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Infected infarcts of the testis: A study of 18 cases preceded by pyogenic epididymoorchitis

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SYNOPSIS Eighteen cases of infected infarcts of the testis are presented, and evidence is put forward that these result from venous occlusions in the epididymis and cord. The venous lesions probably result from thrombosis during the course of an attack of epididymoorchitis.

Granulomatous orchitis was present in some part of half of the orchidectomy specimens, and the clinical histories, bacteriological findings, and histological data all suggest that this form of inflammation results from pyogenic infection of the testicle. What the factor is which determines whether the inflammation is granulomatous or not is unknown.

Apart from torsion and occasional involvement in polyarteritis nodosa testicular infarction is rare, and the receipt of several specimens stimulated interest in the lesion.

Between January 1964 and December 1969 we have received 18 testes with infarcts (excluding cases of torsion) and this paper presents the findings from their study.

The ages of the patients ranged from 26 years to 74 years, the majority being between 30 and 65 years (Table I). Most of the patients had a history of urinary tract disease, mainly of attacks of cystitis, often with haematuria. The common history was of 'cystitis' for seven to 10 days, then of the development of testicular pain and swelling usually diagnosed as epididymoorchitis (Tables I and II). Conservative treatment for three to seven weeks failed to lead to resolution and many developed a fluctuant mass in the testis. In six patients a scrotal sinus developed and in six others its imminence dictated immediate orchidectomy (Tables I and II).

In most of the patients *E. coli* was cultured from the urine, and in all cases in which culture

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Case No.	*Age (yr)*	*Clinical Epididymo-orchitis*	*Haema-turia*	*E. coli Cultured from*		*Previous Surgery*
				Urine	*Testis*	
1	55	+		0[1]	+	
2	43	±		+	0	
3	60			0	+	
4	48	−		+	+	Hernial repair
5	69	−		*Ps. pyo.*	0	Transurethral resection of prostate + hernial repair
6	30	+	+	−	+	
7	56	+	+	0	+	
8	70	−		−	+	
9	30	+	+	+	+	
10	36	+		−	Proteus	
11	26	−	+	0	0	
12	67	−		−	0	Hernial repair
13	71	+	+	+	+	
14	48	+		−	+	
15	42	+		−	+	
16	45	+		+	0	
17	57	+	+	0	+	
18	74	+	+	+	+	Hernial repair and retro-pubic prostat-ectomy

Table I *Clinical summary of 18 cases*

[1]0 = no culture performed.

Case No.	*Testicular Swelling (no. of days before operation)*	*Scrotal Skin Involved*	*Histology of Surviving Testis*
1	50	+	F
2	44		0
3	38		0
4	21		F
5	?	+	F
6	31	+	F
7	51	−	G
8	26	−	G
9	35	+	F
10	40	+	0
11	?	+	M
12	?	+	F
13	64	−	M
14	36	±	F
15	42	+	M
16	28	±	M
17	42	+	G
18	?	+	F

Table II *Length of history, involvement of skin, and histology of surviving testes in 18 patients*

0 = no recognizable viable testis.
F = fibrotic tubules.
G = granulomatous tubules.
M = both fibrotic and granulomatous tubules.

of the testicular tissue was performed *E. coli* was grown. Four patients had had a hernial repair (three ipsilateral and one contralateral) and two patients had had a recent prostatectomy.

Pathology

The specimens were extraordinarily similar so that the naked eye appearances could almost lead one to predict the history of the patient.

There were two types. In the first and most common (12 cases) the testis was of normal size or slightly enlarged. The cord was thickened by grey-white fibrous tissue in which were scattered yellow-brown foci, and the cut surface of the testis was more or less replaced by a yellow-green suppurative mass in which tubules could still be identified (Fig. 1). The surviving testis (if any) was represented by a peripheral rim of pale brown soft tissue. The tunica was usually grossly thickened, and skin was attached to it and communicated with the underlying abscess in seven cases (Figs. 1 and 2).

In those cases with generalized enlargement the testis was replaced by rubbery, firm, creamy-yellow lobulated tissue, from which the infarct could be clearly distinguished (Fig. 3). The cord was thickened as in the first group with yellow foci scattered in dense white fibrous tissue.

