

## **Case report: Evolution of lipedema during pregnancy**

### **Abstract**

Lipedema is a syndrome of subcutaneous deposition of fat in the buttocks and lower extremities in combination with leg edema (1). The prevalence of lipedema is 8-18% in women with enlargement of the lower limb (4, 5, 6). The diagnosis can be made from a thorough examination of the patient's medical history as well as a clinical examination (1). Mostly the lower limbs are affected and the edema typically stops above the ankles (9). The exact pathophysiology is still hypothetical (13-16). The disease cannot be cured but different therapeutical options are proposed, such as medication, kinesitherapy, psychological support and surgery (18-19).

We present a 34-year-old woman who suffers from lipedema since the age of 14. In the first trimester, the lipedema was stable. In the second trimester, subjective symptoms like itching started. In the last trimester, the pain increased and an evolution of the lipedema was observed and measured. The right leg gained 16.4% and the left leg 19.9% of the original contour. Six weeks post partum, there was an overall mild decrease of the circumferences. The most manifest decrease was seen in the upper arms (20%).

This is, to our knowledge, the first publication on the evolution of lipedema during pregnancy. We observed a global increase in lipedema during pregnancy, with measurements higher at the postnatal consultation than at the first prenatal visit. More cases are required to formulate a definite conclusion of what the effect of pregnancy on lipedema is, as well as on what the appropriate prevention and/or treatment should be.

### **Introduction**

Lipedema is a syndrome of subcutaneous deposition of fat in the buttocks and lower extremities in combination with leg edema. It was described for the first time in 1940 by Allen and Hines (1). It belongs to a group of conditions termed "disproportional fatty deposits", such as lipodystrophies, multiple symmetric lipomatosis and dercum's disease (2). The exact etiology of the disease is unknown. Lipedema most commonly manifests during menarche, pregnancy or menopause and affects almost only women (3,4). The prevalence of lipedema is 8-18% in women with enlargement of the lower limb (4, 5, 6). In a research of Child et al., the disease started in 55% of the cases during puberty (7). The prevalence in childhood is 6.5 % (8). In the male population only a few cases have been reported, all in men with liver dysfunction or hormonal deficiencies (7).

### **Diagnosis**

Diagnosis can be made by a thorough investigation of the patient's medical history as well as a clinical examination. The main symptoms are tender or painful legs that bruise easily (Table 1). Lipedema is

typically bilateral and symmetric. The disease affects mostly the lower limb, but fat deposits in the upper extremities have also been reported (3). The edema stops abruptly above the ankles and wrists leaving the hands and feet unaffected. The edema is usually non-pitting. One of the first signs is the disappearance of the retromalleolar sulcus at the ankle (9).

### **Diagnostic criteria of lipedema**

1. Lipedema merely affects women with the diagnosis made by the third decade of life
2. Bilateral and symmetrical fat deposits develop downward from the hips, while the feet are usually spared
3. Non-pitting edema
4. Affected subcutaneous regions are tender, painful and characterized by bruising easily
5. Resistance to diet and elevation of the extremities
6. Increased vascular fragility

Table 1. Six criteria suggested to make the diagnose of lipedema (1).

The diagnostic difficulty lies in the overlap and concomitant occurrence with other diseases. It is often associated with chronic venous and lymphatic insufficiency, early degenerative articular disease and obesity (10). Lipedema evolves in a small percentage of patients into secondary lymphatic dysfunction, called lipolymphedema (3). In lipedema, the swelling is not reduced by elevation, differentiating it from lymphedema and lipolymphedema. The disease is refractory to diet. Half of the people are obese, but the upper body can have a 'normal size' (3). Diagnostic imaging is not indicated. (4). An MRI, if used, is most relevant. On an MRI, an increase in the subcutaneous fatty tissue layer can be seen and the skin may or may not be thickened (11).

In many women, lipedema will remain relatively stable, but in a proportion of patients a gradual progression is observed, and in some, an abrupt development of the condition and/or evolution to lipolymphedema can occur. It is thought that exacerbation can be caused by pregnancy or trauma, including surgery, similar to the triggers for primary lymphedema (4,12).

### **Pathophysiology**

The pathophysiology is still unclear. There is no evidence-based theory, but several hypotheses have been made:

- Hormonal: estrogen may directly regulate body lipogenesis and lipolysis (13).
- Genetic: in 10-60% of patients, an inheritance is suspected, probably polygenetic (7, 14-16).

- Neurological: abnormal innervation can lead to increased adipocyte tissue (17).
- Lymphatic: lymphatic leaks and loss in skin elasticity can lead to secondary changes in blood and lymphatic (micro)circulation (4,17).

### **Treatment**

There is no cure, nor is there a standard symptomatic treatment for lipedema. Different therapeutical options are proposed, such as medication, kinesitherapy, psychological support and surgery.

Medical options are beta-adrenergic agonists, glucocorticoids, cimetidine and beta glucan. The working mechanisms of these therapies are unclear, the efficiency is limited. Beta-adrenergic medication and glucocorticoids have a positive influence on the non-pitting edema. Cimetidine can alleviate pain and beta glucan increases the local immune response (18-19).

