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PARENCHYMATOUS KERATITIS IN TRYPANOSOMIASIS IN CATTLE AND IN DOGS, AND IN MAN*

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IN the course of trypanosomiasis in cattle and in dogs, the result of experimental inoculation, there is frequently developed parenchymatous keratitis. Experimental dogs inoculated with nagana in Zululand included many which became blind. A series of seventeen used in Nyassaland contained eight which went blind (David Bruce). Warrington Yorke in the experimental farm at Runcorn found frequent occurrence of interstitial keratitis not only in dogs, but in horses, donkeys, and goats. Morax, referring to work by Stock, states that, after inoculation into the anterior chamber of dogs and rabbits of infected blood, keratitis develops, with oedema of the cornea, the development of deep vessels and mononuclear infiltration. Abundant trypanosomes were found at the margin of infiltration and at the edge of healthy tissue. The same author states that in the goat the disease is absolutely comparable with syphilitic interstitial keratitis in human beings. In the course of a few weeks the cornea became opaque and gradually whiter and whiter. This was followed

*The illustrations of this paper were shown at a meeting of the Comparative Section of the Royal Society of Medicine on January 5th, 1927, when microscopic sections were displayed.

by a slow clearing of the opacity so that in a few months only a few striae of cicatrization remained. Similar is the condition in the horse. Iritis or irido-cyclitis also occurs with this condition, but not invariably. The trypanosome has been demonstrated in the aqueous and in the iris and ciliary body. Stock describes the appearance in the cornea in this experimental keratitis as an opacity which is porcelain-white in colour and contains deep vessels. He found no organisms in the cornea but a few in the aqueous. Daniels reported in 1911 the development of keratitis in a brown dog affected with the disease. In this case, injections of arsenophenyl-glycin caused a rapid clearance of the greater part of the corneal opacity, which relapsed later after an interval of a few days. The opacity was again abolished by a repetition of the treatment and again recurred. In each case with the reappearance of the interstitial keratitis, trypanosomes were found in the blood. Warrington Yorke described cases of parenchymatous keratitis in some goats and a horse; in some of these cases he found trypanosomes present in the inflamed cornea. Descriptions of the course of the clinical condition in the eye were included. Woods describes in detail his findings in experimental trypanosomiasis keratitis in a dog. de Schweinitz and A. C. Woods, in an experimental investigation on dogs, inoculated the animals intraperitoneally with infected blood, and increased the virulence by successive passages. Ocular signs appeared in from five to twelve days of the time of first discovery of trypanosomes in the blood. The clinical signs were clouding of the cornea, haemorrhage and exudate into the anterior chamber, and severe iritis. Pathological examination revealed thickening and infiltration of the cornea, the formation of new capillaries, and the presence of trypanosomes between the corneal lamellae, stained by alum-iron haematoxylin. There was cell infiltration of the iris, but no trypanosomes were discovered here or in the ciliary body. The ciliary processes were embedded in a fibrinous exudate containing a few organisms.

Dr. Muriel Robertson wrote in 1921 to the author that she had many times seen dogs develop keratitis in acute trypanosomiasis of the Gambiense-Brucei group.

The writer describes below in detail the histological findings in an eye affected with parenchymatous keratitis in a dog infected with the disease. The specimen was from a dog examined by Dr. C. W. Daniels. The writer is indebted to Mr. E. Treacher Collins for permission to examine the eye and to report on the condition, and to Moorfields Eye Hospital for laboratory facilities. The salient points are vascularization of the cornea in all its layers, marked cell infiltration in the peripheral parts and the presence of abundant trypanosomes in the infiltrated area of the cornea. The cellular exudate in the anterior chamber also contains abundance of

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poorly stained trypanosomes. The iris and ciliary body show slight infiltration, with abundance of trypanosomes, whilst the ligamentum pectinatum is markedly affected.

Several reports of the occurrence of an interstitial keratitis in men affected with trypanosomiasis have been made (Shirecore five in twenty-nine cases, Thiroux one in four cases), also of irido-cyclitis. Daniels reported a total of forty-two cases of trypanosomiasis in men in Rhodesia, Nigeria, Uganda and the Congo—cases which were examined in England. Among these there were thirteen

FIG. 1.

