

# Multiple lipomatosis after stem cell trasplant and chemotherapy: a case report

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**Abstract. – BACKGROUND:** Lipomas are the most common type of soft tissue benign tumor. They can be either isolated entities or involved in a multiple lipomatosis, which may have a familial basis or be an acquired condition.

**AIM:** Chemotherapy and/or blood stem cell transplantation may be plausible causes of multiple lipomatosis.

**MATERIALS AND METHODS:** A 28 year-old patient was diagnosed with non-seminomatous germ cell left testicular cancer. The patient was addressed to chemotherapy and peripheral blood stem cell chemomobilization. After stem cells collection, the patient underwent autologous peripheral blood stem cell transplant.

**RESULTS:** A subsequent *de novo* multiple lipomatosis onset developed.

**CONCLUSIONS:** Although this is a preliminary study and further elaborations are needed, dermatologists and surgeons facing with multiple lipomatosis should consider previous chemotherapy and peripheral blood stem cell mobilization/transplant as possible causes of its onset.

*Key Words:*

Lipomatosis, Chemotherapy, Blood stem cell.

with partial remission. Subsequently he received peripheral blood stem cell chemomobilization with carboplatin, etoposide and Granulocyte Colony-Stimulating Factor (G-CSF). Three cycles of TIP (paclitaxel/ifosfamide/cisplatin) followed. After stem cells collection, the patient underwent autologous peripheral blood stem cell transplant. His chemotherapy was completed in 2010. The lipomas had developed *de novo* in 2011.

He was followed up with clinical assessment, full blood count, liver and renal function tests, electrolytes, tumor markers levels and total body-CT scan. He had no recurrence on follow-up. He had no significant medical history. He was a non-diabetic, non-smoker and non-alcohol consumer. He had neither family history of testicular cancer nor of lipomas.

At our Centre, thirty-two encapsulated lipomas were enucleated completely under general anaesthesia (Figure 1). The histology showed mature lobulated adipose tissue (lipoma), occasionally with many small blood vessels containing fibrin, compatible with an angioliipoma.

## Introduction

A 28 year-old man presented to the Plastic Surgery Outpatient Clinic with multiple, subcutaneous, soft, and mobile lesions on his trunk, back, upper and lower limbs. They were of various dimensions and were clinically consistent with lipomas. They had recently increased in size and become unpleasant and annoying. He was diagnosed in 2009 following a left supraclavicular lymph node biopsy with non-seminomatous germ cell (embryonal carcinoma with areas of choriocarcinoma) left testicular cancer (stage III C). The patient was addressed to chemotherapy comprising standard PEB scheme (cisplatinum/etoposide/bleomycin) for 3 cycles

## Discussion

Lipomas are the most common type of soft tissue benign tumor, with a prevalence of 2.1 per 1000 people<sup>1</sup>. They are an example of fat accumulation, encapsulated or not. When in association with vascular proliferations of capillary size they are called angioliipomas. They often occur in young adults and have a predilection for the subcutaneous fat of the upper limbs and, less commonly, the trunk.

Lipomas and angioliipomas can be either isolated entities or involved in a multiple lipomatosis, which may have a familial basis or be an acquired condition.



**Figure 1.** Thirty-two lipomas/angioliipomas were enucleated under general anesthesia.

Lipomatosis is most often associated with specific congenital, familial, or idiopathic syndromes. In the Familial Multiple Lipomatosis (FML)<sup>2</sup>, lipomas are usually painless and a dominant autosomal route of inheritance is usually observed. Unlike lipomas, lipomatous tissue in this syndrome is non-encapsulated, with the ability to infiltrate spaces between adjacent subcutaneous and muscular structures. The lipomatous tissue is characterized by normal-sized or smaller than expected fat cells.

Conversely, a commonly reported cause of acquired lipomatosis is the Launois-Bensaude syndrome or Madelung's disease. It can also be known as benign symmetrical lipomatosis or multiple symmetrical lipomatosis. It is typically characterized by massive symmetrical fat deposits located mainly in the neck and shoulder region. The majority of cases are sporadic. Ninety percent of the cases are associated with alcoholism. The disease also occurs in patients who do not drink alcohol and but have metabolic disorders (hyperuricaemia, hyperlipidaemia, hyperlipoproteinaemia and diabetes mellitus).

