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THE EFFERENT CARDIAC LYMPHATIC PATHWAYS IN THE MACAQUE MONKEY

M. Eliskova, O. Eliska, A. J. Miller, A. Palmer, A. DeBoer, Z. Usman

Department of Anatomy (ME,OE), Charles University, Prague, Czechoslovakia, and Departments of Cardiology and Cardiothoracic Surgery (AJM, AP, AD, ZU), Northwestern University Medical School, Chicago, Illinois, USA

ABSTRACT

In ten postmortem hearts of the Macaque monkey (M. mulatta), *the coronary lymphatics were visualized using an India ink suspension in 2% gelatin. The left coronary lymphatic initially passed to the dorsal surface of the aortic arch. In five hearts, this lymphatic went directly to the cardiac lymph node, whereas in the others, it first ascended to the left superior tracheobronchial node and then interconnected with the cardiac lymph node. The right coronary lymphatic usually passed in front of the ascending aorta and common arterial (brachiocephalic) trunk and entered the cardiac lymph node. In two hearts, however, the right coronary lymphatic first ascended to an anterior transverse mediastinal node and from here lymphatics joined the cardiac lymph node. Those lymphatics that passed cephalad from the cardiac lymph node to the right anterior mediastinal nodes and the right paratracheal nodes ultimately emptied into the right venous angle. Those lymphatics that passed cephalad from the cardiac lymph node to the anterior transverse mediastinal nodes ultimately emptied into the left venous angle.*

*In five other Macaque monkeys (*M. mulatta *and* M. fascicularis*) after marker injection (T1824 blue dye and micropulverized barium sulfate) into the living heart or pericardium, lymphatic drainage beyond the base of the heart could not be demonstrated.*

Whereas postmortem morphologic studies suggest that the monkey coronary lymphatic system is amenable to obstruction by removal of the cardiac lymph node and interruption of its adjacent lymphatic connections, effective methods for visualizing the mediastinal lymphatic collecting system in the living monkey must be developed before experimental cardiac lymphatic ablation can be accomplished in this species.

The monkey is an important experimental subject for the study of coronary atherosclerosis with the *Macaca mulatta* ("Rhesus") and *Macaca fascicularis* ("Cynomolgus") being the species most often used. Because of a hypothesized relationship between deficient pericoronary arterial lymphatic drainage and progressive coronary atherosclerosis (1-4), we attempted to delineate the monkey cardiac lymphatic anatomy for purposes of future experimentation. Many studies of mammalian cardiac lymphatic anatomy and pathology are available but with special emphasis on that of man and dog. More recent studies of Aagaard (5), Patek (6), and Kampmeier (7) complement many older anatomical studies of mammalian coronary lymphatics (4), but detailed descriptions of the coronary lymphatics in the monkey remain scarce. Although McKinney (8) and Lemole (3) describe abnormalities following cardiac

lymphatic obstruction in monkeys, the topography of the lymphatics interrupted are not clearly described. Moreover, classic articles on the vascular system of the monkey (e.g., Lineback) (9) do not address the coronary lymphatic pathways. In order to devise consistent experimental methods to manipulate cardiac lymphatics in this species, we now describe our attempts to detail the cardiac lymphatic anatomy in the living intact monkey and in postmortem specimens in a cooperative venture between the lymphatic research groups in Prague and in Chicago.

MATERIALS AND METHODS

Living intact hearts (T1824 dye and barium sulfate suspension)

Two *Macaca mulatta* ("Rhesus") and three *Macaca fascicularis* ("Cynomolgus") were studied. Each monkey was operated upon under general anesthesia (sodium thiamylal; 10-15mg/kg B.W.) and maintained with supplemental small doses of this agent or with Halothane 1.5%, administered with standard inhalation equipment after tracheal intubation. Respirations were kept at 8 to 12 per minute. Two monkeys (one *M. mulatta* and one *M. fascicularis*) were operated upon under sterile conditions; the other three were operated upon prior to euthanasia as part of other institutional experiments that did not involve the heart. The operative technique was similar in each monkey. The chest was opened with a sternal-splitting incision. In four, the pericardium was incised longitudinally and a pericardial sling was fashioned. In one monkey, operated upon at the Arteriosclerosis Research Center at the Bowman Gray Medical School in Winston-Salem, the pericardium was left intact. In each monkey, 0.5ml of T1824 (Evans) blue dye diluted 1:1 with saline solution was injected either directly into the apex of the left ventricular muscle or in one indirectly through the intact pericardium. Thereafter, sketches were made and photographs were taken.

