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New Approaches to Sympathetic Blocks as Treatment of Postmastectomy Lymphedema

Report of a successful case*

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Introduction

The presence of lymphedema following mastectomy still constitutes a serious problem in spite of improved methods of surgery and other forms of cancer therapy. In a recent study about 17% of the patients who had undergone mastectomy combined with radiation therapy the arm volume on the side of the operation was increased to on average 110% or more of that the contralateral side. There was a similar difference in respect of 10% of the patients who had had no radiation therapy (21). Even slight edema can give rise to pain and annoying sensations of pressure, tension and paresthesia, especially when the edema is located in the hand or at the level of elbow. Edema of the hand in particular is often experienced as a social handicap (20).

The mechanisms of lymphedema following mastectomy are incompletely understood, and numerous causes have been postulated. Examples are: obstruction of the lymphatic circulation following removal of axillary lymph nodes, and lymphangitis, either as an allergic reaction, or due to infection (2, 3, 6, 11), venous obstruction caused by strangulation of the axillary veins (16), thrombophlebitis and fibrosis in the axillary veins (16), thrombophlebitis and fibrosis in the axilla leading to strangulation of both veins and perivascular lymphatic vessels (5), and, finally, obliteration of lymphatic and blood vessels of small diameter as a direct result of radiotherapy (8, 15). Long periods of heavy static work (17, 23) and overweight (6) have been considered predisposing factors for lymphedema after mastectomy. As a further cause smooth-muscle spasm in arteries, veins and lymphatic vessels had been discussed.

The possibility of treating postmastectomy lymphedema by stellate blocks is well documented in the early literature (14). However, sympathetic blocks as a method of relieving edema in postmastectomy patients appear not to be part of current therapy. The reason for publishing the present case report is to draw attention to this possibility. In this particular patient, who has been followed for about three years, the sympathetic block therapy was tried because it had been noticed incidentally that the postmastectomy lymphedema was much reduced as a result of percutaneous cordotomy, which is known to have a moderate blocking effect on the sympathetic system. As a temporary stellate block had no significant influence on the edema, the recently developed method of regional sympathetic block by intravenous guanethedine injection was instituted and found to be most effective.

Methods

The assessment of lymphedema in the arm was performed using a volumetric method previously described in detail (18, 19, 21).

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The volume of the affected arm is expressed as a percentage of the volume of the contralateral healthy arm. The accuracy of this method has been shown to be highly satisfactory, the standard error of the mean being less than 1%, which in this context corresponds to 5–15 cm^3 of the volume of a normal female arm.

Percutaneous cordotomy was performed by the lateral approach at the level C:I-C:II. The location of the needle was checked by fluoroscopy and electrical stimulation.

For sympathetic block of the arm regional intravenous injection of guanethedine by the technique described by *Hennington-Kiff* (7) was used. With the arm elevated a tourniquet was applied as close as possible to the shoulder and insufflated well above the arterial pressure. Guanethedine, 15–30 mg in 20–40 ml of saline, was injected intravenously in the arm, and after 10–15 minutes the tourniquet cuff was released. Digital pulse plethysmography and cold provocation were performed on the day prior to, and the day after, guanethedine block. Cold provocation was performed with the hand immersed 15 minutes in water at 15 °C. After 0.5, 5, 10 and 15 minutes the skin temperature of the dried and bare hand was measured. Volumetric measurements of arm lymphedema were performed on the same day as, and on the day after, the block, and then repeated once a week until the next block.

Sympathetic thoracic block was performed by injecting 5 ml of 6% phenol in water in the sympathetic chain at the level of the second and third thoracic vertebrae. The location of the tip of the injection needle was monitored by computed tomography using a recently designed method for obtaining a sympathetic block in this region for hyperhidrosis (12).

Case report

For ductal mammary cancer without demonstrable spread the patient had at 67 years of age undergone left-sided mastectomy, with removal of the axillary lymph nodes. No irradiation therapy was given. The postoperative course was uneventful but the shoulder mobility was considerably reduced.

