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Peripheral Arteriography Using the Reactive Hyperemia*

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Various kinds of vascular surgery for occlusive diseases of peripheral artery have become rather popular and fairly good results have been obtained. One of the most important factors influencing the results of operation is the condition of peripheral outflow tracts. Therefore, an arteriography extended to the very peripheral region is necessitated. Concerning the lower extremities, especially in the case with occlusive lesions, it is fairly difficult to have good visualization from the thigh down to the foot with usual methods. To dissolve this problem, the author tried to take the arteriography experimentally and clinically under the various conditions which were presumed to dilate arteries such as spinal anesthesia, sympathectomy, intra-arterial injection of Imidalin or Procaine and reactive hyperemia, and knew that we could have satisfactory results using the reactive hyperemia. Although it was quite possible that sympathectomy might promote the development of collaterals, the experimental proof was not yet sufficient. Applying the author's method, this problem has been dissolved experimentally. Arteriogram under the reactive hyperemia could be presumed to give the dynamic and functional interpretations. We have applied this new method upon many patients with various circulatory disturbances, and had several interesting findings. In this report, only the basic points are described.

RECENT ADVANCES in various vascular surgery for occlusive diseases of peripheral arteries are remarkable and the operative results have been fairly good. One of the most important factors influencing the operative results is a condition of peripheral outflow tracts. In order to reveal this condition an arteriography extended to the very peripheral region is necessitated. This is not so difficult technique in the upper extremities, but fairly difficult in the lower extremities especially in the foot when an occlusive disease is present.

To dissolve this problem, the author

added each factors considered to dilate the arterial system to the technique of arteriography, and found that the arteriography under reactive hyperemia gave the most clear arteriogram showing very peripheral fine arteries and also gave other various advantages. This is a report of this new method of arteriography and applying this method, the author also found roentgenologically that collateral channels could be markedly developed after sympathectomy.

METHODS

Twenty adult mongrel dogs were used, ar-

* Outline of the study was reported at the 17 Kanto-Koshinetsu Regional Meeting of the Japanese Circulation Society in May, 1960.

teriograms after sympathectomy, intra-arterial injection of Imidalin** or Procaine, and under reactive hyperemia were compared. Influence of sympathectomy on the development of collateral channels was also studied. Since the autumn of 1958, further observations were made clinically on 155 cases with mainly occlusive arterial diseases such as thromboarteritis obliterans. Two hundred and fifty peripheral arteriographies were performed on those cases and the effects of lumbar anesthesia, sympathectomy, intra-arterial injection of Imidalin or Procaine and reactive hyperemia were compared.

Arteriography of canine hind legs.

Thirty mg. of Nembutal per kg. were injected intravenously with insertion of tracheal tube. Laparotomy was performed with median incision and polyethylene catheter was inserted through the caudal artery into the terminal aorta. Thirty ml. of 76% Urografin was injected in 8 to 10 seconds and arteriograms of bilateral hind legs were taken on one film under same condition.

Arteriography of human lower extremities.¹⁾²⁾

Only local anesthesia was applied on the inguinal region and the common femoral artery was punctured directly through the skin using No. 18 gauge needle. Forty ml. of 76% Urografin was injected by hand and arteriogram was taken with single exposure using 3 separate films. The duration of injection of contrast medium was differed between 14 to 18 seconds depending on each case. For example, the injection was done rather slowly for such case as the occlusive lesion was presumed to be extensive.

Roentgen apparatus machine used for this study has rotating anode made by Toshiba Electric Co. Just before the completion of injection of contrast medium, the arteriogram was taken with 65-70 KV. 100-150 mA. and exposure of 0.15 seconds.

Arteriography of human upper extremities.¹⁾²⁾

In the middle part of the upper arm, the brachial artery was punctured directly through the skin, or the brachial artery was operatively exposed and then punctured. In other way, subclavian artery was directly punctured from supraclavicular fossa and the contrast medium was injected. Duration of injection was 5 to 10 seconds for the brachial artery puncture.

1) *Peripheral Arteriography under the Spinal Anesthesia.*

Ten clinical patients underwent lumbar anesthesia with 2.5 ml. of Percamin-S before arteriography of lower extremities. An extent of the anesthesia was around up to the umbilicus. No vasoconstrictive drugs were given.

