Scintigraphy and indirect lymphography

Practical aspects

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Lymphoedema is a life-long disease which may be improved but not healed by our therapy. Therefore it seems to be desirable to ascertain the clinical suspicion of lymphoedema or to rule out this diagnosis at least once in the life of a patient suffering from chronic swelling of the extremities. The most appropriate methods for that purpose are lymphoscintigraphy and indirect lymphography.

Radionuclide lymphography and indirect lymphography are based on a similar principle: lymphatic drainage is assessed after „indirect“ application of a tracer into the tissue, in contrary to the „direct“ injection of contrast-material performed in conventional lymphangiography. Labelled compounds are used for scintigraphy, and newly developed, water-soluble contrast media for indirect lymphography.

While radionuclide lymphography has become the most important diagnostic tool for diagnosing compromised lymph-drainage, indirect lymphography has been established only in few centres, mainly for scientific reasons.

Scintigraphy and radionuclide lymphography

The essential function of the lymphatics to clear the interstitium from large molecules can be tested by introducing labelled proteins or colloids into the tissue. Scintigraphy by gamma camera allows the assessment of the distribution of the tracer in the leg and its storage in the lymph nodes. Using new high-resolution techniques (“lymphangioscintigraphy LAS “) images of lymph nodes and also of lymphatics may be obtained The function of the lymphatic

drainage can be assessed by comparing the uptake of radioactivity in the lymph nodes with the injected dose. Nodal scintigraphy has gained some new importance for the assessment of sentinel lymph nodes in different areas of cancer-surgery .

Labelled tracers

It has been suggested that the optimal particle size for a lymphatic tracer is in the range of 10 nm. After injection into the tissue these particles enter the initial lymphatics, some part being incorporated into macrophages, and are transported towards the lymph nodes.

Commonly used compounds are antimony sulphide colloid, rhenium sulphate, human serum albumin nanocolloid and DTPA serum albumin, all labelled with technetium (99m Tc) .Labelled gold colloids are not used anymore.

Injection

Injection volume should be small (0.1-0.2 ml) and should have high specific activity.

For routine diagnosis of lymphoedema subcutaneous injections are recommended into the web space between the first and second finger of the hand and between first and second toe of the foot. Several subcutaneous injections may improve diagnostic accuracy.

For special information injections into the area of interest, e.g. around leg ulcers , scrotum etc can be performed.

Subfascial lymph transport can be assessed after intramuscular injection of the tracer into the distal third of the calf.

Stress-tests

In order to enhance lymph -transport active movement, e.g. exercise with a foot ergometer or walking on a treadmill is recommended. This is essential if the assessment of the lymphatic

drainage function is mainly based on the amount of radioactivity recovered in the regional lymph nodes. It has been shown that sensitivity and specificity of static images obtained one hour after injection are increased by muscular exercise. However, some authors prefer to assess static images taken in different time-intervals after injection without any stress test.

Measurement of radioactivity

Different kinds of techniques have been described:

The registration of time-activity curves over the injection site reflects the local clearance. It has been shown that the correlation between the clearance of the tracer from the depot and its uptake in the lymph nodes is very poor. However, this parameter has been used especially to demonstrate therapeutic effects.

Pictures taken from the whole extremity by a gamma camera and whole body images may show pathological distribution of the injected substance due to dermal back-flow or a block of lymph collectors.

The uptake of radioactivity in the lymph nodes is the most reliable single parameter for assessing the lymph-transport. It can be documented by simple scintigraphy, measured with a scintillation probe or a gamma camera, or using a combined transmission- emission-procedure in order to correct for different depth of the inguinal and iliac lymph nodes. By comparing the injected dose with the corrected lymph node activity quantitative information can be given .

The appearance-time after the injection of the tracer alone, which should be shorter than 40 minutes under normal conditions, is an unreliable parameter.

Semiquantitative scoring systems considering different parameters of tracer kinetics and calculating a transport index have been proposed . For routine diagnosis visual interpretation of images may be sufficient in the majority of cases.

Results

Based on visual interpretation the sensitivity of isotope lymphography in diagnosing lymphoedema was reported to be 97 % and its specificity 100% .

Intracutaneous tracer-injection is not able to separate lymphoedema from non-lymphoedema. The normal storage values after intracutaneous tracer-application in patients with lymphoedema, even caused by metastases in the lymph nodes, demonstrate the fact that intracutaneous networks of initial lymphatics may act as an effective collateral pathway. Therefore intracutaneous application of the tracer is useful to detect sentinel lymph nodes or to visualize pathological skin- lymphatics filled by dermal backflow as it is intended by the LAS-technique. When quantitative measurement of the lymph-node activity is taken as the deciding parameter subcutaneous tracer administration is to be preferred. Using quantitative lymphoscintigraphy we were able to diagnose subclinical forms of lymphatic damage e.g. on the normal appearing contralateral leg of patients with hereditary lymphoedema.

It has been shown that lymphatic function declines with age, markedly so after the age of 65 years.