Histology

All sections were stained with haematoxylin and

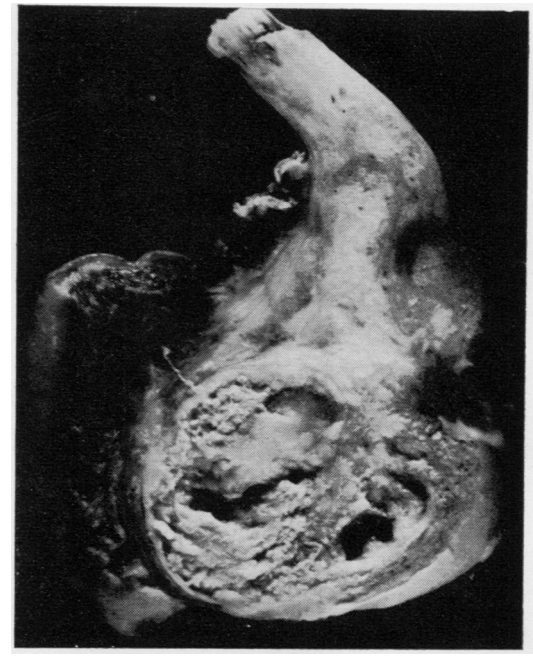

Fig. 1 *Sagittal slice of orchidectomy specimen shows necrosis of most of the testis. A thin rim of surviving parenchyma is seen at the bottom right-hand corner of the photograph.*

The fibrous thickening of the cord is well shown, and attached scrotal skin is indistinctly visible at the left-hand side of the specimen.

Case 11: histology of epididymis is shown in Figures 9 and 10.

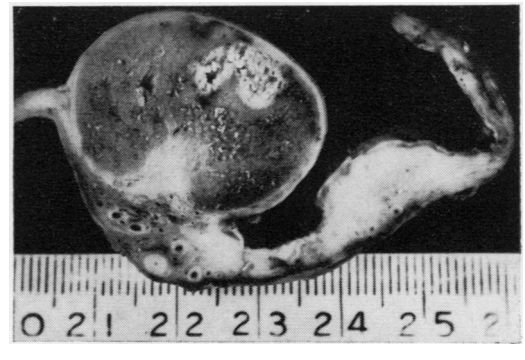

Fig. 2 *Horizontal slice of orchidectomy specimen shows a small sharply demarcated zone of necrosis in the anterior part of the testis. Note the gross thickening of the tunica. The viable testis showed fibrotic seminiferous tubules.*

Case 12: histology of border of necrotic zone is shown in Figure 4.

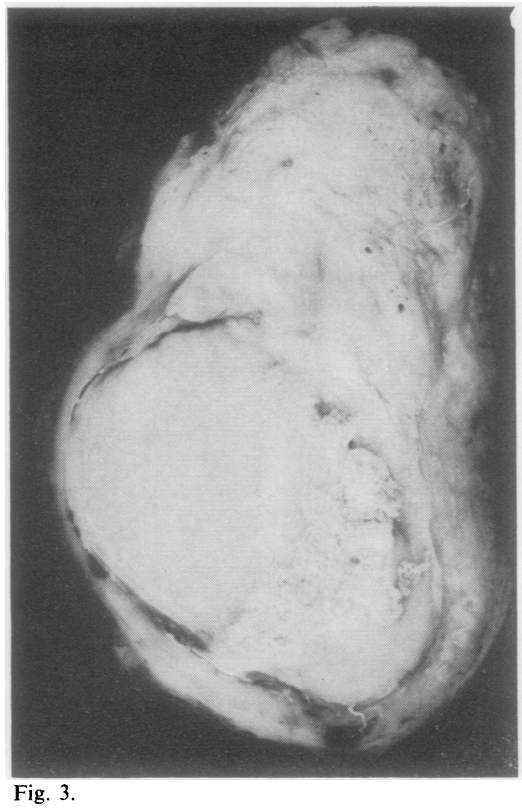

Fig. 3.