2) *Peripheral Arteriography after Sympathectomy.*

Laparotomy with median incision was made on dogs under intravenous Nembutal anesthesia, and unilateral sympathectomy was performed from the height of renal arteries down to the aortic trifurcation which is corresponded to L₃-L₆. Arteriograms of the bilateral hind legs were taken immediately after, 7 days after, and 2 weeks after sympathectomy and the films of both sides were compared.

As clinical observation, arteriograms were taken on 21 lower extremities 7 days to 3 years after sympathectomy.

3) *Peripheral Arteriography after Intra-arterial Injection of Imidalin.*

Bilateral canine femoral arteries were exposed and 2 ml of Imidalin was injected unilaterally and for the other side, only puncture with needle was done as a control. Ten to thirty seconds after this procedure, arteriography of bilateral hind legs was done and both sides were compared.

In human cases, spotted or diffuse flush was seen on the skin of the area pertaining to the artery 10 to 30 seconds after intra-arterial injection of 2 to 4 ml of 1% Imidalin. Under such situation, arteriographies of lower extremities were done on 15 cases.

4) *Peripheral Arteriography after Intra-arterial Procaine Injection.*

Bilateral canine femoral arteries were exposed and 10 to 20 ml. of 2% procaine was injected unilaterally, and for the other side, only puncture with needle was done as a control. Twenty to thirty seconds after this procedure, arteriography of bilateral hind legs was done and both sides were compared.

Three clinical patients underwent slow intra-arterial injection of 20 to 40 ml. of 2% Procaine taking 20 to 60 seconds and arteriogram of the same side was taken immediately after this procedure.

5) *Peripheral Arteriography using the Reactive Hyperemia.*

Manchette was applied on the middle part of canine unilateral thigh and the peripheral was brought to the ischemic condition for 7 to 8 minutes. The manchette was then released and bilateral arteriograms were taken.

In human cases, manchette was applied on the upper part of the leg, which had been elevated to avoid the venous engorgement. Then the pressure of manchette was elevated above arterial blood pressure of the pertaining leg.

** Benzol Imidazoline, or Priscol

Fig. 1.
Peripheral arteriography using the reactive hyperemia, after the release of 7-8 minutes occlusion, arteriography is performed.

After the procedure, the leg was returned to the horizontal position and left for 7 to 8 minutes to induce ischemia. Contrast medium was injected 10 to 20 seconds after release of the manchette, and arteriograms from thigh to foot were taken. (Fig. 1)

Roll film was used for 4 cases, and serial angiographies every one second were performed and these were compared with that of single exposure.

6) *Experiments concerning the Collaterals after Sympathectomy.*

The fact that collateral channels might increase after sympathectomy is easily believed from various reports based on skin temperature measurement³⁾⁴⁾⁵⁾ or from evaluation of late results of sympathectomy.⁶⁾ However, literatures have not yet revealed any clear-cut experimental or clinical evidences on this matter.⁷⁾

The author investigated this problem by arteriography using 8 dogs, and the following experiments were performed.

In the upper part of bilateral thigh, superficial femoral arteries were exposed under intravenous anesthesia by 30 mg of Nembutal per kg. They were ligated and severed. Then, laparotomy was performed by median incision and the caudal artery was ligated with 1 cm left for the convenience of later procedure of aortography. The internal iliac arteries were also ligated twice at their origin. Unilateral sympathectomy was done from the height of renal arteries down to

aortic trifurcation which was corresponded to L_3-L_6 .

Seven days to 6 weeks after operation, laparotomy was again performed with a median incision and sympathectomy of the opposite side was done. Immediately after this procedure, polyethylene catheter was inserted through the caudal artery to the terminal aorta and the first (plain) arteriography of bilateral hind legs was performed with 20 ml. of 76% Urografin.

Then, the abdominal aorta was occluded below the renal arteries with a vascular clamp. Five to 10 minutes after occlusion, the clamp was released and 10 seconds later, the second arteriography (under reactive hyperemia) was done with injection of contrast medium.

RESULTS

1) *Effects of Spinal Anesthesia on Peripheral Arteriography.*

None of patients complained of pain when contrast medium was injected. However, no difference was noticed between arteriograms under spinal anesthesia and those of control.