Careful mediastinal dissections were made superior to the heart to identify lymph nodes and lymphatics colored blue by the T1824 dye. In both monkeys operated upon under sterile precautions (one with an intact pericardium and one in which the pericardium was closed after having been incised), 2.0ml of a suspension of micropulverized barium sulfate in isotonic saline solution was injected into the pericardial sac. In both, the chest was closed and the monkeys were allowed to recover from the operation. Postoperative chest x-rays were taken and then repeated monthly for 6 months.

In the three monkeys operated upon under non-sterile conditions prior to euthanasia, suspensions of micropulverized barium sulfate and T1824 blue dye were injected into the apices of the left and right ventricular muscle. Sketches were then made and photographs were taken.

Postmortem hearts (India ink)

In 10 postmortem hearts of *M. mulatta*, injections of India ink in 2% gelatin were made subepicardially. When the subepicardial lymphatics became visible, they were cannulated, injected with the India ink-gelatin suspension, and the lymphatic pathways were followed with the aid of a dissecting microscope (10).

RESULTS

Living intact hearts

Injection of T1824 blue dye into the apex of the left ventricle (*M. mulatta*) demonstrated a beaded ascending lymphatic adjacent to the anterior descending coronary artery, that passed cephalad to the base of the heart. In another monkey (*M. fascicularis*) in which the pericardial sac was unopened, T1824 blue dye injected into the left ventricular apex was seen through the pericardium to be in lymphatics ascending towards the base of the heart. In a third monkey (*M. fascicularis*), the T1824 blue dye injection failed to reveal lymphatics but

injection of the micropulverized barium sulfate into the left ventricular apex demonstrated lymphatics ascending towards the base of the heart. In two other monkeys (*M. fascicularis* and *M. mulatta*) no lymphatics were seen after injection of either T1824 blue dye or micropulverized barium sulfate into the ventricular apex. Instead, the T1824 blue dye and the micropulverized barium sulfate remained as "blobs" at the injection site for at least 15 minutes without visualization of ascending lymphatics. Despite careful dissection, in none of the five monkeys studied were we able to delineate mediastinal lymphatics or lymph nodes that drained from the heart. In two monkeys we identified small lymph nodes but these did not color with either marker. These findings were in striking contrast to our earlier observations in the dog (4), where mediastinal lymphatic pathways readily became visible after markers were injected into the cardiac apex.

In the two monkeys that had micropulverized barium sulfate injected into the pericardial sac and were followed with serial x-rays for up to 6 months, no mediastinal lymphatics were visualized by plain chest x-ray. This finding is again in contrast to our experience in the dog (4).

Postmortem hearts

a. Lymphatic pathways to the mediastinal nodes

After subpericardial injection of India ink, a left and right coronary lymphatic drainage system was visualized *(Fig. 1)*. The left coronary lymphatic received two main branches. The posterior branch emanated from lymphatics in the posterior interventricular groove and from the adjacent dorsal portions of the right and left ventricles. It ascended to the left atrioventricular groove and then ran anteriorly. The anterior branch of the left coronary lymphatic started at the apex, passed cephalad in the anterior interventricular groove and received lymphatics from the adjacent areas of the right ventricle and from the ventral portion of the left ventricle. Between the left atrial appendage and the margin of the pulmonary trunk, the anterior and posterior branches joined to form the main left coronary lymphatic. The latter then ran posterior to the pulmonary trunk to the dorsal surface of the aortic arch. In half the specimens *(Fig. 1, left)*, this main left lymphatic channel passed upwards to the right, continued between the superior vena cava and the common arterial (brachiocephalic) trunk (the first branch of the aortic arch), and entered the cardiac lymph node. In the other monkeys *(Fig. 1, right)*, the left coronary lymphatic passed upwards and to the left, behind the aortic arch to the area of the main left bronchus where it entered the left superior tracheobronchial node. From this node an efferent lymphatic passed along the left edge of the trachea, crossed in front of the trachea behind the common arterial trunk, and entered the cardiac lymph node.

