Xenograft Studies in Leprous Neuropathy

TO THE EDITOR:

We have utilized xenografting techniques ([1-3]) to investigate primarily the behavior of leprous human Schwann cells on feeding them to normal mouse axons and, secondly, to observe the fate of transplanted intracellular *Mycobacterium leprae*. A preliminary observation appears interesting and worth reporting.

One tuberculoid and two lepromatous nerves, all obtained from untreated leprosy patients were each individually grafted into the right sciatic nerve of two, random-bred, Swiss white mice. These mice were immunosuppressed by anti-Thy-1.2 (donated by Dr. Mitchison, London) administered twice weekly.

The grafts, along with the proximal and the distal segments of the host nerves, were biopsied after two months and six months. The ungrafted left sciatic nerves of these mice biopsied at the same time served as controls. All of the nerve biopsies were fixed in buffered 3% glutaraldehyde and processed for electron microscopy. The right and left foot pads, spleens, livers, and ears of these mice were separately harvested for acid-fast bacilli as per the method of Shepard ([4]).

Tuberculoid nerve graft. The donor nerve was an ulnar funicle which had minimal degree of damage and a few small foci of infiltrates. No bacilli were seen. A cross section of the middle of the graft at two months revealed good axon innervation and myelination. Fibers were arranged in small regenerating units. No other inflammatory cells were seen. The distal segment revealed uniformly distributed axon innervation and myelination. A sixth-month biopsy was not available for study.

Lepromatous nerve graft no. 1. The donor nerve was an index branch of the radial cutaneous (IRC) nerve. This nerve had very few myelinated fibers, a good population of Schwann cells, and a few infiltrating macrophages. There was moderate bacillary load (4+), mostly solid forms within Schwann cells.

A cross section of the middle of the graft at two months revealed a picture similar to the donor nerve. There was good vascularity, but axon innervation was very poor and no myelination was seen. Bacilli were seen mainly within large membrane-bound vacuoles of cells with indistinct morphology (Fig. 1). Endoneurial collagen appeared denser than in the donor nerve.

The distal segment had few axons but they were well myelinated. Evenly distributed Schwann cells were seen. No bacilli or any other cells were seen in the distal or proximal segment of the nerve.

A middle of the graft cross section at the sixth month revealed a single, well-defined fascicle surrounded by 3–4 loosely arranged layers of perineurial cells. There was good vascularity. A number of both myelinated and unmyelinated fibers were seen to be arranged in small clusters. Perineurial-like cells

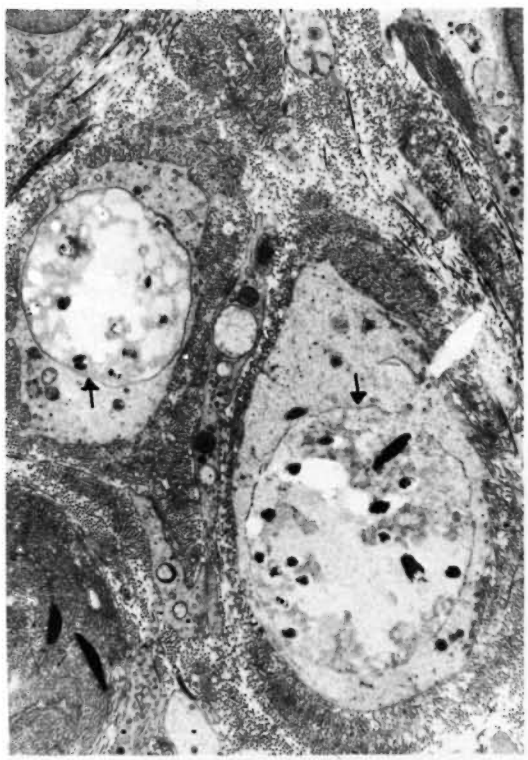

FIG. 1. Transverse section of the middle of lepromatous graft no. 1 biopsied at two months. There are two cell processes with indistinct morphology carrying a large bacillary load within membrane bound vacuoles (arrows) (×5000).

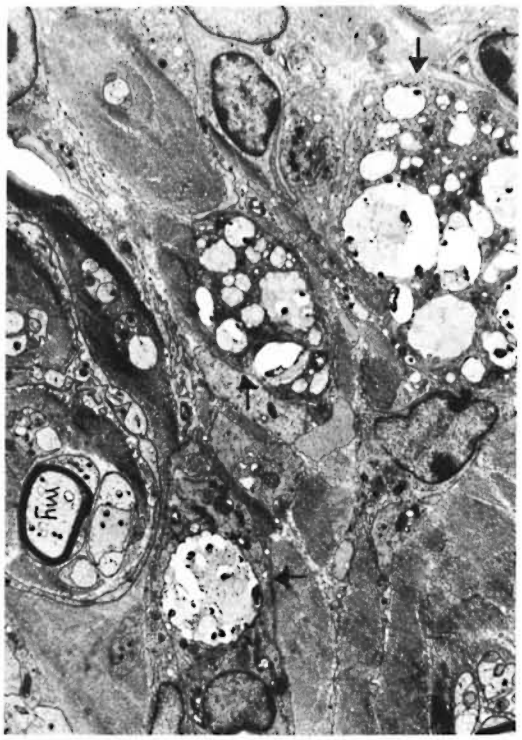

FIG. 2. Transverse section of the middle of lepromatous graft no. 1 biopsied at six months. There are three large, foamy macrophage-like cells with bacilli (arrow). Myelinated fibers are also seen (×3000).

formed a network within the endoneurium, segregating small groups of fibers. In addition, there were large aggregates of macrophage-like cells with foamy cytoplasmic changes mostly at the subperipheral region (Fig. 2) and along the perineurial septa. These cells harbored a large bacillary load, both solid and fragmented forms. None of the Schwann cells in association with myelinated or unmyelinated fibers showed any bacilli. The endoneurial collagen had varying diameter and appeared more compact. The picture of the nerve was compatible with a chronic, long-treated lepromatous nerve.

Lepromatous graft no. 2. The donor nerve was an IRC obtained from an active LL case. There was extensive damage with a total loss of fibers. The nerve was heavily bacillated (6+) and infiltrated with macrophages.

The middle of the graft at two months as well as at six months revealed a total lack of axon innervation. The two-month picture compared with the donor nerve, except for the increased foaminess of the cells. At the sixth month, the cells in the central region of the fascicle showed degenerative changes, and highly fragmented bacilli were seen within these cells. In both experiments, the proximal and the distal segments at the second and sixth months failed to show any bacilli. Multiple harvests, including foot pads, done at two months as well as at six months also failed to show any detectable bacilli.

The axonal innervation and extent of myelination of the tuberculoid graft at two months compared with the sixth-month picture of the first lepromatous graft; whereas the second lepromatous graft failed to show any axon innervation even at the sixth month. Such a difference could be due to variation in the initial damage which was maximum in the second lepromatous graft. Since only one mouse was studied at each interval, a technical failure in not obtaining a good junction cannot be ruled out.

None of the Schwann cells in association with the regenerating fibers in the graft segment, at two months or at six months, revealed any bacilli. The origin of these Schwann cells as well as the foamy macrophages with bacilli needs to be established by graft rejection experiments. It is possible that the grafted Schwann cells harboring bacilli either did not survive or failed to associate with the incoming axons. Six months may be too short a time for bacillary dissemination into the foot pads and other sites. However, what is intriguing is why the bacillary load remained confined to the macrophage-like cells. What prevented them from crossing over and spreading into the neighboring Schwann cells, within the graft and along the length of the nerve into the proximal and distal segments in this T-cell suppressed mouse model?

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