People can benefit from wearing compression stockings, especially when they have lipolymphedema. Compression or complex decongestive therapy (CDT) is considered the standard therapy for lipedema and is a combination of manual lymphdrainage and compression therapy (20-21). If lipedema is present without edema, compression therapy will not result in volume decrease. However, the therapy is not tolerated by all patients due to the pain (22).

Clinical evidence for all therapeutic options is low and the main treatment purpose is stabilization of the disease and avoidance of complications. Since obesity often accompanies lipedema, a good diet and lifestyle is important. The prognosis is positively influenced when therapy is started before the age of 35 (4).

### **Quality of life**

A significant impact is seen on the quality of life. Not only are there physical complaints, the emotional impact and low self-esteem that are associated with the disease are significant (4).

### **Case report**

We present a 34-year-old woman with lipedema, G0, who wants to become pregnant. Her complaints started in puberty (age 14) but the diagnosis was made 16 years later in 2012 after uncountable doctor visits. Since her diagnosis, she wears compression stockings, has a healthy and active lifestyle and gets manual lymph drainage therapy. Her BMI is 32. Before the correct diagnosis was made, she underwent an operation placing bilateral lymphovenous shunts, with no clinical benefit.

During her preconceptional visit, she asked how her lipedema would evolve during pregnancy. Since literature on lipedema in pregnancy is scarce, a clear answer could not be provided.

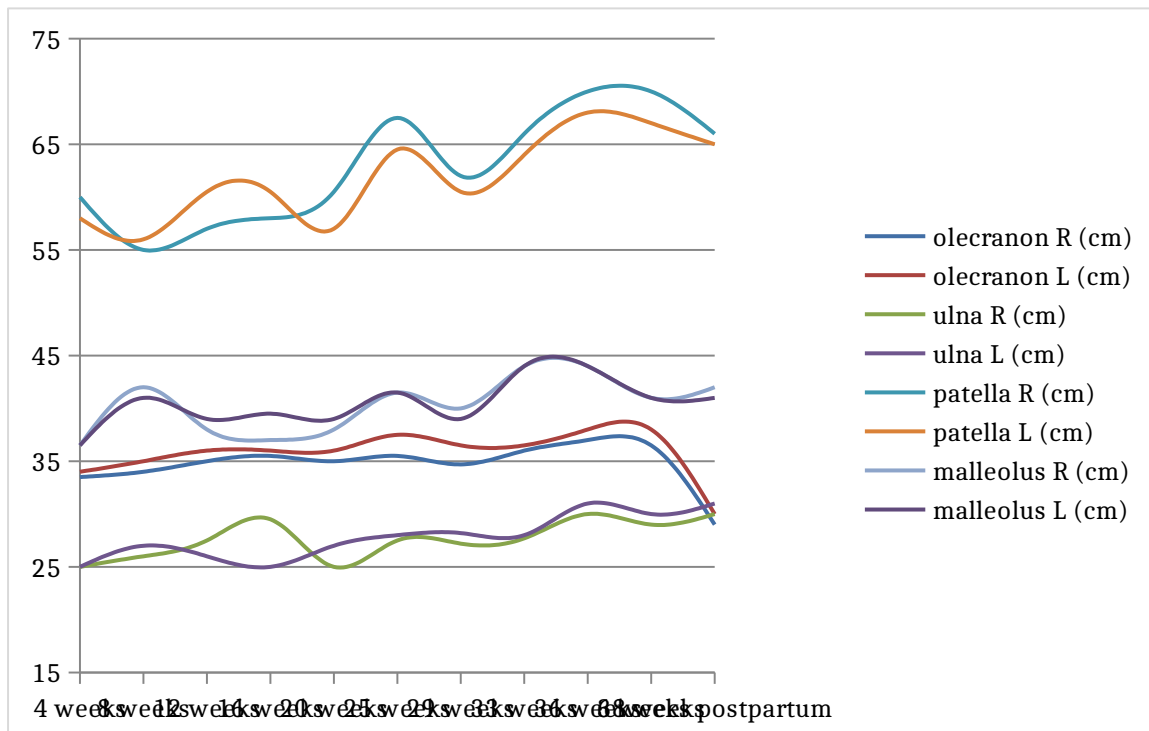
Her first prenatal consultation was at 4 weeks of pregnancy. It was discussed that she would continue her regular treatment of compression therapy, healthy lifestyle and lymph drainage therapy. Due to the knowledge gap on lipedema in pregnancy, it was decided to measure the circumferences of her arms and legs and monitor symptoms at each prenatal consultation. A standardized procedure for measuring was used, measuring 10 cm above the olecranon and the ulna for the upper limbs and 10 cm above the patella and malleolus bilateral for the lower limbs (Table 2).

