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THE GENERALIZED SHWARTZMAN REACTION IN ASSOCIATION WITH E. COLI ENTEROTOXEMIA IN A PIG

By

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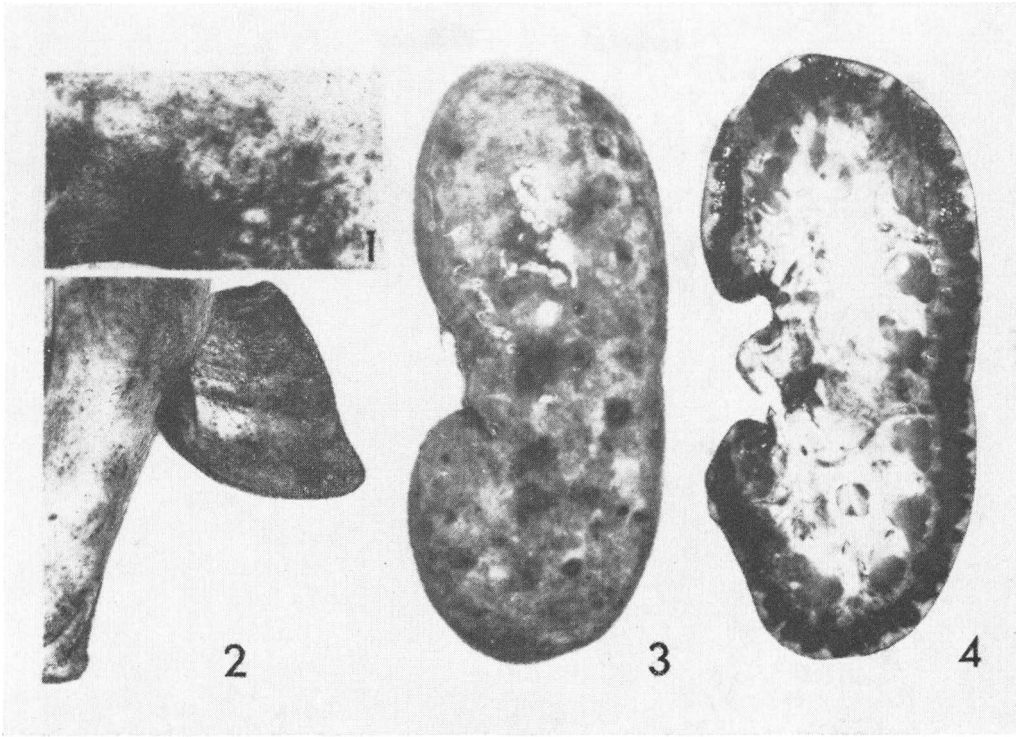
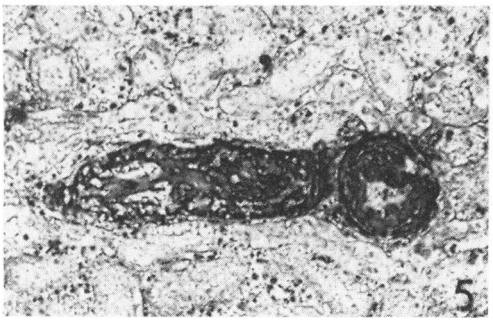
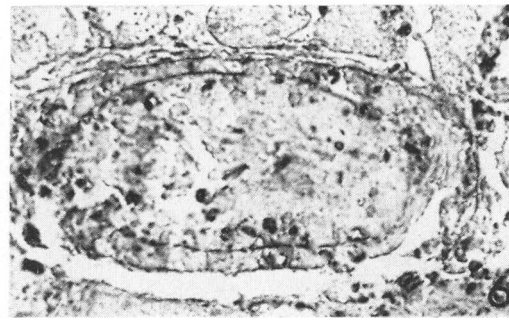
TEIGE, JON jr. and HANS GAMLEM: *The generalized Shwartzman reaction in association with E. coli enterotoxemia in a pig.* Acta vet. scand. 1977, *18*, 316—322. — A pig at the age of approx. 10 weeks died after four days of illness. Distinct necrotic changes were found both in the skin and the cortex of the kidneys. The histological examination revealed fibrinoid thrombi in skin vessels. In the kidneys similar thrombi were observed in capillaries of the glomeruli and in their afferent arterioles and in the interlobular arteries. In these vessels there were also a fibrinoid mural necrosis. These changes were in accordance with those expected to occur in the generalized Shwartzman reaction (GSR). The diagnosis of Escherichia coli enterotoxemia was based on the pathomorphological changes in the alimentary tract. The E. coli enterotoxemia was considered the cause of the GSR-changes.

generalized Shwartzman reaction; pig; E. coli enterotoxemia; edema disease; bilateral cortical necrosis.