As a result, the case herein described has not any of the aforementioned aetiologies. In fact, it is likely an acquired condition induced by some exogenous factors stimulating fat development and subcutaneous accumulation.

Although a clear aetiology has never been defined, in our case three possible causes have been hypothesized: stem cell mobilization or transplant and chemotherapy.

As far as stem cell mobilization and transplant are concerned, no data about adipose cell proliferation as a renowned side-effect are reported in the literature. However, it would be intriguing to demonstrate that the agents used for chemomobi-

lization may induce a proliferation involving adipocytes besides blood cells. In fact, it is well-known the exciting action mediated by Macrophage Colony-Stimulating Factor (MCSF) on the adipocytes<sup>3</sup>, whereas nothing regarding G-CSF has been documented. Nevertheless, a recent study by Skurk et al<sup>4</sup> referred an increased release of G-CSF in association with the augmentation of cultured adipocyte sizes, suggesting a correlation.

Furthermore, it should be studied if peripheral blood stem cell injection as in transplants may stimulate adipose tissue hyperplasia. After the infusion, the collected stem cells locate in bone marrow and proliferate. No influences on other kind of cells have ever been noted before. Furthermore, adipocytes differentiation should be mediated by factors which are not conventionally administered during the mobilization.

However, it has been demonstrated in mice that adipose tissue is an effective and reliable reservoir for hematopoietic stem and progenitor cells (HSPCs)<sup>5</sup>. In fact, adipose tissue is composed of lipid-filled mature adipocytes and other nonadipocyte cells, the stromal vascular fraction (SVF) containing a heterogeneous population of cells with a potential to differentiate into several lineages. In particular, after G-CSF injection, an increase of HSPCs in the SVF followed the augmentation of HPSCs from the bone marrow, suggesting a strict relation with adipose tissue.

Increased cell release from the bone marrow reservoir is part of the immune system host defence during inflammation as a result of infection- or injury mediated release of stress signals. This release is induced clinically by chemotherapy and G-CSF.

Cisplatin-based chemotherapy has been associated with several long-term complications<sup>6</sup>: renal toxicity, vascular toxicity (Raynaud's phenomenon), neurotoxicity (especially the sensory fibers), pulmonary toxicity (pneumonitis) and secondary malignancies. However, multiple subcutaneous lipomatosis induced by this treatment has never been reported before.

Cronin et al<sup>2</sup> recently reported the first case of multiple lipomas onset coinciding with chemotherapy. However, differently from ours, the patient had followed a cytotoxic treatment based on the MOPP scheme (mechlorethamine, vincristine, procarbazine and prednisolone), which involves steroids. Treatment with corticosteroids, as well as the use of anti-HIV drugs, has already demonstrated to be responsible for fat development<sup>7</sup> either subcutaneously or not.

Some Authors indicated anticancer drugs like bortezomib as lipomatosis inducers<sup>8</sup>. Anyway, in the case mentioned, it may have been underestimated the role of dexamethasone combined with bortezomib in the treatment of myeloma. Cases of iatrogenic lipomatosis have been recently described after therapy with Peroxisome proliferator-activated receptor (PPAR) gamma agonists<sup>9</sup>, drugs (rosiglitazone, pioglitazone) used in the treatment of type 2 diabetes mellitus. In fact, they promote fatty acid uptake and storage in subcutaneous adipose tissue, increase adipocyte proliferation, and redistribute adipose tissue from visceral to subcutaneous fat.

Despite an unknown underlying mechanism, the cisplatin-based chemotherapy may appear the major contributor. Cisplatin has an alkylating-like action, binding DNA and eliciting apoptosis. Although the proliferation of fat cells induced by an antimitotic drug may appear paradoxical, it is important to note the body changes due to cisplatin. In fact, increased body mass index and metabolic syndrome are possible consequences, which may be related to hormonal changes caused by chemotherapy, such as testosterone deficiency<sup>6</sup>.

### Conclusions

Even though this is a preliminary report and further studies are needed, dermatologists and surgeons facing with multiple lipomatosis should consider previous chemotherapy and peripheral blood stem cell mobilization/transplant as possible causes of its onset.

### Conflict of Interest

The Authors have not declared any conflicts of interest.

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