2) *Effects of Sympathectomy on Peripheral Arteriography.*

In dogs, many spot like densities were noticed in the pattern of the side with sympathectomy. Pattern of a dog is corresponded to the human heel.

From these densities, almost all contrast medium passed into the superficial vein which corresponded to the human saphenous vein, and a part of the medium directly to deep veins. In the opposite side without sympathectomy, only a few spot like densities were noted and a small amount of contrast medium moved into deep veins (photo. 1 & Fig. 2).

Visualization of fine arteries in the muscles was a little better immediately after sympathectomy. However, no difference between arteriograms of both sides was noticed 7 or more days after the sympathectomy.

In human case, arteriograms of 21 cases were taken 7 days to 3 years after sympathectomy. No significant differences were noticed when they were compared with pre-operative arteriograms or arteriograms of the opposite side.

Photo. 1 & Fig. 2.

Arteriogram of canine hind legs immediately after sympathectomy, right side is operated. Many spot like densities are noticed in the right pattern, and contrast medium passes through these densities into the superficial vein.

Photo. 2 & Fig. 3.

Arteriogram of canine hind legs after intra-arterial Imidalin injection, injection is done to the right common femoral artery. Many spot like densities are noticed in the right pattern, and contrast medium passes from these densities through the superficial vein to deep vein.

Sympathectomy did not relieve the pain at the time of injection of contrast medium. After thoracic sympathectomy, air plethysmography of fingertip showed markedly decreased pulse wave immediately after the injection of contrast medium, as well as in the opposite control side. From this fact, it was presumed that contraction of arteries occurred.

3) *Effects of Intra-arterial Injection of Imidalin on Peripheral Arteriography.*

Arteriograms of dogs after intra-arterial injection of Imidalin revealed many spot like densities in the pattern more markedly than noticed in the arteriograms immediately after sympathectomy.

From this region almost all contrast medium passed through superficial veins to deep veins, and a part of it passed directly into deep veins. Visualization of fine arteries in muscles were somewhat better than the opposite side. (Photo. 2 & Fig. 3).

In human cases, visualization of arterial branches was better in the thigh with intra-arterial injection of Imidalin. However, no such differences were noticed in lower legs. Pain at the time of injection of contrast medium was not relieved by this procedure.

4) *Effects of Intra-arterial Procaine Injection on Peripheral Arteriography.*

In dogs, fine arteries in muscles were well visualized in arteriograms after intra-arterial injection or 2% Procaine compared with control. It was noticed that contrast medium moved through accompanying venules to deep veins which is obviously different from the findings after sympathectomy or intra-arterial injection of Imidalin (photo. 3 & Fig. 4).

In human cases, patients complained of dullness in the whole lower extremities after intra-arterial injection of Procaine. But they complained of pain when contrast medium was injected. This was almost the same as control. In the thigh, visualization was a little better than control. However, no significant effect was noted in the lower leg.

Photo. 3 & Fig. 4.

Arteriogram of canine hind legs after intra-arterial Procaine injection, injection is done to the right common femoral artery. Fine arteries in muscles of the right leg are well visualized, and small amount of contrast medium moves through accompanying venules to deep vein.

5) *Effects of Reactive Hyperemia on Peripheral Arteriography.*

In dogs, fine arterial branches in muscles were very well visualized in the area distal to the manchette. It was noticed that contrast medium passed through accompanying venules to deep veins which was the same finding in arteriograms after intra-arterial injection of Procaine.

In human cases, manchette was applied on the upper part of the lower leg. Fine arterial branches were visualized very obviously in and distal to the area where manchette was applied. In cases without disorders of arterial or venous system, it was noticed by delayed exposure that contrast medium moved from fine arteries through the accompanying venules to deep veins.

When manchette was applied on the thigh, good visualization of arterial system in the lower leg could not be obtained, of course, in those cases with occlusion below the popliteal artery and even in those cases with occlusion at the height of the thigh. Consequently, manchette should be always applied on the upper part of the lower leg, and the injection time should be prolonged a few seconds when occlusion is suspected in the thigh.

These findings were same when this procedure was done after lumbar anesthesia or after sympathectomy.

Even in such a patient who had peripheral tissue necrosis, pain did not inhibit the performance of the procedure. No aggravation of circulatory disturbances was seen in 125 cases who had had this kind of arteriography during 3 years since April 1959. Almost all patients who had peripheral tissue necrosis complained of severe pain when contrast medium was injected intra-arterially without this method. However, pains were relieved in some extent when arteriograms were taken under reactive hyperemia.