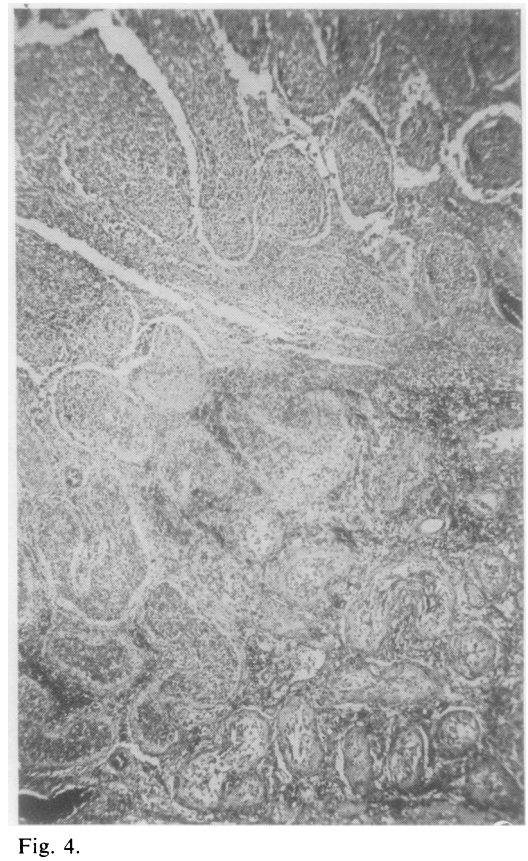

Fig. 4.

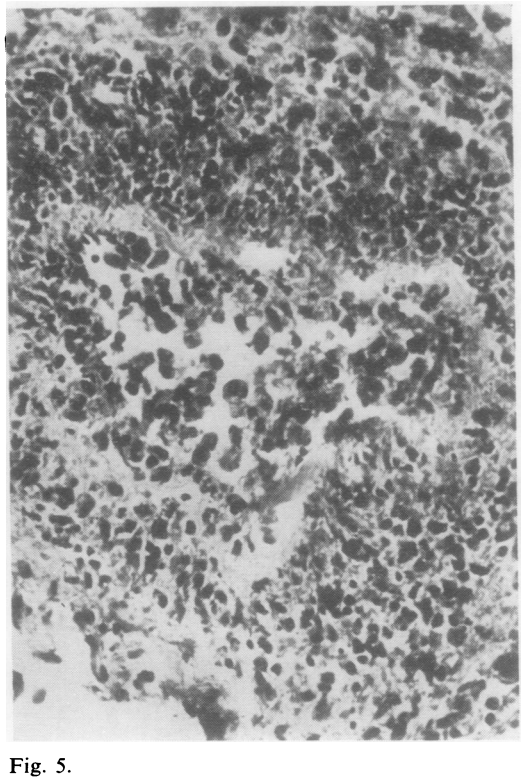

Fig. 5.

Fig. 3 *Testis enlarged by firm, pale tissue, with a distinct zone of necrosis in the lower part of the specimen. Cord grossly thickened.*
Case 13: history of testicular swelling for 64 days. Histology in Figs. 6 and 7 shows a mixture of granulomatous and fibrotic tubules.

Fig. 4 *Area of necrosis of tubules at the top of the photograph, with fibrotic, viable tubules at the foot. A thin haemorrhagic zone between the two areas runs diagonally across the photograph. Specimen is shown in Figure 2.*
Case 12: haematoxylin and eosin × *54.*

Fig. 5 *Outline of a seminiferous tubule surrounded by inflammatory infiltrate.*
Case 17: history 42 days. H and E × *750.*

Fig. 6.

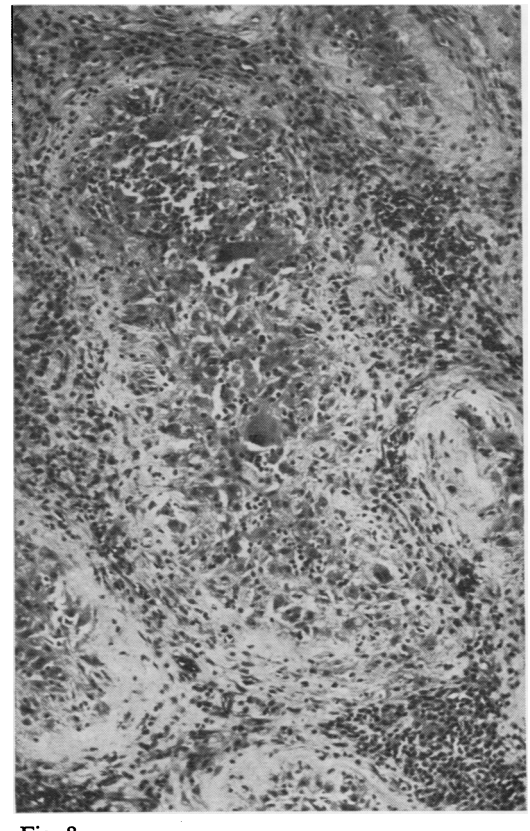

Fig. 8.

