LYMPH-NODE CHANGES DUE TO POLYVINYL PYRROLIDONE

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(RECEIVED FOR PUBLICATION APRIL 27, 1956)

Polyvinyl pyrrolidone has been widely used in recent years as a plasma expander, and a few side-effects have been reported, mostly reactions considered due to allergic or similar mechanisms. A few histological changes have been noted in man such as the liver lesions reported by Gall, Altemeier, Schiff, Hamilton, Braunstein, Giuseffi, and Freiman (1953) and the work of Vickery (1956), but in general little is known about the tissue reactions it may stimulate. It may thus be of interest to record briefly unusual lymph-node changes which appear almost certainly to be due to polyvinyl pyrrolidone. Here the material was not given as an intravenous infusion, but was used as an absorption-retarding agent in a drug which the patient gave herself by subcutaneous or intramuscular injection in the thigh over a period of about a year.

Case Report

The patient was a nurse aged 28 years who had an adrenalectomy for hypertension performed by Professor Patrick FitzGerald in St. Vincent's Hospital early in November, 1955. At operation the surgeon noted that many of the para-aortic lymph nodes were moderately enlarged and rather pale, so he removed one for histological examination. Sections revealed the unexpected picture to be described later, and investigations were begun to find the cause of this lesion. At first, lipid material in some form was suspected, and the patient was interrogated about the injection of oily substances. After much questioning, she remarked that the only substance that she had received by injection was hexamethonium bromide in a proprietary form, which she had given herself over a period of about a year, stopping 18 months before her operation. Inquiries from the manufacturers revealed that the absorption-retarding agent used was polyvinyl pyrrolidone, but that its use was being discontinued in view of some reports of undesirable side-effects. They were unaware of any lesions similar to those in this case, and they knew of no method of staining the substance in tissues. The problem then arose of identifying the material as polyvinyl pyrrolidone.

The lymph node had been fixed in 4% formal-saline and frozen and paraffin sections were cut. In addition to routine haematoxylin and eosin, these were stained by the periodic-acid-Schiff method, by phloxine-methylene blue for inclusions, by Sudan 111 and osmic acid for fat, by iodine and methyl violet as for amyloid, and by the Congo red-light-green method described by Freiman and Gall (1955). Examination revealed marked changes in the node (Figs. 1, 2, and 3). The sinuses were dilated and filled by vacuolated cells with the nucleus pushed to one side, and in many cases one got the impression that there was some transparent material present. The lymph follicles were reduced in size and contained numerous giant cells with both peripheral and central nuclei, and many had prominent asteroid inclusion bodies reminiscent of those sometimes seen in sarcoidosis. Examination under polarized light showed that the material was not optically active. Fat stains were negative, and the material was Schiff-negative using the McManus technique (McManus, 1948), although it may be stained by the Mowry modification (Vickery, 1956). At this stage the assistance of Dr. A. G. Everson Pearse was invoked, and a portion of the lymph node was sent to him; fortunately, too, the paper by Freiman and Gall on the staining of polyvinyl pyrrolidone in tissue sections came to hand (Freiman and Gall, 1955). The material gave similar results both in our hands and with Dr. Pearse. It was stained bright red by Congo red, and, using the light green counterstain and glycerine jelly as a mounting agent, an attractive, but unfortunately impermanent, result was obtained, the green stain diffusing out rather rapidly. A watery iodine solution stained the deposits dark brown, so that both this and the Congo red reactions resembled those of amyloid. However, the material was not stained by methyl violet. From these results, Dr. Pearse agreed that there could be but little doubt that the material stored in the lymph node was, in fact, polyvinyl pyrrolidone (Pearse, 1956).

Comment

That the material, after injection into the thigh, found its way to the para-aortic nodes and was stored there for over 18 months seems indis-

FIG. 1

FIG. 2

FIG. 3

FIG. 1.—A low-power view showing the general appearance of the lymph node. Haematoxylin and eosin, $\times 90$.

FIG. 2.—A high-power view showing a lymph follicle containing giant cells, one with a prominent asteroid inclusion body. Haematoxylin and eosin, $\times 410$.

FIG. 3.—The sinuses are packed with vacuolated cells containing polyvinylpyrrolidone. Haematoxylin and eosin, $\times 410$.

putable. In view of the relatively small amounts given it is interesting to note that, where polyvinyl pyrrolidone has been identified in the reticulo-endothelial cells of experimental animals, it has been after repeated large infusions over relatively long periods of time and the foci have not been associated with any tissue reaction. Turner, Butler, Smith, and Scudder (1949) found reticulo-endothelial hyperplasia in the spleens of dogs, with the formation of giant cells resembling megakaryocytes. Bull, Ricketts, Squire, Maycock, Spooner, Mollison, and Paterson (1949) found serological evidence of polyvinyl pyrrolidone being stored in lymph nodes and spleens of rabbits subjected to multiple injections, as well as varying amounts in other organs, although chemical methods gave negative or equivocal results. In this case, some of the polyvinyl pyrrolidone may have undergone changes in the macrophages (Pearse, 1956), and it seems certain that it provoked the changes seen. That a similar picture does not appear to have been described before is no doubt due to the fact that it is usually given

as an intravenous infusion, and opportunities for examining tissues after other forms of injection must be extremely rare.

Summary

Lymph-node changes presumably due to polyvinyl pyrrolidone are described.

Staining methods to confirm the diagnosis are described.

My thanks are due to Professor Patrick FitzGerald for access to this, his case; to Dr. A. G. Everson Pearse for his interest and valuable help; and to Miss Patricia Byrne, who was responsible for all the histological preparations.

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