Dog. Path. No. 1536 (Moorfields Eye Hospital). $\times 6$. Anterior portion of eye shows peripheral infiltration and vascularization, *a*.

deaths, and fifteen cases with ocular lesions (35.7 per cent.). Daniels emphasizes the importance of the signs which occur in the eye as directing suspicion to a possible trypanosome infection. The affected eye is often painful, the condition always noticeable, and in some cases it has been the first symptom that caused the patient to consult a medical man. The lesions are described as being similar to those in dogs but of a milder form. Daniels noted ciliary congestion, slight keratitis and iritis. One of his cases was shown by Leslie Paton at a meeting of the Ophthalmological Section of the Royal Society of Medicine and is described as having had very slight photophobia and irido-cyclitis, with a rash resembling bruises of the skin of the body, and enlarged glands and slight pyrexia. No reference to pathological examination in man has been found.

Pathological Examination

Dog. Royal London Ophthalmic Hospital, Pathological Specimen No. 1536.

Keratitis in Trypanosomiasis.—Right eye of a black dog. This specimen was given to Mr. E. Treacher Collins in 1911 by the School of Tropical Medicine. The writer acknowledges his gratitude to Mr. Collins for the remaining portion of the specimen. The half eye was treated with gum solution and frozen sections were prepared in the ordinary way. A portion was embedded later in paraffin. Various methods of staining with Giemsa's stain were tried, and also Ehrlich's haematoxylin and

FIG. 2.

Corneo-scleral junction, $\times 7$, iris, and part of anterior chamber; shows peripheral vascularization, *a*, at all depths of the cornea; mass of coagulum in anterior chamber. The portion, *b*, is reproduced at greater magnification in Fig. 3.

eosin. The most satisfactory sections were obtained by the latter method of staining in the case of paraffin sections.

Microscopical Examination.—The cornea shows intact epithelium. There is infiltration of the substantia propria, greatest at the periphery and fading off towards the centre from both sides. The infiltration is most marked in the deeper layers of the periphery and is composed of polymorphic cells for the most part, with very diverse forms. There is present a zone, as seen in the sections, of cell infiltration and proliferation which encloses the central deeper parts of the substantia propria. Within this zone can be traced a falling off of the staining power of the corneal cells only in the deepest central layers. This indicates necrosis of this portion of the substantia propria. There are the stained nuclei of a few cells of infiltration

(polymorphic). Peripheral to the zone of infiltration there is a narrow zone of slighter infiltration. Some delicate capillaries penetrate the cornea from the corneo-sclerotic junction. Amongst the vessels is a high degree of infiltration. The capillaries pass inwards beneath the limbus at all depths of the substantia propria, and for a distance

FIG. 3.

× 90, shows a small portion of the above, including the extreme periphery of the angle of the anterior chamber. (a) Posterior lamellae of cornea with masses of normal pigment. (b) Posterior glass membrane (Descemet) with endothelium on its posterior surface. In front of this, a small amount of cell infiltration is visible. (c) Cell exudate in angle of anterior chamber with lighter stained fibrinous material. This cellular exudate is continuous with cellular infiltration of the ligamentum pectinatum. (d) Anterior surface of iris, deeply pigmented. The substantia propria in the photograph shows an excess of cells above the normal and some cell infiltration around the vessel near the middle of the photograph.

of about 1.5 mm. mesial to the limbus on each side of the section examined. On one side immediately anterior to Descemet's membrane is a collection of red corpuscles which has the appearance of a haemorrhage, by which the layers of the substantia propria are pushed apart. Trypanosomes are to be seen in various parts of the substantia propria particularly numerous within a short distance of the capillaries. Most of them appear to be in or on the lamellae of the substantia propria,

a few are seen in spaces between the fibres. As many as 15 trypanosomes were counted in a single field in examining with a 1/12th oil immersion objective and No. 4 eyepiece (Zeiss). In another part the trypanosomes were so closely packed as to be uncountable.

FIG. 4.