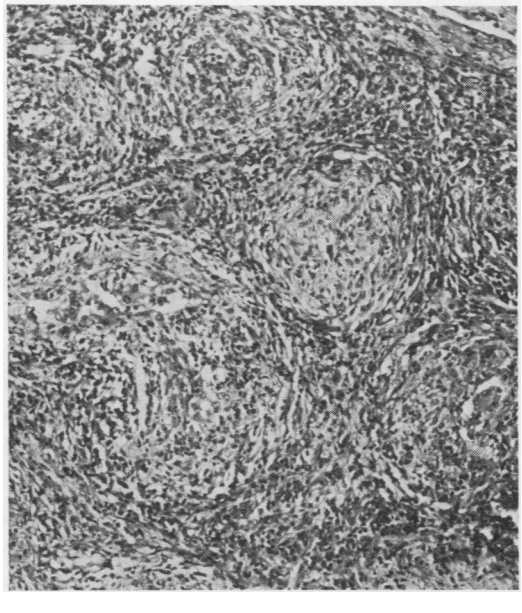

Fig. 7.

Fig. 6 *Fibrotic seminiferous tubules, lined by a single layer of mononuclear cells. These cells usually contained lipid, and are probably modified Sertoli cells. Same case as in Figures 3 and 7.*
Case 13: history 64 days. H and E × 180.

Fig. 7 *Intratubular granulomata, with intense interstitial inflammation.*
Case 13: history 64 days. H and E × 180.

Fig. 8 *A single seminiferous tubule lies vertically in the photograph, and is filled by large, pink, mononuclear cells. Multinucleated giant cells can be seen, and polymorphs are identifiable within the upper and lower ends of the tubule.*
Case 17: history 42 days. H and E × 180.

Fig. 9 *Interstitial histiocytic and lymphocytic infiltrate between epididymal tubules. Specimen is shown in Figure 1.*
Case 11: H and E × 180.

Fig. 10 *Intratubular exudate in epididymis. Note peritubular histiocytes.*
Case 11: H and E × 300.

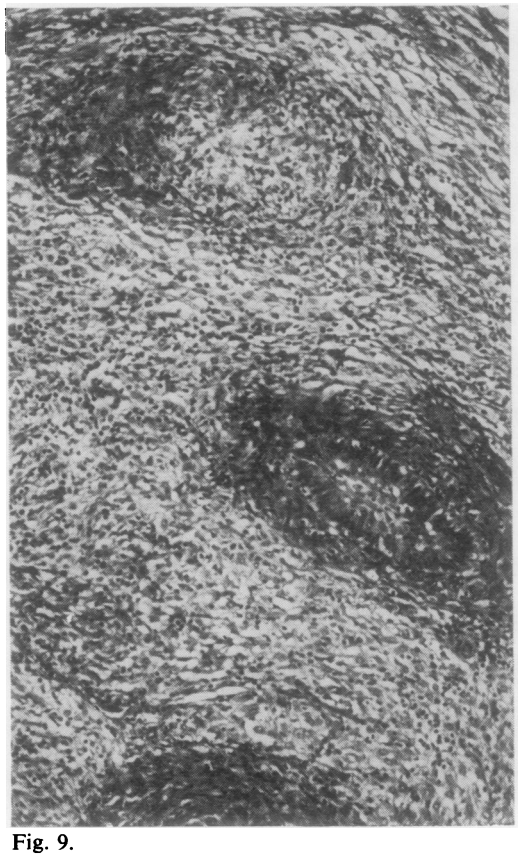

Fig. 9.

