Injury and repair of smaller muscular and elastic arteries

A light microscopical study on the different healing patterns of rabbit femoral and carotid arteries following dilatation injuries by a balloon catheter

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Summary. 26 rabbits of the Danish country strain were subjected to mechanical dilatation injury of the left femoral and carotid arteries with Fogarty's embolectomy catheters F2 and F3 respectively. The rabbits were killed 2, 7, 14 and 28 days after the dilatation injury and the arteries examined histologically. Initially both of the arteries exhibited necrosis of the media and infiltration of the vessel wall with neutrophils and mononuclear cells. From day 7, intimal thickening was observed in both types of arteries, progressing in thickness during the later stages. However, thrombosis occurred in the majority of the carotid arteries, whereas this was only infrequently seen in the femoral arteries. In all of the dilated arteries, the elastic laminas were stretched or fragmented and never regained their normal appearance. In the carotid artery, giant cells accumulated around the fragmented elastin and calcified areas, located primarily at the intima-medial border. These changes were never observed in the femoral artery. At the twenty-eight days stage, proliferation of the smooth muscle cells more or less led to restitution of the media in the femoral artery, whereas the carotid artery showed medial restitution only to a lesser extent. The similarities between the injured carotid artery and human temporal arteritis, and the utility of the model as an animal model for the study of temporal arteritis are underlined.

Key words: Carotid artery – Dilatation injury – Femoral artery – Rabbit – Temporal arteritis

Introduction

Injury and repair of arteries have for long been considered important for the initiation and pathogenesis of arterial diseases e.g. arteriosclerosis and different types of arteritides. In arteriosclerosis, primary attention has been paid to the endothelial damage and the secondary intimal thickening (Ross and Glomset 1977). Consequently, attempts have been made to perform experiments with selective endothelial abrasion carried out with various methods, to study the repair processes of the endothelium and subendothelium under different conditions. Care has normally been taken to avoid more profound lesions of the underlying media, although some injury is always present (Schwartz et al. 1975; Fishman et al. 1975; Ross and Glomset 1977; Christensen et al. 1979; Reidy and Schwartz 1981; Ramsay et al. 1982; Clowes et al. 1983; Clowes and Schwartz 1985; Reidy and Silver 1985).

In some human arterial diseases, degenerative and inflammatory medial changes are, however, severe and frequently combined with an extensive intimal thickening and thrombosis. This is true of giant cell arteritis. In this disease, deterioration of the internal elastic membrane, accumulation of giant cells around the fragmented membrane, and inflammation and repair processes throughout all layers of the vessel wall are seen (Albert et al. 1982). The arteries involved in giant cell arteritis are of the muscular and the elastic type.

The present study was undertaken to compare the arterial response to severe injury in a muscular and a smaller elastic artery with the findings in giant cell arteritis (Lorenzen et al. 1987). Furthermore, the alterations in the smaller arteries were compared with our previous studies on injury and repair in the rabbit aorta (Lorenzen 1963; Helin et al. 1971a, b; Garbarsch 1976).

Material and methods

In 26 rabbits of the Danish country strain, 2–3 months of age and weighing about 2.5 kg, dilatation of the left common carotid artery and the left femoral artery was performed. In all...
operations the animals were anaesthetized with sodium pentobarbital (50 mg/kg body weight, intravenously). The left femoral artery was exposed at knee level. Through an incision, a Fogarty embolectomy catheter 2F was introduced and advanced to the external iliac artery. The balloon was filled with 0.05 ml water and the catheter redrawn 3 times before removal, after which the artery was ligated. Then the left external carotid artery was exposed through a midline incision in the neck. A Fogarty embolectomy catheter 3F was introduced, and dilatation of the common carotid artery was performed similarly after inflation of the balloon with 0.075 ml water. The left external carotid artery was ligated, and the wounds were closed. The right femoral artery was ligated at knee level and used as undilated control artery.

After 2, 7, 14 and 28 days the femoral and the common carotid arteries were removed bilaterally in 6, 6, 6 and 7 animals respectively, and the animals killed by intravenous injection of 200 mg sodium pentobarbital. In order to avoid interference of the incision and the ligature, 1 cm of the arteries next to the ligature were discarded.

The arteries were fixed in 0.5% cetylpyridinium chloride in 4% formalin (Williams and Jackson 1956), before dehydration and embedding in paraffin. Five μm sections were cut, and the following methods of staining applied: 1. Haematoxylin and eosin, 2. van Gieson staining for collagen fibers, 3. Orcein staining for elastic fibers (Lillie and Fullmer 1976), 4. 0.1% toluidine blue in 30% ethanol for glycosaminoglycans (Kramer and Windrum 1955), 5. Alcian blue 8GX (Gurr), 0.3%, at pH 1 and 2.5 for glycosaminoglycans (Pearse 1968), 6. The Calcium Red methods for calcium (McGee-Russel after Pearse 1972). 7. Mallory's phosphotungstic acid hematoxylin (PTAH) technique for fibrin and myofilaments (Lillie and Fullmer 1976).

**Results**

**Microscopic anatomy**

The control arteries

The right femoral arteries appeared undamaged, and were unchanged throughout the observation period. The media had circumferentially oriented smooth muscle cells amongst which delicate dispersed elastic fibers were observed. The intimal endothelial cells rested apparently directly on the internal elastic lamina, which was distinct and continuous (Fig. 1) apart from fenestrae, which connected the subendothelium with the media. A distinct subendothelial layer could be seen using light microscopy. The adventitia consisted of loosely arranged connective tissue with collagen fibers and dispersed elastic fibers. A well-developed external elastic lamina separated the media from the adventitia.