OCCURRENCE OF MACROPHAGE CELLS IN THE SEMEN AND IN THE EPIDIDYMIS IN CASES OF MALE INFERTILITY

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(Received 21st March 1961)

Summary. In certain cases of male infertility, there are present in the semen, certain mononuclear and multinuclear cells which exhibit phagocytic activity. These spermiophage cells are witnessed in large numbers in the epididymal juice in cases of obstructive azoospermia. Serial sections of epididymis in such cases demonstrate intraluminal sperm phagocytosis by macrophage cells. The site of origin of these spermiophage cells is uncertain.

INTRODUCTION

During routine semen examination, one is occasionally struck by the presence of certain mononuclear and multinuclear cells in fair numbers. Theoretically, it is possible that the cells from the lining epithelia and the precursors of spermatozoa are likely to make their appearance in semen. In certain infertile semen samples, cells in the process of spermiogenesis are present in fair numbers. Apart from the above-mentioned cells, there are present in the semen certain mono- and multinucleated cells whose origin and function is uncertain. In this paper, we have made an attempt to investigate the nature of these cells.

MATERIAL AND METHOD

Several hundreds of semen samples of infertile patients who attended the Family Welfare Bureau in the last 2 years were scrutinized. Thin smears of semen were stained by Ehrlich’s haematoxylin and eosin. The slides were coated with a thin layer of Mayer’s albumin, prior to the preparation of the smear to ensure fixation. These smears were then kept at 65° C for ½ hr before they were stained. The staining procedure was little modified in that 95% alcohol was used for differentiation instead of conventional acid alcohol, which according to Gray (1954) produces diffusion of the nuclear stain in the cell cytoplasm. Wet coverslip preparations were studied under the phase-contrast microscope.

Samples of the epididymal juice were obtained while one of us (G. M. P.) performed vaso-epididymal anastomosis operations. Thin smears of the epididymal juice were prepared and fixation was achieved by immersing the slides in ether-alcohol mixture. Saline suspensions of the epididymal juice were
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used for phase contrast work. In twenty-three cases on whom vaso-epididymostomy was performed, a biopsy from the epididymis was obtained and serial sections were prepared for histological study.

RESULTS

Description of the macrophage cells

The size of the mono- and multinuclear spermiophage cells was variable. The cell diameter ranged from 20 to 60 μ. The cytoplasm was foamy and vacuolated. In saline suspensions of the epididymal juice, cells with phagocytosed red blood cells could be demonstrated. The cell margins in the stained smears were mostly circular and well defined.

In live condition under phase contrast, we have noted that the cell cytoplasm had a membranous or petal-like frill which exhibited very slow ameboid movement. In most of the macrophage cells, the tails of the engulfed spermatozoa were not visible, but we also noticed macrophage cells which had partially or completely engulfed the sperm heads with their tails entangled with each other.

The nucleus of these cells is sponge-like, and is usually eccentric in position. It is generally circular but may be indented. In the multinucleated cells, the number of nuclei ranged from one to eleven. The arrangement of the nuclei in only one instance was peripheral akin to the giant cell of Langhans type. Commonly, they formed clusters or were irregularly scattered in the cell cytoplasm like the nuclei of the foreign body giant cell.

Sources of error

In stained smears of semen after a laborious search, one may occasionally note the presence of either single or multiple sperm heads in the cell cytoplasm of mono- or multinucleated cells and thereby get an impression that these mono- or multinuclear cells are phagocytic in nature. Here a word of caution is necessary. In stained smears, a certain amount of overlapping of cells is inevitable. It will give a false impression that the sperm head is engulfed by the cell cytoplasm while in reality it may be just overlapping or adjacent to the cell. To exclude this fallacy with reasonable certainty, wet coverslip preparations should be studied under the phase-contrast microscope.

Exfoliated cells from the lining epithelia of the epididymal ducts appear in large numbers in the epididymal juice and are not to be confused with the spermiophage cells. The nuclei are central; the cytoplasm is not foamy and vacuolated.

Multinucleated spermatids or spermatocytes are not to be confused with the macrophage cells. The nuclei of the spermatids are not sponge-like, are densely stained and the cytoplasm is not foamy and vacuolated. Oberndorfer (quoted by Friedman & Garske, 1949) has called them pseudospermiophage cells. Besides, they are smaller in diameter as compared to the multinucleated giant cells.

When the tails of the engulfed spermatozoa are visible, they may be mistaken for the terratoid spermatozoa or head-to-head type of agglutination. The
presence of the separate nucleus of the macrophage cell should clarify the doubt.