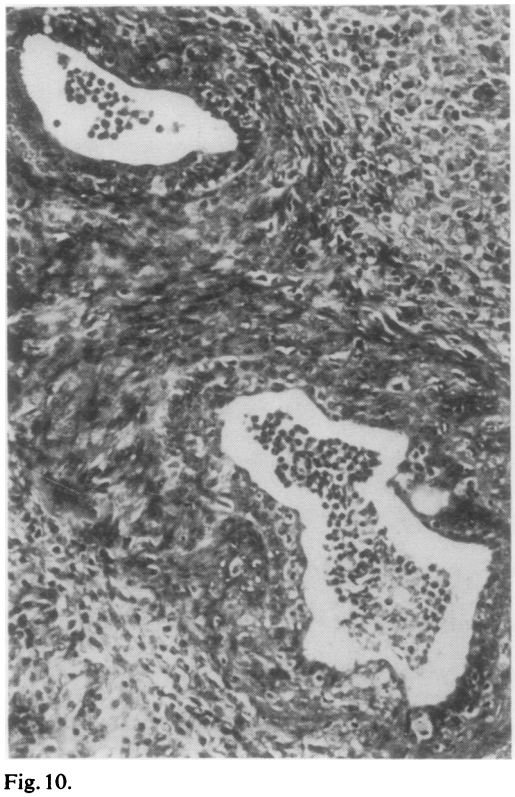

Fig. 10.

eosin, and all suspected vascular lesions were stained with Sheridan's method for elastic tissue. Ziehl-Neelsen stains were performed on all granulomatous specimens. Brown pigment was stained with Perls's acid ferrocyanide method for haemosiderin, and with a long Ziehl-Neelsen method for acid fastness. Frozen sections were stained for fat with oil red O.

There was again a general resemblance between the cases. No normal tubules or spermatozoa were identified in any specimen. In the testes of normal size the central necrotic zone showed a mixture of infarction and suppuration (Figs. 4 and 5) with polymorphs infiltrating necrotic tubules, the outlines of which were still detectable (Fig. 5). Occasional haematoidin crystals were seen within the necrotic zones. A thin haemorrhagic border was present separating necrotic from viable tubules in some specimens (Fig. 4). The surviving peripheral area of testis showed fibrotic tubules lined by Sertoli cells with occasional intratubular granulomatous zones (Fig. 6).

The larger testes were swollen by a granulomatous intratubular reaction (granulomatous orchitis, Figs. 7 and 8) with some fibrotic tubules in peripheral areas, but their necrotic zones were similar to those of the smaller testes.

Inflammation of the epididymis was present in all cases. In many it was purely histiocytic while in others polymorphs were scattered in the histiocytic infiltrate and in the neighbouring fibrous tissue. Exudate was always present both between and within tubules (Figs. 9 and 10), although tubules were difficult to identify in some specimens. The cord was commonly thickened by fibrous tissue and scattered foci of lymphocytes and histiocytes, while dilated lymphatics and sclerosed blood vessels were prominent.

A feature of 17 of the specimens was the presence of totally occluded veins in the epididymis and cord (Fig. 11). Many of these contained haemosiderin granules and were heavily infiltrated with plasma cells and lymphocytes (Fig. 12) while others were recanalized and showed immature collagen between the new channels (Figs. 13 and 14). Endophlebitis (Fig. 15) and extreme narrowing of veins by intimal collagen were common findings (Fig. 16).

Frozen sections were available from nine specimens, including sections of epididymis and testis in each case. Lipid was demonstrated by oil red O. Large aggregates of lipid-laden histiocytes were present in the epididymis but the venous occlusions were uniformly negative for fat. Many of the seminiferous tubules were lined by lipid-containing cells. In general, those lined by a single layer contained more lipid than those filled by granuloma. Interstitial lipid was focally present but not prominent.