Table I summarizes the results of lymphoscintigraphic studies in several pathologic conditions.

Table I: Lymph-drainage in different conditions. Summarized findings reported in the literature (DVT = deep vein thrombosis, PTS= postthrombotic syndrome). ⇓=decreased, ⇑=increased

Lymph transport	**Praefascial**	**Subfascial**
Lymphoedema	⇓	
Venous oedema	(⇑)	
	⇓	
DVT	(⇑)	⇓
PTS	(⇑)	⇓
leg-ulcers	⇓	⇓
Lipoedema	⇔	

Practical consequences

Today isotope lymphography is the most appropriate method to ascertain the clinical suspicion of lymphoedema. This method is also important to rule out lymphatic involvement in different forms of swollen extremities with unknown origin. It is easy to perform and not invasive. However, its routine use is mostly restricted to nuclear medical departments with clinical partners in the background who are interested in lymphology and who admit their patients to scintigraphic investigations.

Unfortunately up to now no broadly accepted consensus has been reached concerning a standardized protocol for lymphoscintigraphy. It has to be underlined that “normal findings” very much depend on methodological details and are not always able to rule out lymphoedema.

Indirect lymphography

Skin lymphatics may be opacified by intradermal injection of newly developed contrast media. This method gives a valuable picture of the local dermal lymphatics in a region of interest and may provide important clues about the lymphatic drainage of the limb as a whole. However, lymph nodes are opacified only rarely so that this method cannot substitute conventional, direct lymphography.

Method

Non-ionic, water soluble, dimeric, hexaiodinated contrast media such as Iotasul or Iotrolan are constantly infused subepidermally by a motor pump (0.12 ml/min) using thin, butterfly needles with a total amount of 2-4 ml per injection site. The tip of the needle has to be situated in the uppermost part of the dermis so that a bluish, glassy-appearing wheal will develop. Under normal conditions, lymphatics begin to fill after a few minutes that can be observed by an image converter and documented on mammography films at 5-minute intervals. Xeroradiography may be a valuable alternative; computer-tomography with three-dimensional reconstruction gives impressive pictures.

Indications

This method may be helpful regarding a differentiation of various forms of lymphoedema like in hypoplasia of distal lymphatics versus proximal hypoplasia with distal distension. It has a high sensitivity for diagnosing lymphoedema (97%) with a moderate specificity (89%) .Pathological changes of skin lymphatics can be demonstrated in areas of lipodermatosclerosis due to chronic venous insufficiency and in the vicinity of leg-ulcers. Localized lymphoedema as e.g. after trauma, inflammation or in morbidly obese patients is characterized by pathological initial lymphatics in certain skin areas while large collectors may appear normal . Patients with lipoedema show a typical flame-like pattern of the dye distribution, which is one of the very few pathognomonic features of this entity.

Fascinating results may be obtained after replantation-surgery.

Results

The infused contrast agent forms growing depots, which taper into peripheral lymph-collectors. Under normal conditions these collectors can be followed for an average length of 10-30 cm. Retrograde flow may fill small skin lymphatics as a sign of dermal backflow due to incompetence of lymphatic valves.

In principle, four different patterns have been described in lymphoedematous skin :

Type I: No lymphatics are opacified. Instead, contrast may spread in a cuff-like pattern obviously marking the adventitial space of blood vessels. This feature is found especially in congenital lymphoedema and fits well with findings obtained by microlymphangiography.

Type II: A dense network of small skin lymphatics corresponding to precollectors, but only sparse lymph collectors are opacified. This pattern is found mainly in patients with peripheral lymphoedema praecox and tardum.

Type III: Precollector skin lymphatics and lymph collectors are both enlarged, possibly due to proximal obstruction. Most patients with descending form of lymphoedema due to primary proximal obstruction and with involvement of the entire limb tend to show this constellation. This pattern is also seen after infusion of the dye into skin-areas with papillomatosis cutis.

Type IV: Neither precollectors nor lymph collectors can be seen. This pattern may be explained by a „die-back“-mechanism of lymphatics in the presence of proximal abnormalities. However, also technical problems in patients with extremely dense and thick skin can also yield a similar picture.

In patients with chronic venous insufficiency morphological changes of dermal lymphatics may also be demonstrated in pathological skin regions. Precollectors are fragmented, filled by dermal backflow and show extravasations of the dye into the tissue. Prefascial collectors are

enlarged and show often increased contractility. Even lymph nodes in the groin may be opacified. These features of wide and well-filled lymph-collectors correlate with an increased praefascial lymph transport demonstrated by radionuclide lymphography.

Injecting the dye into the border of venous ulcers can fill no lymphatics.

Lipoedema, which is often confused and sometimes combined with lymphoedema, shows a very characteristic and quite specific pattern.. The depot of the dye injected into the oedematous parts of the lower leg forms a typically flame-like structure.

Practical consequences

Indirect lymphography is a kind of radiological patent blue-test, but with a much better resolution. Exact injection technique is a prerequisite for adequate results. The value of this method is rather restricted to scientific than to practical information.

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