The right coronary lymphatic channel received lymphatics from the ventral, lateral, and adjacent posterior part of the right ventricle. It ran on the ventral side of the right ventricle into the right coronary groove, passed to the right border of the pulmonary trunk, and from there between the pulmonary trunk and the aorta. In three specimens there was a small node in a lymphatic network at this latter site. The right coronary lymphatic passed cephalad in front of the ascending aorta, pierced the pericardium, passed in front of the common arterial trunk and entered the cardiac lymph node *(Fig. 1, right)* (8 specimens). In two specimens, the right coronary lymphatic entered a node located superficially to the left of the cardiac lymph node below the left brachiocephalic vein. This node (classified in man by Rouviere as the group "nodi mediastinales anteriores transversi") (11) had lymphatic connections to the cardiac lymph node.

b. Lymphatic pathways from the cardiac lymph node

The cardiac lymph node was located in

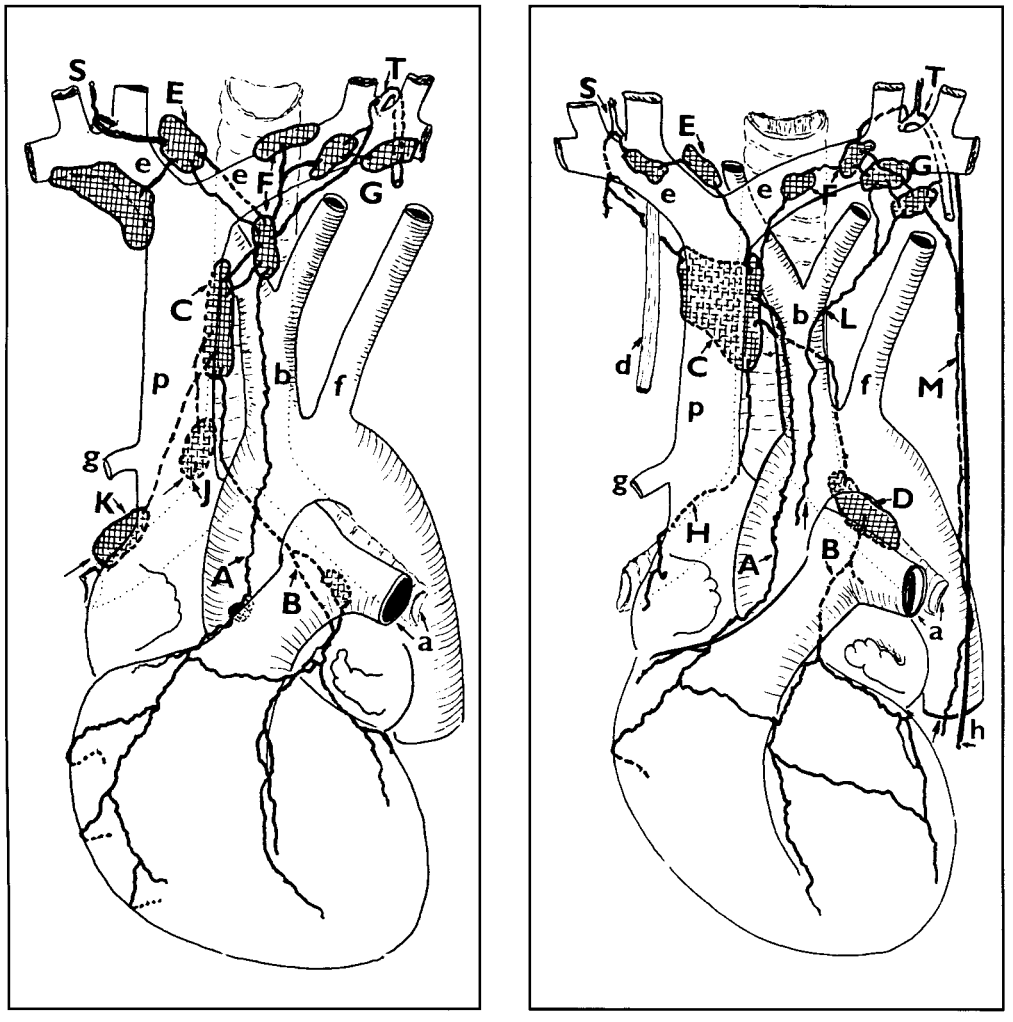

*Fig. 1. Patterns of efferent lymphatics and lymph nodes draining the heart in the monkey (*Macaca mulatta*). Left — main left coronary lymphatic passes directly to the cardiac lymph node. Right — main left coronary lymphatic passes first to the superior tracheobronchial node, and then to the cardiac lymph node.*