Foci of intracellular brown pigment were found in the interstitium of the epididymis and in occasional seminiferous tubules; most of this pigment

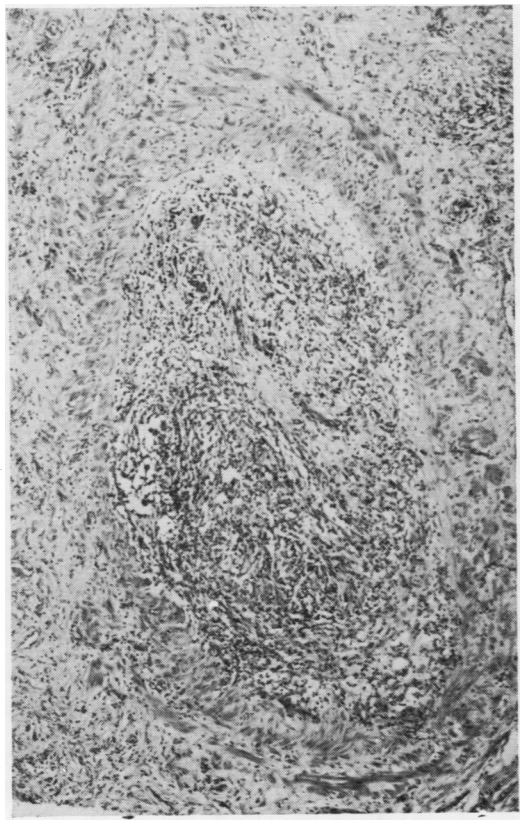

Fig. 11 *Totally occluded vein in spermatic cord. Heavy cellular infiltrate occupies lumen. Case 7: history 51 days. H and E × 750.*

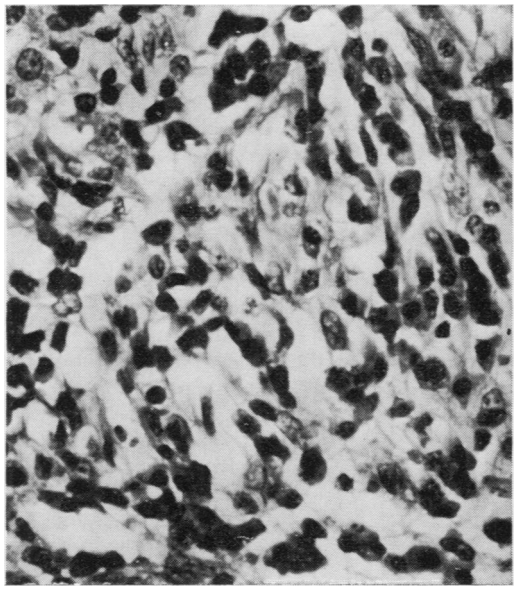

Fig. 12 *Higher magnification of intravascular tissue in Figure 11. Largely lymphoid cells with some histiocytes and intercellular connective tissue. Case 7: history 51 days. H and E × 1,200.*

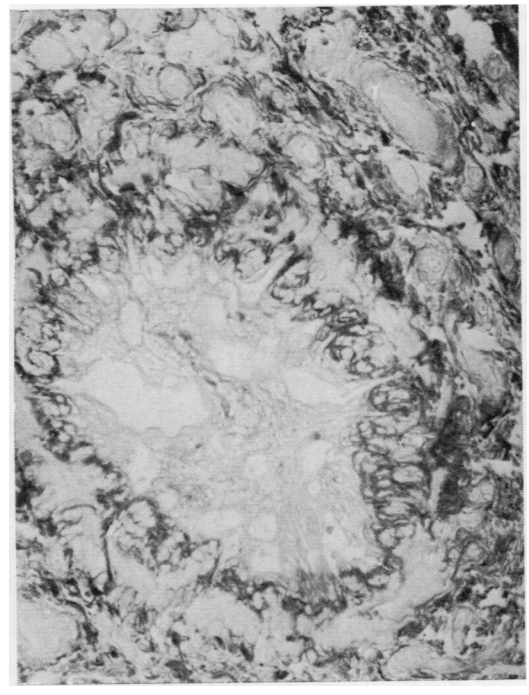

Fig. 13 *Multiple channels of recanalized vein. Case 17: history 42 days. Sheridan's elastic stain, counterstained with van Gieson stain × 180.*

