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## Review Article

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### Adiposis Dolorosa – A Scientific Review

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#### ABSTRACT

Adiposis dolorosa was described by American neurologist Francis Xavier Dercum in 1892, adiposis dolorosa is a relatively unknown condition characterized by great and localized adiposity with pain, deposition of subcutaneous fatty tissue may occur in many parts of the body by applying pressure to the nerves and mental phenomena including emotional instability. Middle-aged females are more affected in menopausal age. In some cases women of 67-years old are prone to the Dercum's disease after the intake of tocilizumab, an anti-interleukin-6 reported monoclonal antibody to treat rheumatoid arthritis. In some case reports demonstrate successful symptomatic treatment of the patient by lidocaine of 5mg/kg body weight by the intravenous infusion to relieve the pain lasting several weeks or even months. These fatty tissue deposits had shown significant reduction of pain on surgical excision or liposuction. The upper arms, elbows, stomach wall, thigh, or knees are the most commonly affected parts by Dercum disease.

**Keywords:** Dercum's disease, adiposis dolorosa, obesity, chronic pain

#### ARTICLE INFO

##### CONTENTS

1. Introduction . . . . .	35
2. Pathophysiology. . . . .	36
3. Treatment. . . . .	36
4. Conclusion . . . . .	37
5. References . . . . .	38

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### 1. Introduction

Dercum disease is also known as adipose tissue rheumatism. It is a rare disease characterized by the great and localized adiposity with tenderness to pressure over the fat pads. Pathologically the disease can be characterized by changes in the endocrine organs such as sclerosis, International Journal of Pharmacy and Natural Medicines

hypertrophy. The lipomas mainly occur on the upper arms, upper legs, and trunk. Adiposis dolorosa, first described by Dercum, is characterized by the following syndrome:

- Great and localized adiposity with pressure over the fat pads

- Fatigability or marked asthenia,
- Epilepti form seizures and psychoses;
- Ulcers on the extremities,

Decreased metabolic rate and tendency towards hemorrhage may also present in the subnormal temperature, by the changes in the endocrine organs such as sclerosis with atrophy in some instances and hypertrophy is characterized by the disease pathologically. The lesion is very variable, the primary lesion is situated in the hypophysis cerebri. There is no manifestation history of tenderness over the fat masses.

**Synonyms:** Dercum's disease, morbus dercum, adiposis dolorosa, adipose tissue rheumatism, Adiposalgia, lipomatosis dolorosa

#### Signs and symptoms:

Four cardinal symptoms have been used as diagnostic criteria.

- ❖ formation of fatty tumors
- ❖ obesity
- ❖ fatigue and weakness
- ❖ epilepsy
- ❖ depression
- ❖ confusion

The other associated symptoms in dercum disease include fatty deposits, emotional instability, anxiety, rapid heartbeat, fatigue, weakness, joint muscles aches, sleep disturbances

#### Causes:

- Nervous system dysfunction
- Trauma
- Adipose tissue dysfunction
- Mechanical pressure on nerves

#### Diagnosis:

Patient history and physical findings plays a key role in the diagnosis of dercum disease, Ultrasound and magnetic resonance imaging can play a major role in diagnosis. Diagnosis is based on clinical criteria, and it is made by systemic physical examination. Diagnosis is made by physician with broad experience.

#### Genetic Counselling:

In most of the cases, dercum disease occurs sporadically. A→G at position A8344 of mitochondrial DNA cannot be detected in patients with dercum's disease. Any correlation between typical antigens and the presence of the condition has not revealed by HLA (human leukocyte antigen).

#### Epidemiology:

Adiposis dolorosa most commonly appears between age of 35-50 years, women are more prone to dercum disease than man, and the condition mainly affects postmenopausal woman, it is five to thirty times more common in women.

## 2. Pathophysiology

The understanding of the mechanism and pathogenesis of adiposis dolorosa was unknown. The induction of pain is obscure, and the disease is better known as a clinical entity rather than a metabolic and physiologic process. Fatty deposit causes nerve compression and results in weakness and pain. The sudden appearance of the disease is slight

increase in the number of inflammatory cells in the fat is pointed towards the presence of disease. In the origin and further development of pain the sympathetic nervous system may plays a major role. The alterations of fat metabolism induced by corticosteroid excess may play a role in the syndrome development. Dercum disease is an autosomal dominant disease characterized by multiple asymptomatic lipomas. The disease segregates in an autosomal dominant fashion with variable phenotypic expressivity, ranging from totally asymptomatic to extremely painful lipomas suggested in dercum disease. Mutational analysis excluded the 8344A→G mitochondrial mutations are present in other patients with multiple lipomas. The A→G transition at the position 8344 in the tRNA gene of mitochondrial DNA has been described in the syndrome myoclonic epilepsy and ragged-red fibers (MERRF). In some of the patients of pedigrees with MERRF harboring the 8344 tRNA mutation.

#### Images:



Figure 1



Figure 2

#### Diet:

By changing, the diet is difficult to achieve the lasting weight reduction, which doesn't appreciate affect the pain.

## 3. Treatment

Dercum disease has been largely unsatisfactory relying on weight reduction and surgical excision of troublesome lesions of traditional management. Acupuncture, cognitive behavioral therapy, hypnosis, and biofeedback may be used as additional to pharmacologic treatment as non-pharmacological approaches.