Two months after the operation progressive lymphedema in the hand developed. There was also some pain. Eighteen months after the operation volumetric measurement showed that the arm volume was 30% greater than that of the sound arm. The fact that the edema was concentrated in the hand and the lower arm rendered purposeful movements of the hand virtually impossible. The skin was very glossy. Electrophysiological examinations revealed injury to the radial, median and ulnar nerves. The edema gradually increased until the arm volume was about 180% of that of the control arm (Fig. 1). At this stage the pain had become excruciating and the patient consumed high doses of narcotic analgesics. Percutaneous cordotomy was therefore performed so as to produce total analgesia up to a level corresponding to C:III, thereby banishing the pain completely.

Shortly after the operation the edema decreased considerably, and at two months the volume of the arm was only 115% of that of the control side. This effect slowly subsided, however, and the arm again tended to increase, so that after eight months it had attained a volume of 180% of that of the control arm. Pneumatic compression treatment was given daily, but without significant effect. As it is known that cordotomy may sometimes lead to decrease in sympathetic tone the reduction of edema in this patient after cordotomy was ascribed to a sympatheticolytic effect. An attempt to block the stellate ganglion – deemed a rational measure – proved to be entirely ineffective. In a further attempt to reduce the edema by lowering the sympathetic tone a regional intravenous guanethedine block was performed. This treatment resulted in an immediate and dramatic decrease in arm volume from 200 to 150% (Fig. 1). A second block performed the following week caused a further reduction to 130%. This effect lasted for about four weeks, when a new block had the same effect. Altogether eight guanethedine blocks were performed, the greatest duration of a single block being eight weeks. Eventually the effect tended to diminish, and local swelling of the hand

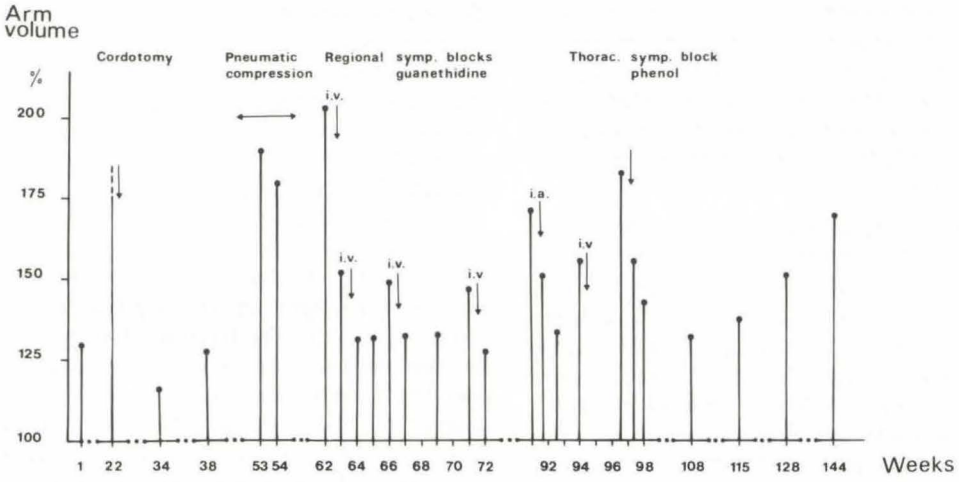

Fig. 1 Changes in the relative volume of the edematous arm following various kinds of treatment over a period of three years

and arm made injections difficult. It was therefore decided instead to perform an intrathoracic sympathetic block with phenol. At that time – 97 weeks after cordotomy – the arm volume was about 180% of that of the control arm. As a result of the intrathoracic block the edema diminished dramatically in the course of 11 weeks to a minimum of 135%. Thereafter, there was again a slow increase, but not until 47 weeks after the phenol block had the volume attained a value of about 160%. Thus, the thoracic sympathetic block with phenol considerably reduced the edema, and part of this effect persisted for up to about one year.

Pulse plethysmography before and after the sympathetic blocks showed no significant changes. In contrast, the cold provocation revealed a decrease in vascular reactivity (tendency to vasospasm), as evidenced by enhancement of the increase in temperature following exposure to the cold water. This effect was observed in both arms. This test was not performed in association with the cordotomy.

