

The Regulation of Subcutaneous Blood Flow in Patient with Dercum's Disease

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Dercum's disease or adiposis dolorosa is a poorly understood disorder with painful fatty deposits in the skin localized to the lower extremities. The etiology is unknown. In such a patient the mechanisms of local regulation of blood flow in subcutaneous tissue was investigated by the local $^{133}\text{Xenon}$ washout technique. The patient was reinvestigated one week after treatment with intravenous lidocaine. The local vasoconstrictor response to increase in venous transmural pressure was not present in this patient, but reappeared after lidocaine treatment. Autoregulation of blood flow in subcutaneous tissue was present before as well as after lidocaine treatment. It seems likely that a pain elicited increase in sympathetic activity in the vasoconstrictor fibres abolished the normal vasoconstrictor response to increase in venous transmural pressure. The mechanism of pain relief after intravenous lidocaine infusion is uncertain, but central as well as peripheral mechanisms may be considered. (Received November 27, 1985.)

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Adiposis dolorosa or Dercum's disease (1) is a poorly understood disorder with painful circumscribed or diffuse fatty deposits often symmetrically localized to the lower extremities, predominantly in post-menopausal women with generalized obesity. Dercum's disease is rare, the etiology is unknown, and light microscopic examinations of the affected fatty deposits show normal fatty tissue (2, 3). The fatty deposits is localized to the subcutaneous part of the tissue and although vascular defects are not prominent by light microscopy there may be a primary role for abnormal vascular reactions in the pathogenesis of the disease.

Local regulation of blood flow has been intensively explored by Henriksen (4). In patients with generalized scleroderma Henriksen et al. (5) found that in subcutaneous tissue intrinsic vascular reactions responsible for the autoregulatory response was present, whereas the normal "vasoconstrictor response" to an increase in venous transmural pressure was almost abolished.

Treating the pain of Dercum's disease is difficult, but recently intravenous lidocaine has been used as an effective treatment of the severe pain (6, 7). The aim of the present study was to investigate whether mechanisms of local regulation of blood flow in subcutaneous tissue were affected in a patient with Dercum's disease. Furthermore these mechanisms were restudied following intravenous lidocaine infusion given in an attempt to achieve painlessness.

MATERIAL AND METHODS

An 81-year-old woman with painful circumscribed fatty deposits extending from the hips to the ankles was investigated. The patient was normotensive and no other clinical abnormalities were found. All routine laboratory analyses. ECG, chest X-ray and light microscopic examination of the fatty tissue were normal. A diagnosis of Dercum's disease was made. Treatment with acetylates, ketobemidone and sedatives did not keep the patient painless.

Autoregulation and the local veno-arteriolar reflex in subcutaneous tissue were investigated as previously described (5). Blood flow in subcutaneous tissue was measured by the local $^{133}\text{Xenon}$

washout technique (4). $^{133}\text{Xenon}$ washout (0.1 ml, 3 mCi/ml) was injected slowly subcutaneously on the dorsal part of the distal arm and leg. The patient was placed in supine position and a single investigation consisted of three periods of measurement of blood flow: 1) with the labelled area of the forearm and leg at reference level, jugular notch ($f_{\text{ref.}}$), with the hand or leg lowered 40 cm or elevated 20 cm (f_{test}) and finally 3) with the labelled area placed again at reference level. Each period of measurement lasted 6–8 min. Relative blood flow ($f_{\text{test}}/\bar{f}_{\text{ref}}$) and relative vascular resistance ($R_{\text{test}}/\bar{R}_{\text{ref}}$) was calculated from the washout rate constants, and the estimated arterial and venous blood pressures as previously described (4).

In an attempt to achieve painlessness an intravenous infusion of 200 mg lidocaine in isotone glucose was given over a 30-min period. At the end of infusion the pain had completely disappeared, and the pain-relieving effect lasted 28 days. The local regulation of the subcutaneous blood flow was investigated in the same tissue area immediately before and one week after lidocaine infusion.

Moreover the subcutaneous blood flow was determined with the person in horizontal position before and during lidocaine infusion.

In an attempt to elucidate ultrastructural abnormalities in the subcutaneous fatty tissue and vessels, biopsies from the same fatty deposits were investigated with electron microscopy before and one week after the lidocaine infusion.

During a follow-up period of 7 months the patient was treated with several infusions of both isotone glucose and lidocaine. There was no effect of glucose, but sufficient pain-relief was obtained for about 25 days after lidocaine infusion.

