ducts. Exfoliated inclusion bodies harboring duct cells were observed rarely. The cytoplasmic inclusions gave a strong PAS positive reaction. Minute PAS positive round granules in normal ductus cells were always present.

Discussion

Eight out of 15 guinea pigs exhibit pathognomonic changes of the "Salivary Gland Virus Disease."

These preliminary findings suggest that the disease is widespread and in an active stage in the salivary glands. No lesions were observed in any other part of the body but submaxillary glands. Only in one case mucous and serous salivary glands were both involved in the disease.

Intranuclear inclusion bodies were observed in the epithelium of several ductules; no cytomegaly was found in other parts of the gland tissue. It seems that the virus has a predilection for the duct epithelium of the serous glands, but little affinity for the mucous glands. Sabai [8] claimes that inclusion bodies did also occur in the salivary acinar epithelium of the guinea pigs, which were never observed in our cases.

The intracytoplasmic inclusions of the duct cells were basophilic and gave a strong reaction for mucopolysaccharides, they were

always located on the projecting pole of the enlarged cells. It is believed that these inclusions are metabolic proceses and are the result of a hyperactivity of the hypertrophying cytoplasm. This suggestion is based on the observation that normally numerous PAS positive minute globules does always occur in the cytoplasm of these ductules. Only the differances are that in normal cells the globules are distributed in the whole cytoplasm, whereas the so-called inclusions are much more larger and located in the projecting pole of the cytoplasm. Symmers [11] however, stated that these inclusions appear to be mainly mucopolysaccharide secretory products which have accumulated because the presence of virus interferes with nuclear function. The occurence of cytoplasmic inclusions in tissue cultures has not been reported so far.

Exfolieted cells having both type of inclusion bodies were occasionally observed in the duct lumina. This may indicate that the virus is discharged by the saliva. In infants, cells characteristic of the disease could be found in the urine and can be confirmed by cultivation the respective specimens of the urine in tissue cultures of human fibroblasts. It would be interesting to find out whether the virus of the guinea pigs could be detected in the saliva by using similar methods.

Summary

The literature concerned with "Salivary Gland Virus Disease" in guinea pigs is briefly reviewed.

The finding of the pathognomonic apperances of "Salivary gland virus disease" in submaxillary gland tissue from guinea pigs are recorded.

Histological examination of submaxillary gland revealed typical intranuclear and intracytoplasmic inclusion bodies within enlarged duct cells and with varying degrees of mononuclear cell infiltrations.

The cytoplasmic inclusions gave PAS positive reaction. These were considered to be the result of a hyperactivity of cells harboring intranuclear inclusion bodies.

Özet

Kobaylarda Tükürük Bezinin Viral Hastalığı

Tükürük bezlerinin anormal şekilde büyümüş epitellerinde ve diğer organ hücrelerinde "INTRACYTOPLASMIC" ve "INTRANUCLEAR" inclusion cisimciklerinin teşekkülü ile karakterize edilen insan ve hayvanların viral bir hastalığıdır. Etkeni TÜR-, ÖZELLİĞİ gösterir; yani kobayı hasta eden virus insan ve diğer türler için patojen değildir ve bunun aksi de varittir.

"CYTOMEGALOVIRUS" grubu içinde mütalâa edilen bu etkenler doku kültürlerinde "CYTOPATHIC" tesire maliktirler.

Cytomegalovirus'lar insan (özellikle çocuklarda), maymun, köpek ve çeşitli kemiricilerde tesbit edilmiştir.

Hastalığa ilk defa Veteriner Fakültesi Bakteriyoloji Kürsüsü kobaylarında rastlanmıştır. Hastalık yalnız submaksillar tükürük bezlerinde lokalize olmuştur. Hastalık, kanal epitellerinde tesbit edilen intracytoplasmic ve intranuclear inclusion cisimciklerinden başka oldukça şiddetli fokal interstitiel bir yangı ile seyretmektedir. İntracytoplasmic cisimcikler kuvvetli PAS pozatif bir reaksiyon vermişlerdir.

Hastalık laboratuvar hayvanlarında nadiren ölümlere sebep olmaktadır. Fakat virus denemelerinde bu hastalığı taşıyan kobaylar kullanıldığı taktirde meydana gelebilecek lezionların kıymetlendirilmesinde karışıklığa sebep olabilir.

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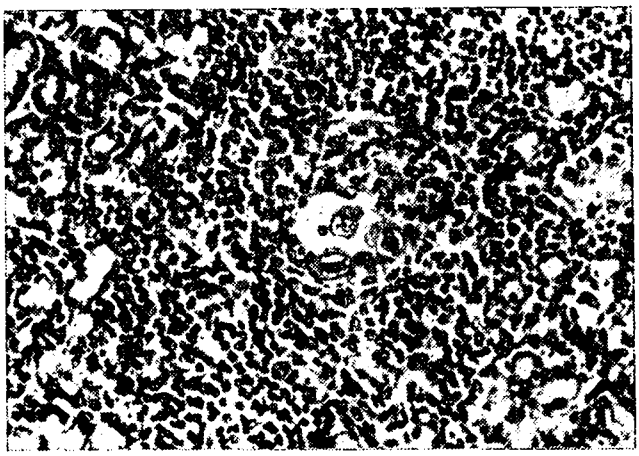

Fig. 1 – Haevy periductal mononuclear cell infiltration. An exfolieted cell within the duct lumen, and two duct epithelium cells with intrenuclear inclusion bodies.
H. and E. stain X125

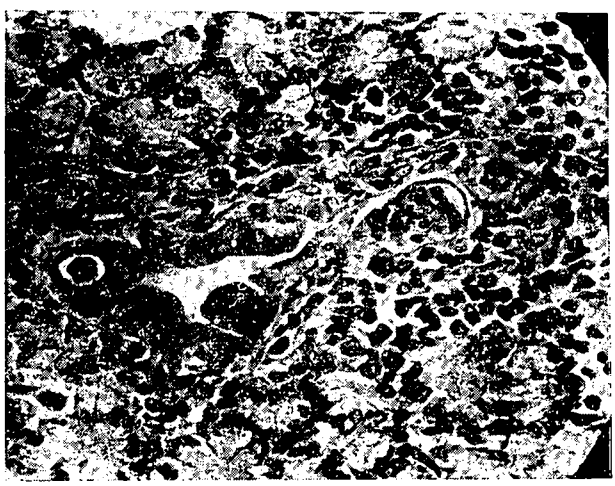

Fig. 2 – Intranuclear and intracytoplasmic inclusion bodies in duct cells, and periductal mononuclear cell infiltration.
H. and E. stain X350

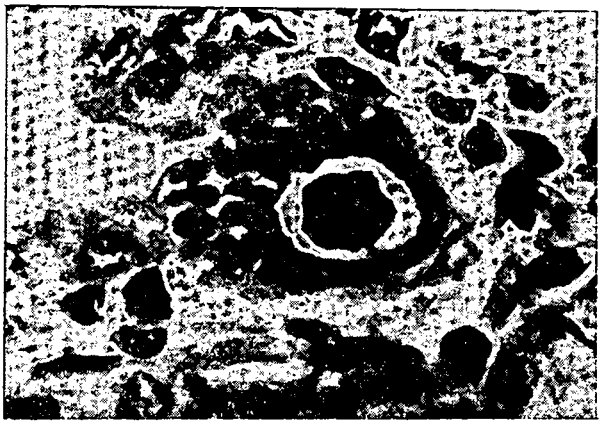

Fig. 3 – Intranuclear and intracytoplasmic inclusion bodies in a hypertrophic epithelium cell.
H. and E. stain, enlarged from X450.