Comments

The literature contains several early reports (14) on the efficacy of sympathetic blocks – mostly performed as a temporary block of the stellate ganglion – in the treatment of postmastectomy lymphedema. This method is, however, seldom practiced now, because such a block often fails, the effect is generally shortlived and the side effects involving the face are poorly tolerated. These shortcomings explain why such blocks are only exceptionally performed with neurolytic agents.

Sympathetic blocks by intravenous regional injection of guanethedine, and neurolytic blocking of the upper intrathoracic sympathetic chain are more persistent in their effect, and have no serious side reactions. Sympatheticolysis of the upper thoracic portion of the sympathetic chain can, of course, be performed as surgical sympathectomy, but this operation incurs considerable risk of complications. The percutaneous method, with computed tomography for controlling the location of the needle, appears to be a safe method and offers many other advantages.

Cordotomy is known sometimes to produce a reduction of sympathetic tone, as evidenced by arterial hypotension (22). When cordotomy is performed with the percutaneous method at the level C:I-C:IV Horner's syndrome is a common sequela. This symptom is, however, ob-

served on the same side of the spinal lesion, and no contralateral sympatheticolytic effects have been reported. The findings in this patient suggest that the spinal sympathetic projections at the high cervical level are bilaterally organized, but this possibility needs to be further explored (10).

Intravenous regional sympathetic block with guanethedine has been introduced as an alternative to conventional blocks of sympathetic ganglia with local anesthetics (7). Guanethedine has a selective blocking effect of peripheral sympathetic nerves, is quickly taken up by the tissues and it is slowly metabolized. It produces a selective blockade of the transmission in postganglionic adrenergic nerve-endings, and peripheral responses to sympathetic activity and to circulating sympathicomimetic amines are inhibited. The substance is taken up by the adrenergic nerve terminals and stored in intraneuronal granules, competing with noradrenalin. Sympathetic activity will thus result in a release of guanethedine as a false transmitter. Moreover, the re-uptake of noradrenalin is impeded owing to a competitive mechansim (4). Guanethedine blocks have been used mostly in the treatment of causalgic pain, often referred to as sympathetic reflex dystrophia (1, 9). The duration of the effect is highly variable, but it may be a matter of months. Moderate peripheral edema occasionally present in such painful conditions is known to be reduced or to disappear as a result of both central and peripheral sympathetic blocks. However, both the pain-relieving effect of sympathetic blocks and the decrease of swelling are poorly understood, and several explanations have been proposed (13).

In the present case the same effect on the lymphedema was obtained after cordotomy, regional intravenous and intraarterial injection of guanethedine and phenol injection in the thoracic sympathetic chain. It is therefore conceivable that a reduction of the sympathetic tone is the causative factor; the effect can hardly be ascribed to any increased mobility following relief of pain by cordotomy, or to some unspecific mode of action of guanethedine.

The mechanisms by which edema may be influenced by vascular tone are incompletely known. The fact that the decrease in sympathetic tone, presumably through its effect on the vascular bed, may lead to a reduction of postmastectomy edema does not necessarily indicate that this swelling is due to sympathetic dysfunction, and that "neurovascular spasm" should be included among the possible causes of this edema. It might well be that the improvement in perfusion resulting from vasodilatation facilitates the drainage of extracellular fluid whatever the cause of this condition may be. It must, however, be remembered that an increase in the peripheral sympathetic activity not only causes contraction of arteries, but it also influences postcapillary resistance. Moreover, there is evidence that the effector organ of the peripheral sympathetic system may also be vasodilator muscle fibres. Thus, the vasomotor sympathetic control is extremely complex, and the effects of manipulating the peripheral sympathetic outflow are difficult to interpret. However, the fact remains that the new method of blocking, or reducing, the sympathetic tone would appear to be a promising alternative to other available methods of dealing with postmastectomy lymphedema. For a further systematic investigation of the usefulness of these methods and for their rational use a better understanding of the dependence of lymphedema on sympathetically controlled vascular tone is needed.