Duration of pregnancy	olecranon R (cm)	olecranon L (cm)	p.s. ulnae R (cm)	p. s. ulnae L (cm)	patella R (cm)	patella L (cm)	malleolus R (cm)	malleolus L (cm)
4 weeks +3 days	33,5	34	25	25	60	58	36,5	36,5
7 weeks +6 days	34	35	26	27	55	56	42	41
12 weeks +2 days	35	36	27,5	26	57	60,5	38	39
16 weeks +2 days	35,5	36	29,5	25	58	60,5	37	39,5
20 weeks +1 day	35	36	25	27	60,5	57	38	39
25 weeks +2 days	35,5	37,5	27,5	28	67,5	64,5	41,5	41,5
29 weeks +2 days	34,7	36,5	27,2	28,2	62	60,5	40	39
33 weeks +2 days	36	36,5	27,7	28	66	64	44	44
35 weeks +6 days	37	38	30	31	70	68	44	44
37 weeks +6 days	36,5	38	29	30	70	67	41	41
6 w post partum	29	30	30	31	66	65	42	41

In the first trimester, the lipedema was stable. The patient had no physical complaints, which was reflected in the stable measurements. In the second trimester, the patient complained of increased itching, mostly in the lower limbs. The patient recognized these complaints as symptoms that precede the aggravation of lipedema. She stopped wearing the stockings because they became too small and switched to support-giving leggings. At 25 weeks of pregnancy, plaques above the patellae were observed during clinical examination. This corresponded to the location of the previous intense itching. The measurements nevertheless remained broadly stable. At this time, the patient had gained 12 kilos. We assume that the measurements of the ulnae at 20 weeks were incorrect and we took them out of consideration. In the last trimester, the pain increased and an evolution of the lipedema was observed and measured. The most extensive increases in circumference were of the legs (6 cm at the right lower leg (16.4 %) and 7 cm (19.9%) at the left lower leg since the beginning of the pregnancy). In total, the patient gained 22 kilos during her pregnancy.

She delivered vaginally at term. A baby girl was born with a birthweight on the p 80.

Six weeks after delivery, there was an overall mild decrease of the circumferences. The most manifest decrease was seen at the upper arms, a decrease of almost 20% right and left (decrease of 7.5 cm at the right and 8 cm at the left since the delivery).



Graph 1. Four weekly measurements during pregnancy. X-axis: gestational age in weeks, Y-axis: circumference in centimeter.

## Discussion

To our knowledge, this is the first case report that reports on the evolution of lipedema during pregnancy.

Only 109 articles could be found using the meshterm “Lipedema”. Knowledge on the disease is scarce, even though it is relatively common and severe. This reflects the frustrating search of the patient for a diagnosis and appropriate treatment.

In our case, an increase of upper and lower limb measurements and a postpartum decrease were observed. The increase was most prominent in the third trimester. This supports the hypothesis that estrogen plays a role in the pathophysiology, as estrogen levels are increasing in the third trimester. Estrogen regulates bone morphogenetic protein-2 (BMP-2). This protein is known to cause an inflammatory reaction with edema (23). It also stimulates adipogenesis (24) and induces osteogenesis (25). The findings at the lower limbs six weeks postpartum are worrying. There is no obvious decrease in circumferences and it is known that gaining weight can affect the prognosis of lipedema due to augmentation of adipose tissue.

When interpreting these measurements, it is important to keep the following limitations and possible confounders in mind. First, different midwives did the measurements. Nevertheless, they were on a standardized location and surveilled by the patient. Second, the patient could not tolerate her

compression stockings during her pregnancy. Not wearing them can have negatively influenced the lipedema. Due to the elevated pressure in the lower venous system during pregnancy, fluid accumulation is frequently and progressively seen in healthy pregnant women. Edema in the upper limb is also frequently reported in pregnancy. Meems published a prospective study where 34% of healthy pregnant women had carpal tunnel symptoms (26). Therefore, part of the increase in measurements could also be due to lymphedema. Third, the patient gained 22 kilos during pregnancy, which is more than the recommended weight gain during pregnancy. In 2009, the Institute of Medicine formulated the recommended weight gain based on body mass index. When the BMI is above 30, the weight gain should be limited to 5-9kg (Thira Samura). It is impossible to differentiate between weight gain due to fat increase, lipedema or lymphedema. Lastly, lipedema normally presents as a symmetrical disease. In our patient, a right left difference in the forearm was seen, starting at 25 weeks of pregnancy. This difference cannot be explained, except for a possible error in measurement.

### **Conclusion**

Although lipedema is a common disease, it is underdiagnosed and frequently confused with obesity. The accuracy of the diagnosis is important for the patient in order to avoid pointless therapies and to provide the right treatment, which can affect the prognosis. To our knowledge, this is the first publication on the evolution of lipedema during pregnancy. A global increase in lipedema during pregnancy was observed, with measurements higher at the postnatal consultation than on the first prenatal visit (except for the upper arm circumference). More case studies are required to formulate a definite conclusion of what the effect of pregnancy on lipedema is, as well as more research on what the appropriate prevention and/or treatment should be.

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