RESULTS

Preinfusion

When the labelled area was elevated 20 cm, blood flow remained almost constant in the distal arm ($f_{\text{test}}/\bar{f}_{\text{ref.}}=1.00$, $R_{\text{test}}/\bar{R}_{\text{ref.}}=0.99$) as well as in the distal leg ($f_{\text{test}}/\bar{f}_{\text{ref.}}=0.98$, $R_{\text{test}}/\bar{R}_{\text{ref.}}=1.02$). When the labelled area of the arm was lowered by 40 cm, corresponding to an increase in vascular pressure about 30 mmHg, blood flow remained nearly unchanged in the arm ($f_{\text{test}}/\bar{f}_{\text{ref.}}=0.92$, $R_{\text{test}}/\bar{R}_{\text{ref.}}=0.96$) as well as the distal leg ($f_{\text{test}}/\bar{f}_{\text{ref.}}=0.99$, $R_{\text{test}}/\bar{R}_{\text{ref.}}=0.98$).

Per- and postinfusion

During lidocaine infusion subcutaneous blood flow in the arm increased by 31% corresponding to a decrease in the vascular resistance of 16%. In the affected tissue on the leg, blood flow increased by 25% corresponding to a decrease in vascular resistance of 21%.

When the above mentioned procedures were repeated one week later blood flow remained constant during arm elevation ($f_{\text{test}}/\bar{f}_{\text{ref.}}=0.97$, $R_{\text{test}}/\bar{R}_{\text{ref.}}=1.06$). However, when the arm and leg were lowered 40 cm, a "vasoconstrictor response" to increase in venous transmural pressure could be demonstrated in the arm ($f_{\text{test}}/\bar{f}_{\text{ref.}}=0.60$, $R_{\text{test}}/\bar{R}_{\text{ref.}}=1.56$) and in the leg ($f_{\text{test}}/\bar{f}_{\text{ref.}}=0.61$, $R_{\text{test}}/\bar{R}_{\text{ref.}}=1.58$).

Electron microscopic examination of the affected tissue showed completely normal fatty tissues and vessels before and after the infusion of lidocaine.

DISCUSSION

In the present study with the patient untreated, blood flow remained constant during elevation of the labelled area both in the arm and the leg, indicating that intrinsic mechanisms responsible for autoregulation of blood flow were intact. There was no vasoconstrictor response to arm and leg lowering, indicating that the sympathetic-mediated local veno-arteriolar reflex was absent. This is in agreement with the findings in situations with increased sympathetic activity, i.e. in patients with acute myocardial infarction (8) or in normals subjected to lower body negative pressure (9). The loss of vasoconstrictor response to venous distension in patients with generalized scleroderma may be due to changes in reactivity of the smooth muscle cells in the arterioles (5).

Lidocaine infusion produced an immediate increase in blood flow in the examined extremities corresponding to a marked decrease in vascular resistance. This might be ascribed to a reduction in local or central sympathetic vasoconstrictor tone, which may be elicited by receptor blockade in the central nervous system as the patient was without pain during the investigations. As the vasoconstrictor response normalized in both extremities following lidocaine infusion this ruled out structural changes in the arterioles or any abolition of the vasoconstrictor fibres (sympathetic neuropathy) playing any role. The normal autoregulation of the blood flow also ruled out autoregulatory escape following prolonged neurogenically mediated vasoconstriction (10).

In the above mentioned study Skagen et al. (8) found, that in patients with acute myocardial infarction there was an increased sympathetic vasoconstrictor tone in subcutaneous tissue. They also found that the increased rate of discharges in sympathetic fibres abolished the effect of the vasoconstrictor response to increased venous pressure. It is therefore very likely that a similar mechanism was acting in our patient before the lidocaine infusion, i.e. a probably pain-elicited increased sympathetic activity in the vasoconstrictor fibres abolished the normal veno-arteriolar reflex. The mechanism of the pain relief after intravenous lidocaine infusion is uncertain but central or peripheral mechanisms may be considered. Atkinson (7) suggested that the pain relief after intravenous lidocaine in Dercum's disease was due to a central mechanism, may be alteration of local concentrations of endorphines in the central nervous system, but future studies are needed to reveal the exact site of action of intravenous lidocaine.

The etiology of this painful disease is still unknown and there is no explanation of the development of the fatty deposits or the severe pain.

The normal light- and electron microscopic examinations and the investigations of the local blood flow regulation suggest a normal peripheral nerve function. Therefore a central mechanism seems to be the most likely explanation of the chronic pain in Dercum's disease. From the results of our study and from the literature it seems reasonable to try intravenous lidocaine as pain-relieving treatment in Dercum's disease, especially as no traditional analgesic treatment is effective.

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