Pathomorphological lesions in pigs indicative of the generalized Shwartzman reaction (GSR) were first noticed in association with septicemic salmonellosis in pigs by *Lawson & Dow* (1966), although total bilateral cortical necrosis (BCN), which has been recognized as the hallmark of GSR (*Thomas* 1959), is not present in porcine salmonellosis (*Lawson & Dow, Nordstoga* 1970). However, there are several reports on experimental GSR including BCN in pigs (*Nordstoga* 1967, *Nordstoga & Fjølstad* 1967, 1970, *Teige et al.* 1973, *Quast* 1973), where injections of disintegrated cells of Haemophilus parainfluenzae, Salmonella choleraesuis and Escherichia coli or endotoxin from Escherichia coli were used.







Figures 1 and 2. Hemorrhagic lesions in the skin of the abdomen, ears and ventral parts of the head.

Figure 3. On the decapsulated surface of the kidney hemorrhagic spots are seen in a tissue which is paler than normal.

Figure 4. Cut surface of the same kidney as in Fig. 3. Widespread hemorrhagic necrosis in a swollen cortex.

Figure 5. An interlobular artery with fibrinoid mural necrosis and occlusive thrombosis. Lendrums acid picro-Mallory method, × 40.

Figure 6. An interlobular artery which is distended. Mural necrosis with disruption of the internal elastic membrane and occlusive thrombosis. Stanining: el. v. G., × 100.

Fibrinoid thrombi and necrosis in the kidneys of pigs have been observed prior to 1966 (*Röhrer* 1932, *Hjärre et al.* 1951, *Thomson & Ruhnke* 1963, *Jones & Smith* 1964, *Dade* 1966). The changes reported have, however, not been interpreted as an expression of GSR. The present report refers to a pig with GSR-changes which seemed to have developed in connection with an E. coli enterotoxemia.

MATERIALS AND METHODS

The pig was the subject of routine necropsy. Tissue samples were collected from myocardium, lungs, liver, kidney, skin, brain and stomach for histological examination. The sections were stained by haematoxylin and eosin, elastin van Gieson and Lendrums acid picro-Mallory method (*Lendrum et al.* 1962).

CASE REPORT

The pig, which was approx. 10 weeks old, became ill two days after arrival to the farm. It was found in lateral recumbency and seemed to be paretic in the hind legs. It was then given a parenteral injection of antibiotics (Procamycin®). Later on the same day the animal developed a reddish discoloration of the skin. The pig was paretic until it died, four days after the first clinical signs were recognized. Another pig in the same pen showed similar skin lesions and after a few days the distal parts of ears became necrotic.

Gross lesions

Ecchymotic hemorrhages appeared in the skin of the ears, abdomen and the perineal region (Figs. 1 and 2). The kidneys were swollen. On the decapsulated surface of the kidneys, irregular, focal hemorrhages were seen (Fig. 3). The cut surface of the cortex appeared very hemorrhagic except for a narrow subcapsular rim (Fig. 4). The gastric and jejunal mucosa were hyperemic. The latter was also covered with mucus. The mesenteric lymph nodes were hyperemic and moderately swollen. Edema appeared in the wall of the stomach, gall bladder and abdomen, and also in the mesentery of the spiral colon. There was a red mottled cut surface of the myocardium.

Histological lesions

Distinct necrotic lesions were found in the skin. In the cortex of the kidneys large hemorrhagic and also necrotic areas appeared. The glomeruli were swollen, partly necrotic with an eosinophilic and homogenous content in the capillaries. The lesions were most pronounced in the juxta medullary part of the kidneys. A granular degeneration appeared in the myocardium. The interalveolar septa of the lungs were infiltrated with a moderate number of mononuclear cells. With the acid picro-Mallory staining, fibrinoid thrombi were found in small vessels of the corium, myocardium, liver, stomach and lungs. In the kidneys similar thrombi appeared in the glomerular capillaries, their afferent arterioles and the interlobular arteries (Figs. 5 and 6); the latter vessels also showed fibrinoid mural necrosis.

*Bacteriological examinations**

The samples were examined by routine methods and aerobic cultivation. From jejunal and colon samples anhemolytic E. coli was isolated. Examinations of samples from liver, kidney and spleen revealed either no bacteria or an unspecific flora. Salmonella spp. and Haemophilus spp. were not isolated from the samples.