Serial angiography of the lower leg was performed and effect of reactive hyperemia

Photo. 4 & Fig. 5.

Arteriogram of canine hind legs under the reactive hyperemia, manchette was applied on the middle part of the left thigh. Fine arterial branches in muscles are very well visualized in the area distal to the manchette.

was noticed in completely same way as noticed in single exposure.

6) *Effect of Sympathectomy on the Development of Collaterals.*

The first (plain) arteriograms taken immediately after the second sympathectomy showed more collateral channels in the side of the second operation than in previously operated side. From this finding, it was likely that the effects of sympathectomy was temporary and it did not promote the development of collaterals (Photo. 5 & Fig. 6).

However, arteriograms under reactive

hyperemia (the second arteriogram—when arterial system was extremely dilated) showed better development of collaterals in the previously sympathectomized extremity than in the opposite side (the side of second operation) (Photo. 6 & Fig. 7).

So, it was presumed that sympathectomy has a effect of promoting a development of collaterals, but no significant difference was noticed between arteriograms of 10 days and 6 weeks after sympathectomy. As far as this experiment, it could be thought that development of collaterals reaches to some

Photo. 5 & Fig. 6.

Collaterals after sympathectomy, plain arteriography. Left lumbar sympathectomy was done first. Seven days later, right lumbar sympathectomy was done and then this film was taken. Collaterals are more prominent in the right than in the left.

Photo. 6 & Fig. 7.

Collaterals after sympathectomy, arteriography under the reactive hyperemia. This film was taken after the release of aortic occlusion. Collaterals are more prominent in the left than in the right.

constant level in the fairly short period of time.

COMMENT

In the experiments using dogs, arteriograms immediately after sympathectomy and those after intra-arterial injection of Imidalin revealed the same findings, and arteriograms after intra-arterial injection of Procaine and those under reactive hyperemia revealed the same findings. Each groups suggested that fine arteries were dilated.

Furthermore in the former group, contrast medium revealed many spot like densities in the pattern after filling the arterial trees and it passed through these densities mainly to superficial veins. In the latter group; contrast medium moved from fine arteries in muscles through the accompanying venules to deep veins.

The same kind of spot like densities as seen in the former group were noticed in tips of fingers of men where arterio-venous anastomoses were believed to be normally present by histological investigations.⁸⁾ This fact may suggest that the spot like densities seen in the pattern of dogs represent arterio-venous anastomoses.

Intra-arterial injection of Imidalin or sympathectomy may open arterio-venous anastomoses and this may let contrast medium move directly to venous system. Intra-arterial injection of Procaine and reactive hyperemia may have a different mechanism, namely, contrast medium moved from dilated fine arteries through capillaries to the accompanying venules. It may reasonable to presume that contrast medium passes through arterio-venous anastomoses also in this situation, because it moves very fast. The author would like to believe that arterio-venous anastomoses were present in skeletal muscles.¹⁰⁾

Among 4 methods of clinical experiments using vasodilating procedures, reactive hyperemia was only one method which was noticed to have been useful. When a medicine is injected intra-arterially, it enters into blood vessels proportionally to blood

flow. Consequently, in the case of circulatory disturbances, peripheral distribution of a medicine would not be enough to cause sufficient effect of vasodilation. As to sympathectomy, arteriography immediately after the operation in clinical case was not performed, but it could not be expected that peripheral region below lower leg might well visualized selectively.

The author's new method using reactive hyperemia by manchette applied in the lower leg, has a significance that it causes vasodilatation selectively in peripheral region below lower leg.

Arteriograms of Buerger's disease or arteriosclerosis obliterans using this method revealed many unexpected occlusion of small arterial branches with many small collaterals connecting above and below (Photo. 7).

Photo. 7.

T. F. 36 yrs. male, Buerger's disease, femoral arteriography using the reactive hyperemia. Occlusion of the posterior tibial artery and other small arteries are revealed, many fine collaterals are also noticed.