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Invited Commentary

The authors describe a patient following mastectomy and axillary dissection for breast carcinoma. Two months post op. lymphedematous swelling of the hand and forarm, a 30 percent volume increase, developed. In addition, the patient experienced pain. In which neural segments or nerves is not stated, electrophysiological examination revealed injury to the median, ulnar and radial nerve. The swelling of the arm incrased as did the pain. This was abolished by a percutaneous cervical cordotomy. It cured the pain and reduced, for 8 months, one third of the lymphedematous swelling. Subsequent pneumatic compression as well as a stellate ganglion block was ineffective. But eight regional intravenous guanethidine blocks obtained temporary reductions of the swelling up to 25 percent. An intrathoracic sympathetic block with phenol gradually diminished the edema volume for 35 percent during 11 weeks. The swelling recurred to reach 90 percent of the original severity 2.7 years post operationem.

According to the description of the authors, the patient has two problems: due to axillary surgery a painful infraclavicular brachial plexus palsy. This was cured by cervical cordotomy, without any side-effects. The authors must certainly be congratulated for solving this difficult problem. Never have I seen in over two

hundred patients lymphedema being responsible for intractible pain in the arm nor injuring peripheral nerves.

The patient's second problem: the diagnosis of the arm swelling is certainly secondary arm lymphedema. Its extent may increase, vary and plateau without therapy as described in 41 patients followed up to 20 years (1). In contrast to the many mechanisms, mentioned by the authors as leading to secondary lymphedema, its cause has been defined by a reduction of the lymphatic transport capacity and the extra-lymphatic mastering of plasma proteins in presence of a normal lymphatic load (2, 3). The reduction of the lymphatic transport capacity was effectfully produced by the axillary dissection, which also lead to the neurological symptoms as mentioned.

The temporary action of chemical and surgical sympathetic blocks reducing the amount of lymphedema (presumably without any additional therapy) up to one third of its excess volume in this single patient is interesting and needs, in my mind, experimental verifications.

The authors call this a successful case, although according to Fig. 1, there is an overall increase of the arm volume to 160 percent at 144 weeks. Despite all possible explanations given by the authors on the basis of their observations, the reviewer likes to urge them and the readers to experimentally investigate in lymphedema the actions of the sympathetic innervation upon the structures of the lymph formation and lymph circulation (structures of the capillary wall by which the ultimate lymphatic load enters the interstice, interstitial tissue channels, initial lymphatics, lymph-collectors, thoracic duct). Then this case report will be a lymphological success, because *Claude Bernard* teaches us: "Observation shows, experiment teaches".

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Reply:

We much appreciate Doctor *Clodius*'s commentary to our report and would like to give some additional comments. In particular, we want to draw attention to the fact that percutaneous cordotomy in this case led to a rapid reduction of the lymphedema so that the volume of the arm decreased with about 2/3, i.e. from 180% to 115% of the control arm. This change took place from week 22 to week 34 (Fig. 1). Even though this effect did not last longer than about six months it is of interest for the understanding of possible mechanisms for the development of lymphedema. The same applies to the effect to sympathetic block with regional guanethedine injection which dramatically reduced the volume of the arm from 200% to 130% in two weeks' time (week 62 to 64).

With regard to the possible relationship between lymphedema and severe pain it might be that the text in our report is somewhat ambigous and needs to be clarified. We have never claimed that the development of pain in this case was the result of lymphedema, nor were the neurological deficits. The pain was presumably of neurogenic origin and it could be effectively and immediately abolished by a percutaneous cordotomy which apparently had the additional effect of pro-

ducing with some delay a marked reduction of the lymphedema.

It is true, that on a longterm base this patient can not be considered to be a successful case in the true sense. However, in spite of the poor final outcome after about three years we consider the new approaches to an old and well-known method of dealing with lymphedema to be promising, in particular in view of the fact that conventional methods of treatment never produce such dramatic results in a short period of time. We fully agree with Doctor *Clodius* that the mechanisms by which sympathetic blocks may reduce lymphedema should be further explored experimentally, and this was one reason why we thought that this case was worth reporting.

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