#### The pharmacological treatments include the following:

Prednisone 20 mg daily has been reported to provide some relief from pain. However, in some cases, the induction of disease was associated with consumption of high-dose of

corticosteroids. The lipomas are unresponsive to analgesics, and acetaminophen combined with an opioid analgesic is the first choice. Cortisone/anesthetic injection, alternatively with sterile water given intracutaneously or more deeply are used to treat the localized pain sometimes. The analgesic effect of IFN therapy was unexpected and occurred 3 weeks after treatment with 3 million units, 3 times per week, for 6 months. Antiviral effect of mechanism are used to relief pain with IFN, to the production of endogenous substance to the interference of INF with interleukin 1 and tumor necrosis factor –alpha cytokine production, which are involved in cutaneous hyperalgesias, remains unclear.

- a. Daily intake of mexilitine orally, an antiarrhythmic had described pain relief in some case reports.
- b. While on infliximab, with and without methotrexate to ankylose spondylitis reported improvement of a patient's dercum disease. By the discontinuation of these drugs the patient experienced recurrent weight gain and lipoma pain.
- c. Treatment with a lidocaine (5%) patch, reported on successful therapy with pregabalin with manual lymphatic drainage.

In the convincing process, large studies on the treatment of dercum disease have been conducted. The main target towards the treatment of dercum disease is pain relief rather than lipoma removal. Not enough studies have been done to substantiate that diet supplements could help the disease to cure.

**The modalities which include in the treatment methods are following:**

**Traditional analgesics;**

The pain in dercum disease is often reported to be refractory to analgesics and non steroidal anti-inflammatory drugs (NSAIDs). However, this has been contradicted by the findings of Herbst et al. They reported that the pain diminished in 80% of patients (n=89) when treated with NSAIDs and when treated with narcotics analgesics (n=37) 97% of patients are reported.

**Lidocaine:**

Early reports showed that the intralesional injections of procaine (Novocain) relieved pain in few cases from 1934. Different types of local treatment of painful sites with lidocaine patches (5%) (Lidoderm) or lidocaine / prilocaine (25 mg /25 mg) cream (EMLA) have shown a relief of pain in some cases. But the mechanism of reduction of pain by lidocaine in dercum disease is unclear. May be it block impulse conduction in peripheral nerves, and there by disconnect abnormal nervous impulse circuits. Cerebral activity is also depressed that could lead to increased pain thresholds. In some cases the combination of lidocaine and mexilitine (mexitol), also shown reduction of pain because of its similar pharmacological properties as lidocaine. Iwane et al. performed an EEG during the administration of lidocaine by intravenous route. In this report, EEG showed slow waves appearing 7 minutes after the start of the infusion and disappearing within 20 minutes after the completion of the infusion. After the end of infusion pain relief effect is greatest about 20 minutes. Atkinson et al. have suggested that an effect on the central nervous system.

Cerebral metabolism is decreased and also depressed consciousness by the lidocaine. Skagen et al. demonstrated that a patient with dercum's disease lacked the vasoconstrictor response to arm and leg lowering, which indicated that the sympathetic mediated local veno-arteriolar reflex was not present. This could suggest increased sympathetic activity. Some authors suggested that the pain relief was caused by a normalization of up-regulating sympathetic activity. The blood flow in subcutaneous tissue was increased by an infusion of lidocaine and normalized the vasoconstrictor response when the limbs were lowered.

**Methotrexate and infliximab:**

A patient's symptoms are improved by the administration of combination of drugs methotrexate and infliximab. However, in some cases the effect of methotrexate was discrete. To reduce neuropathic pain caused by the peripheral nerve injury in a study of rats methotrexate was used. In case study the mechanism of decrease in microglial activation subsequent to nerve injury. Further studies has shown that the infliximab reduces neuropathic pain in patients with central nervous system sarcoidosis. Tumour necrosis factor inhibition is the mechanism, which is mediated.

**Corticosteroids:**

Treatment with systemic corticosteroids (prednisolone), a few patients noted some improvement in the reduction of pain. Weinberg et al. treated two patients with juxtra-articular dercum's disease with intralesional injections of methylprednisolone (depo-medrol). The patients reported a dramatic improvement. But pain relief ability of corticosteroids is unknown in some cases. One of the mechanism is that they inhibit the effect of substance, such as serotonin, bradykinin, prostaglandins and histamine.

**Interferon -2b:**

To find whether the mechanism could be the antiviral effect of drug by the production of endogenous substances, such as interference with the production of interleukin-1 and tumour necrosis factor. Factors which are involved in cutaneous hyperalgesia are interleukin-1 and tumour necrosis factor.

**Calcium-Channel Modulators:**

Some of the calcium channel modulators have been used; for instance, pregabalin (lyrica) (anticonvulsant) and oxcarbazepine (trileptal) (anticonvulsant). The activation of calcium neuronal channels is inhibited by the calcium channel modulators and they inhibit the release of substances such as excitatory amino acids, which are necessary for central sensitization. These drugs are used to treat neuropathic pain.

**4. Conclusion**

Dercum's disease is a rare condition characterized by painful subcutaneous lipomas, there are three types of dercum disease are; type 1 involves, classically the knees; type 2 is diffuse and generalized; types 3 is nodular, which causes intense pain. The presence of pain which is required for diagnosis; is most commonly described as a burning or aching sensation. There are some additional symptoms to pain are; weakness; confusion; depression; dementia. It

might be an autosomal dominant disorder with variable expression; dercum disease is suspected if patient has the multiple painful nodules; in subcutaneous tissue. Due to overlapping symptoms; it occurs in male even those who have normal BML (Body Mass Index). It is important to have a multidisciplinary approach encompassing medication; surgery; and mental health.

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