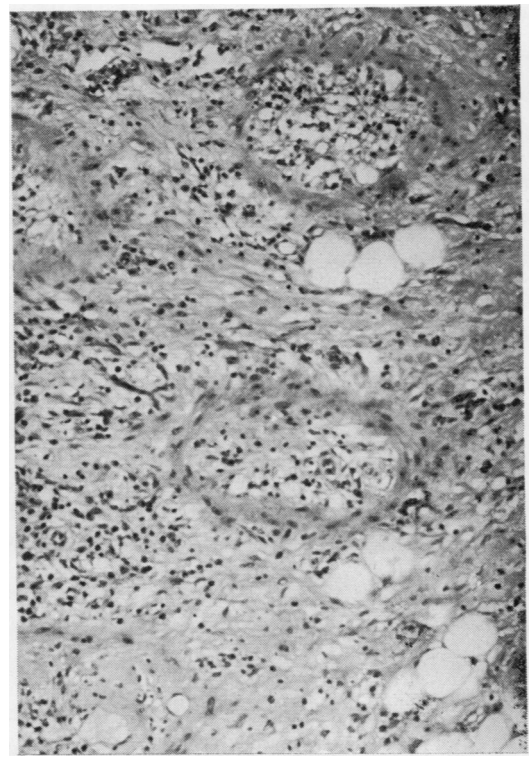

Fig. 14 *Four small occluded veins in spermatic cord. Interstitial and intraluminal lymphoid infiltrate. Case 14: history 36 days. H and E × 180.*

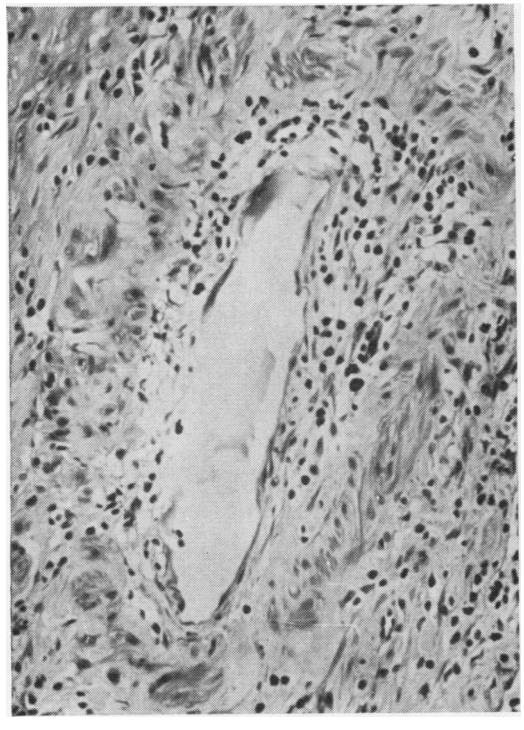

Fig. 15 *Lymphoid intimal infiltrate of vein. Case 17: history 42 days. H and E × 750.*

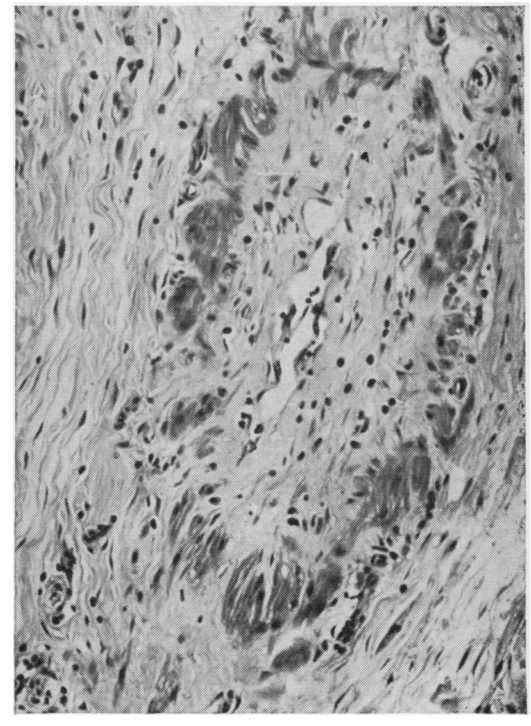

Fig. 16 *Severe intimal fibrosis of vein. Case 17: history 42 days. H and E × 750.*

stained as lipofuscin of ceroid type, but in the epididymis some stained as haemosiderin.

The interstitium of the testes showed an intense infiltrate of plasma cells, lymphocytes, and histiocytes in those with a granulomatous response, but the areas of fibrotic tubules showed a minimal inflammatory infiltrate. No interstitial Leydig cells were identified in any specimen. Giant cells were exceedingly rare within granulomatous tubules, being seen in only two cases, but a central collection of polymorphs was commonly present within the lumen of the granulomatous tubules (Fig. 8).