Various devices of treatment of occlusive arterial diseases by intra-arterial injection have been tried, but none of them was

proved to have been sufficiently effective. One of the important reason of inefficacy is because the injected medicine does not reach to the peripheral region below the occlusion where the medicine is most needed. From this reason, the author applies reactive hyperemia also when intra-arterial injection of some medicine is used for a treatment.

Serial angiography may catch desired part, but at present, no X-ray apparatus for wide area such as from thigh to foot is not obtained. Marked X-ray exposure also inhibit its routine clinical use. Band radiation method (Scanographic technique)⁽¹⁰⁾⁽¹¹⁾ which is a method of exposure through a narrow slit moving with a X-ray tube is also dangerous because of marked irradiation.

The author's method applying reactive hyperemia is simple and easy procedure which can clearly visualize arterial system from thigh to foot with only one exposure. This is especially excellent for visualization of peripheral fine arteries in the region distal to lower leg, and proved itself to be a very useful means for determination of indication for operation and following up of clinical course.

The author performs arteriography of extremities routinely by local anesthesia only. Our arteriography applying reactive hyperemia has another advantage that pains by injection of contrast medium are relieved in some extent.

The degree and duration of reactive hyperemia depends upon room temperature, presence of vascular diseases and its site and degree. Because it is reported that maximal dilatation of arteries is obtained after release of vascular occlusion of 4 to 8 minutes in normal person,⁽¹²⁾ the author begins injection of contrast medium 10 to 20 seconds after release of vascular occlusion of 7 to 8 minutes. Manchette should be applied after elevating the lower extremities to avoid blood congestion in vascular bed because sufficient reactive hyperemia is not obtained under the condition of blood congestion in peripheral region.⁽¹³⁾

It is likely that blood flow occlusion for the cases with peripheral tissue necrosis

might be dangerous procedure, but none of cases showed aggravation of their circulatory disturbances after this procedure.

Rise of central blood pressure, pressure gradient between central and peripheral arteries, deposition of metabolic substances or "Tissue Needs" are factors concerning the development of arterial collaterals.⁽¹⁴⁾ Reflex action also would be related to this because regional skin temperature rises after denervation. However, because long persisting rise of skin temperature is caused partly by stopping of sweating, it does not necessarily mean circulatory improvement through collaterals. On this problem, Dr. Hidai, one of my coworkers will soon publish as his original article. Although it is believable that sympathectomy must improve circulatory disturbances by development of collaterals, no literature proving clearly this problem could not yet be seen.

On this point, the author performed a series of experiment as described in (6) and found that after denervation, markedly increased collaterals were revealed in arteriograms under reactive hyperemia namely when arteries are at most dilated. As arteries are reached to the maximum dilatation under reactive hyperemia, arteriogram in this condition is thought to be indicating the ability of exercise.

From the experiment of (2) and (6), regain of vascular tonus was simultaneously noticed already one week after sympathectomy. If this fact is supposed essentially same in human case, it could be well understood that more than 70 per cent of 150 sympathectomized patients in our clinic showed fairly marked increase in ability of exercise in the late results, despite that blood flow under without any load, returned nearly to the preoperative level after marked increase seen immediately after operation.⁽⁶⁾⁽¹⁵⁾

SUMMARY

Using dog's hind legs, arteriographies after sympathectomy, intra-arterial injection of Imidalin or Procaine and under reactive hyperemia were performed and compared.

Arteriograms after sympathectomy and those after intra-arterial injection of Imidalin were thought to be essentially same. They revealed dilatation of fine arteries in muscles and opening of arterio-venous anastomoses of the pattern through which contrast medium passed to superficial veins.

Arteriograms after intra-arterial injection of Procaine and those under reactive hyperemia were presumed to be essentially same. They revealed dilatation of fine arteries in muscles and opening of arterio-venous anastomoses in muscles and it was noted that contrast medium passed rapidly through accompanying venules to deep veins.

When reactive hyperemia is applied clinically for the lower extremities, especially when they have occlusive disorders, this method is very sufficient for selective visualization of peripheral region and pains by injection of contrast medium is relieved in some extent.

This new arteriographic method devised by the author is simple procedure and always gives excellent arteriograms. It would be very useful for the diagnosis of occlusive diseases and determination of indication for operation.

Furthermore, from the experiments using dogs, it could be proved roentgenologically that sympathectomy promote the development of collaterals. This fact could be revealed in this new method of arteriography applying reactive hyperemia.

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