**Frequency of occurrence of macrophage cells**

The presence of large numbers (over 10 millions/cm³) of spermatozoa cells in the semen is not a common occurrence. Out of hundreds of semen samples scrutinized, the spermatozoa cells were found in appreciable numbers in semen in fifteen cases. However, an occasional macrophage cell can be detected in practically every sample.

In our studies of the twenty-three epididymal biopsies in cases of obstructive azoospermia, we noted the presence of the spermatozoa in the interstitial tissues of the epididymis in only one case. But there also, there was no evidence of phagocytosis in the interstitial tissues of the epididymis by the macrophage cells. Though we have not come across any specimen where the phagocytosis of the spermatozoa was witnessed in the interstitial tissues of the epididymis, in five biopsy specimens we could see the spermatozoa cells in the lumina of the epididymal tubules. There was no evidence of hyperplasia of the macrophage cells in the interstitial tissues of the epididymis. In one case, we noted perivascular focal accumulation of plasma cells. In sections where the tubules contained macrophage cells, there was no suggestion of damage to the tubular epithelium.

**DISCUSSION**

In cases of obstructive azoospermia, the occurrence of the spermatozoa cells in large numbers in the epididymis is self-explanatory. Probably, they act like other scavenger cells in the body which are engaged in the task of removing the products of cell disintegration.

There was no correlation with the percentage of abnormal spermatozoa in the semen or the motility of the spermatozoa and the number of spermatozoa cells, nor were they dominant in cases of necrozoospermia. Samples of semen voided after a prolonged period of abstinence did not show an increase in the spermatozoa cells. Spermatozoa cells are most commonly observed in the initial semen samples after the obstructive azoospermia is corrected by vaso-epididymostomy.

Rumke & Hellinga (1959) mention evidence that in cases of obstructive azoospermia there may be extravasation of spermatozoa in the interstitial tissues of the epididymis where they may come in contact with the blood vessels and lymphatics. This is how they explain the occurrence of auto-antibodies against the spermatozoa in such cases.

In a few of our cases, auto-antibodies against the spermatozoa were detected in the blood by Dr Shanta Rao. Mostly, these were cases of obstructive azoospermia which was cured by anastomosis.

Extravasation of spermatozoa in the interstitial tissues of the epididymis has been described by Steinberg & Strauss (1947), Friedman & Garske (1949), Sunderrao (1955), Glassy & Mostofi (1956) and others in connection with the formation of sperm granulomas. All these observers have noted large numbers...
of spermatozoa in the interstitial tissues of the epididymis phagocytosed by the macrophages and surrounded by fibrosis.

Oberndorfer (quoted by Freidman & Garske, 1949) believed that phagocytosis of the spermatozoa entirely occurs in the interstitial tissues of the epididymis and not in the lumina of the epididymal tubules. But Steinberg & Strauss (1947) observed intraluminal phagocytosis as well in cases of sperm granulomas.

Apart from autolysis, which seems to be the most common method of the body for disposing of the dead spermatozoa in cases of obstructive azoospermia, phagocytosis also plays a significant role. In cases of obstructive azoospermia, despite the absence of spermatozoa in the interstitial tissues of the epididymis, the presence of the auto-antibodies in the blood serum could possibly be explained by sperm phagocytosis by the macrophage system of cells.

As regards the origin of these cells, there is no clear cut evidence. The multinucleated giant cells, like those elsewhere in the body, are probably formed either by the fusion of the mononuclear cells or by the amitotic division of the nucleus of the mononuclear cells without the corresponding division of the cell cytoplasm.

Most writers have expressed dissatisfaction with the view that the spermiosphage cells are derived from the lining of the tubular epithelium, though Grant (1958) has demonstrated in albino rats, the phagocytic properties in the basal layer of the epithelial cells lining the tubules of the epididymis.

In the tubules of the epididymis where the spermiosphage cells are lying free in the lumina, no similar macrophage cells in the lining epithelium could be identified in the serial sections. Further work in this direction is necessary to assess the significance of macrophage cells in the semen in cases of oligospermia.

ACKNOWLEDGMENTS

We are thankful to Dr V. R. Khanolkar, m.d., Director, Indian Cancer Research Centre, for his constructive criticism and guidance. The detection of auto-antibodies in the blood serum against the spermatozoa was carried out by Dr Shanta Rao of the Indian Contraceptive Testing Unit, Bombay.

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