Drawing of portion of above under magnification by 1/12 oil immersion objective and No. 4 E.P. (Zeiss). (a) Red corpuscles in capillary in the substantia propria. (b) Trypanosomes. In a section of the cornea, the whole of a trypanosome is rarely seen in one position of the focussing. It is only by racking up and down that the whole length of the trypanosome is visible. Some trypanosomes are only present in part in sections. Presumably these have been divided by the microtome knife.

The anterior chamber contains masses of inflammatory cells among which are many poorly stained trypanosomes.

Some sections show much cell infiltration of the ligamentum pectinatum, and continuity of this with abundance of inflammatory cells in the anterior chamber and many also in the ciliary body. In

the spaces of the ligamentum pectinatum, numerous trypanosomes can be seen with the oil immersion objective. The iris in one place, near its pupillary border, contains a dense nodule of cells, most of which are polymorphonuclear. Examination of the vitreous cavity

FIG. 5.

× 600. Section of part of vascularized and infiltrated cornea showing trypanosomes, t^1 , t^2 ; t^1 indicates part only of a trypanosome, immediately below which is a complete organism. In the upper left hand quarter of the photograph are very numerous trypanosomes. (Microphotographs by F. Welch.)

on one side at the ora serrata reveals a few inflammatory cells, and among them many trypanosomes.

A fact of practical importance in the examination of the trypanosome in sections of tissue is that this organism appears very considerably smaller than when seen in smear preparations or blood films. In the latter it becomes flattened out and hence appears to be much wider than when fixed in tissue.

Conclusions

In trypanosomiasis in animals of various species, and perhaps also in man, a parenchymatous keratitis is often produced. In some cases this is accompanied by iritis and cyclitis. Pathological examination in animals reveals a severe degree of inflammation of these structures, with marked new formation of vessels in all layers of the cornea and in one case (dog) some necrosis in the centre of the cornea. As far as has been ascertained it bears the closest resemblance clinically and pathologically to distemper keratitis in dogs and to syphilitic interstitial keratitis in man. In the more severe cases of the latter, necrosis of part of the cornea takes place with consequent dense scar formation and very serious impairment of vision. It is probable that pathological examination of late stages of severe cases of distemper in dogs and of trypanosomiasis in various animals would reveal a similar scar formation in the centre of the cornea—as a cause of serious visual impairment. Pathological examination of periodic ophthalmia in horses, of tuberculous keratitis in man and in cats, and of leprous keratitis in man, reveals similarities but also various differences. In distemper in dogs, trypanosomiasis and syphilis in man and animals, the affection of the eye is a local manifestation of a blood infection, the lesions being due in the case at least of trypanosomiasis to the immediate action of the organisms or the effect of their toxins in the vicinity and is an important physical sign of disease.

BIBLIOGRAPHY

- Bruce.—Roy. Soc. Rep. Sleeping Sickness Comm. No. XVI. p. 40.
- Yorke, Warrington.—*Ann. of Trop. Med. and Parasitology*, Vol. IV, p. 385, 1911.
- Morax.—*Pathologie oculaire*.
- Daniels, C. W.—*Jl. of Trop. Med. and Hyg.*, Vol XIV, p. 161, 1911; *Ophthalmoscope*, Vol. XIII. p. 595, 1915; *Proc. Roy. Soc. Med.*, Vol. IX, 1915; *Ophthalm. Sec.*, p. 2; *Brit. Jl. of Ophthalm.*, Vol. II, p. 83, 1918.
- Woods, A. C.—*Arch. of Ophthalm.*, Vol. XLVI, p. 431.
- de Schweinitz and Woods, A. C.—*Trans. Amer. Ophthalm. Soc.*, Vol. XV, p. 106.
- Shirecore.—*Trans. Soc. Trop. Med. and Hyg.*, p. 131, Feb., 1913.
- Thiroux.—*La maladie de la sommeil*. Libr. Baillière et Fils, Paris, p. 29, 1911.
- Kolle and Wassermann.—*Hand. d. Path. Mikro-organismen*, Vol. VII, p. 474, Jena, 1913.
- Collins, E. Treacher.—*Proc. Roy. Soc. Med.*, *Ophthalm. Sec.*, Vol. IX, p. 5, 1915.
- Paton, L.—*Ibid.* p. 2.