DISCUSSION

BCN has been considered the pathomorphological criterion of GSR (*Thomas & Good* 1952, *Thomas* 1959). *McKay* (1963) suggested that GSR should be defined as a renal capillary thrombosis leading to renal cortical necrosis. In this pig a necrotic and hemorrhagic cortex of the kidneys was found. The histological examination revealed fibrinoid thrombi and fibrinoid mural necrosis in various vessels of the kidneys. According to both definitions cited the lesions observed should therefore be indicative of GSR. The edematous lesions found in the alimentary tract of the pig are generally accepted as typical of edema disease (*Emerson* 1967). The diagnosis of E. coli enterotoxemia in the pig can therefore be based on the pathomorphological lesions observed. The bacteriological findings may further support this

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diagnosis. The absence of other microbes known to provoke GSR in pigs is also of importance in this connection. Experimental studies have shown that endotoxin from E. coli has produced GSR in pigs (*Teige et al.* 1973, *Quast* 1973). It seems reasonable therefore that also an E. coli enterotoxemia can provoke GSR in pigs. A spontaneous case of GSR caused by an E. coli enterotoxemia has not been reported previously.

In this connection it should be mentioned that three other pigs with GSR-lesions probably caused by an E. coli enterotoxemia have been observed (Unpublished observation). A red-violet discoloration of the skin and kidneys with a broad and distinctly hyperemic cortex were found in the same pigs. The lesions observed, however, were in accordance with the descriptions of septicemic salmonellosis and Haemophilus-infection in pigs (*Lawson & Dow* 1966, *Nordstoga & Fjølstad* 1967, *Nordstoga* 1970). *Skjørten* (1966) stated that the GSR-lesions are located in target organs and may vary according to the experimental or clinical conditions. The pigs had macroscopic changes and fibrinoid thrombi, particularly in the vessels of the kidneys and skin. In previous descriptions of GSR in pigs, the lesions were located to the same parts of the body (*Lawson & Dow, Nordstoga & Fjølstad* 1967, *Teige et al.*). In human GSR, the kidneys and sometimes the skin are the target organs (*Hjort et al.* 1964, *Skjørten*).

The histological examinations revealed dilated capillaries of the glomeruli with a homogenous content which had the staining properties of fibrin. In afferent arterioles and interlobular arteries and in vessels outside the kidney, similar contents were observed. *Nordstoga* (1974) found the same glomerular lesions in an experimental investigation with salmonellosis in pigs. Electronmicroscopic examination showed that the content in the glomeruli consisted of disintegrated erythrocytes. The same author held the opinion that a pronounced stasis preceded the erythrocytic damage.

Nordstoga & Fjølstad (1973) stated that a fibrinoid mural necrosis was consistently found in interlobular arteries and also often in the afferent arterioles in animals with obvious GSR-changes in the kidneys. It is therefore not surprising that the pig in the present material had similar vascular lesions. In edema disease, hyaline changes and mural necrosis in arterioles are observed (*Clugston et al.* 1974). The edema disease in the pig

may therefore have been a contributing factor to the development of vascular lesions in the kidneys.

GSR in connection with E. coli enterotoxemia is an uncommon complication. The pig described in this study may therefore have been especially predisposed for GSR. Pigs fed unsaturated fat are found to develop GSR readily (*Teige et al.*). In the same pigs, only one injection of endotoxin was sufficient to provoke GSR. Vitamin E could, to a certain extent, protect against the development of the reaction. Unfortunately the vitamin E balance of the pig in the present study was not known.

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SAMMENDRAG

Generalisert Shwartzman's reaksjon i tilslutning til coli-enterotoksemi hos en gris.

En gris som var ca. 10 uker gammel, døde etter et sykdomsforløp på 4 dager. Ved obduksjon ble det funnet tydelige nekrotiske forandringer både i huden og nyrebarken. Den histologiske undersøkelse viste fibrinoide tromber i hudkar. I nyrene ble lignende tromber sett i glomerulikapillærer, afferente arterioler og i interlobulararterier. De to sistnevnte karene var også sete for en fibrinoid karveggsnekrose. Disse forandringene ble funnet å være i samsvar med de man venter å finne ved den generaliserte Shwartzman reaksjon (GSR). Det er

også hos grisen stilt diagnosen E. coli-enterotoksemi med bakgrunn i de patomorfologiske forandringer i fordøyelsestraktus.

E. coli-enterotoksemien oppfattes som årsaken til GSR-forandringene.

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