No spermatozoa were seen in any specimen. Despite inflammation of the epididymis in all cases, with destruction of some tubules and aggregates of polymorphs and lipid-laden histiocytes, extravasated spermatozoa or sperm heads were not seen.

Discussion

These lesions bear close similarities between each other and show a mixture of infarction and infection of the testes. The appearances are, in many respects, reminiscent of renal papillary necrosis in so far as in each tubules undergo necrosis and are infiltrated by polymorphs and yet tubular outlines remain.

The clinical histories and presentation suggest a banal infection of the bladder which subsequently spreads to the epididymis. The tunica breaks down and allows the formation of a discharging scrotal sinus. There is no fundamental difference between patients with granulomatous and non-granulomatous lesions, and in four instances transitions between fibrotic and granulomatous tubules could be seen, supporting the suggestion that granulomatous orchitis results from a chronic pyogenic infection (Lynch, Eakins, and Morrison, 1968).

The role of the venous occlusions is of great interest; the fact that most were organized or in the process of organization means that they were about four to six weeks old. They may have occurred as thrombi at the time of the initial epididymoorchitis, either as a result of suppurative involvement or of venous stagnation, and led to an area of venous infarction which subsequently became infected, or they may have been many years old, following previous infections or the trauma of surgery (ipsilateral hernial repair in three cases). There is little evidence in favour of suppurative destruction of vein walls as in only one case was there circumstantial support for this in the form of scarring of the medial coat, and the presence of inflammatory cells within most of the

venous occlusions suggests that they were not very old, a conclusion supported by the absence of organized pink-staining collagen with van Gieson stain. The presence of necrotic tubules with an inflammatory or haemorrhagic reaction at the edge of the zone of necrosis would also suggest that these lesions were weeks rather than years old.

Thrombosis during the course of epididymo-orchitis would seem to be the most likely explanation for these vascular lesions, as the interval of three to nine weeks between onset and orchidectomy would allow time for organization to take place. Although the turgid friable organ of venous infarction was not found it is reasonable to suggest that the engorgement with blood had been cleared by cellular activity before the orchidectomy.

Ischaemia has been proposed as the cause of granulomatous orchitis (Dreyfuss, 1956), and many published series include cases with large areas of testicular necrosis similar to those described here (Spjut and Thorpe, 1954; Lynch *et al*, 1968). Since 1964 we have seen two cases of granulomatous orchitis in which necrotic areas were not evident, but these have not shown venous occlusions and it would appear that vascular obstruction is related more to the development of testicular necrosis rather than to the granulomatous inflammatory reaction.

The grouping of granulomatous and non-granulomatous testes allowed comparisons between the two, and it became clear after histological study that transitions between the two were common and might be seen in a single testis. These findings support the idea of pyogenic infection rather than an immune mechanism as the cause of this unusual histological reaction.

The history of previous repair of an ipsilateral inguinal hernia is of interest, as the possibility of venous injury at this time must be considered. The data on the remaining patients may be inadequate, but it would seem unwise to ascribe aetiological significance to the earlier surgery.

The absence of normal spermatogenesis in the surviving tubules probably reflects a general suppression as a result of the local inflammation, and is responsible for the absence of extravasated spermatozoa around the inflamed epididymal tubules. This, together with the absence of metaplastic epithelium and the indistinctly granulomatous nature of the epididymal inflammation, contrasts with the findings in patients with spermatic granuloma (Glassy and Mostofi, 1956).

The presence of lipid and lipofuscin pigment of ceroid type within cells in granulomatous orchitis and spermatic granuloma has led Phillips (1961) to postulate that spermatozoa have given rise to each of these inflammatory reactions. Similar findings were present in some of the cases presented here, but the evidence for a pyogenic infection seems very strong, and it would appear more likely that the lipid and pigment have resulted secondarily from necrotic cells.

From this study it seems reasonable to conclude that when an abscess develops in the testis of a patient with epididymoorchitis this is associated with multiple occlusions of veins within the epididymis and spermatic cord, and a causal relationship probably exists between the abscess and the vascular lesions. The abscess usually has the histology of an infected infarct, and is generally situated at the antihilar border of the gonad.

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