A=right coronary lymphatic; B=left coronary lymphatic; C=cardiac lymph node; D=left superior tracheobronchial node; E=nodes of anguli innominati-subgroup of right anterior mediastinal nodes; F=anterior transverse mediastinal nodes; G=left anterior mediastinal nodes; H=lymphatic from the area of the crista terminalis; J=paratracheal node receiving lymphatics from the pericardium; K=right superior tracheobronchial node receiving lymphatics from the pericardium; L,M=lymphatics from the pericardium; S=right lymphatic duct; T=thoracic duct; a=left pulmonary artery adjacent to bronchus; b=common arterial trunk (truncus communis); d=vagus nerve; e=right and left brachiocephalic veins; f=left subclavian artery; g=azygos vein; h=phrenic nerve; p=superior vena cava.

front of the trachea, between the left border of the superior vena cava and the common arterial trunk, beneath the terminal part of the left brachiocephalic vein. Usually the node was longitudinally oriented, was 6-9mm in length, and its right border extended a variable distance behind the superior vena cava.

Some lymphatics ascended from the cardiac lymph node to right anterior mediastinal nodes located in the angle between the brachiocephalic veins (*nodi anguli innominati*), and ran cephalad behind or in front of the terminal parts of either the right or left brachiocephalic vein. From this group of nodes, lymphatics continued to the right venous angle. Other lymphatics ascended behind the right upper part of the superior vena cava, received a few lymphatic twigs, ran behind the vagus nerve, and opened into the right venous angle. Still other lymphatics ascended from the cardiac lymph node to the anterior transverse mediastinal nodes of Rouviere, surrounding the left brachiocephalic vein. From these nodes, lymphatics passed to the left venous angle. Considerable interconnections existed between various lymphatics and nodes in this area.

c. Anatomical variations of the coronary lymphatics

The right coronary lymphatic diameter (0.3 to 0.4mm) was slightly smaller than the left (0.5mm). In one specimen, the right and left coronary lymphatics united between the pulmonary artery and the aorta to form a single trunk that passed cephalad to the cardiac lymph node by the route usually taken by the left coronary lymphatic. In nine specimens, small lymphatics crossed the pulmonary conus and connected with both the right and left lymphatic channels.

DISCUSSION

Because the anatomy of the thoracic lymph nodes in the monkey (*M. mulatta*) is similar to that described in man by Rouviere (11) and Feola et al (12), we adopted their classification to describe the mediastinal nodes in the monkey. Although the coronary lymphatic drainage pathway in the monkey is similar to that of the dog, there are notable differences (4,10,13). In the dog, the left coronary lymphatic almost always empties directly into the cardiac lymph node. In the monkey, in contrast, the ascending coronary lymphatic often first enters the left superior tracheobronchial node and from there passes to the cardiac lymph node.

The right coronary lymphatic also commonly passes (85%) in the dog to the left anterior mediastinal nodes; in only 15% does it enter the cardiac lymph node. On the other hand, in the monkey (*M. mulatta*), the cardiac lymphatics eventually all reach the cardiac lymph node. This latter node also receives some lymphatics draining the pericardium and the lungs. Because the cardiac lymph node in the monkey often connects with the left mediastinal nodes, it seems reasonable to deduce that cardiac lymph in this species also drains, at least to some extent, to the left venous angle.

Technically, completely obstructing the coronary lymphatic system in the monkey appears feasible and optimally would include excision of the cardiac lymph node and interrupting all of the lymphatics entering this node. It probably would also be desirable to resect the lymphatics passing in front of the common arterial (brachiocephalic) trunk.

For reasons that are unclear, we were unable to demonstrate the mediastinal lymphatic drainage pathways of the intact heart in the living monkey. Even with visualization of subepicardial lymphatics after injection of T1824 blue dye or micropulverized barium sulfate into the ventricular apex, we were unable to see the mediastinal lymphatics, a necessity if monkey cardiac lymphatics are to be obstructed for experimental purposes. This methodologic failure despite the technique having previously been successful in delineating the coronary lymphatic system in the dog is perplexing, and we plan further technical modifications to better "mark" the

cardiac lymph node and the entering and exiting lymphatic pathways in the living monkey.

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Albert J. Miller, M.D.
676 North St. Clair
Suite 1930
Chicago, Illinois 60611 USA