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Essay Paper

The Oleaginous Conglomerate-Multiple Symmetric Lipomatosis

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Preface

Multiple symmetric lipomatosis (MSL) is an exceptional disorder of adipose tissue metabolism and lipid storage. The condition was initially scripted by Sir Benjamin Brodie in 1846 and is additionally designated as Madelung's disease, Launois-Bensaude syndrome or benign symmetric lipomatosis [1].

Characteristically, multiple symmetric lipomatosis displays multiple foci of accumulated, non-encapsulated, mature adipose tissue with predominant infiltration within subcutaneous tissue of cephalic, cervical and upper thoracic region. Multiple, non-encapsulated, symmetrically distributed lipomas which spare distal extremities are enunciated in multiple symmetric lipomatosis [1,2].

The condition can be misinterpreted as simple obesity on account of identical clinical features and symptoms. Therefore, antecedent evaluation of pertinent manifestations and differentiation of dual entities is necessitated. The disease is presumed to be a condition diverse from accumulation of brown adipose tissue. Histological structure of constituent adipose tissue cells is dystrophic with characteristics akin to lipoma and liposarcoma. The condition may be associated with significant morbidity, metabolic disturbances, neuropathy, malignant metamorphosis and sudden death [1,2].

Disease characteristics

Launois and Bensaude defined multiple symmetric lipomatosis as a diffuse, multiple lipomatosis symmetrically incriminating the cervical region [3].

Multiple symmetric lipomatosis demonstrates an incidence of 1: 25000 live births. Middle aged individuals between 40 years to 70 years are commonly incriminated. A male predominance is observed with male to female proportion of 30:1. Lesions incriminating the women are common within proximal upper extremities (91%) and lower extremities (54%). An estimated 60% to 90% individuals are heavy consumers of alcohol [4,5].

Multiple symmetric lipomatosis is categorized into four distinct phenotypes contingent to anatomic distribution of adipose tissue:

- Type I typically exhibits a pseudo-athletic appearance with symmetrical adipose tissue distribution within the upper torso.
- Type 2 individuals are obese on account of occurrence of pathological adipose tissue.
- Type 3 depicts a gynaecoid effect upon inferior segments of the body, especially thighs and medial surface of knee.
- Type 4 incriminates the abdominal region [5].

Enzi classified multiple symmetric lipomatosis as:

- Type I or Madelung collar which manifests as a symmetric accumulation of adipose tissue circumscribing nape of the neck, upper dorsal region, shoulders and upper extremities. The condition is predominant in males who represent as pseudo-athletic individuals with massive cutaneous protrusions [4].
- Type II demonstrates an equivalent gender distribution and is associated with diffuse distribution of adipose tissue specifically within the upper dorsal region, upper extremities, deltoid muscle, gluteal region, hips and upper thighs. Subjects represent with generalized obesity [4].

Type I is further subdivided into "horse collar" lipoma and "pseudo-athletic appearance" [4].

Differentiation of metabolic adipose tissue from accumulated brown fat may be challenging. However, brown fat configured within multiple symmetric lipomatosis is functionally defective [5].

Disease pathogenesis

Of obscure genesis, multiple symmetric lipomatosis is closely associated with alcohol abuse. Therefore, although posited to be engendered with ethanol ingestion, underlying aetiology of multiple symmetric lipomatosis remains unclear [5,6].

Of obscure rationale, subjects within certain geographic zones as the Mediterranean region are commonly implicated whereas the disease is infrequent in female subjects of Asian origin [5].

The condition is associated with overconsumption of alcohol. Clear cut mechanics of alcohol consumption concurrent with localized accumulation of mature adipose tissue remains obscure. Consumption of alcohol deranges adrenergic lipolysis by implicating mitochondrial enzymatic processes. Alcohol consumption appears to be a cofactor which induces modifications within the quantification and function of beta adrenergic receptors and possibly engenders uncontrolled accumulation of adipose tissue [5,6].

Approximately 60% to 90% of individuals manifest chronic alcoholism. Alcohol consumption contributes to adipocyte hyperplasia in concurrence with lipogenesis, anti-lipolysis, decimated lipid oxidation and mitochondrial metabolism [5,6].

Subjects denominate a disorderly differentiation of adipocytes. However, associated hypercholesteremia, diabetes mellitus, thyroid dysfunction, renal and hepatic disease may or may not engender the morphological modification. Although exact metabolic mechanism of disorderly adipocytic differentiation is incompletely elucidated, adipocytes of multiple symmetric lipomatosis are diverse from mature adipose tissue cells demonstrating normal cellular proliferation, hormonal regulation and mitochondrial activity. It is posited that pathological adipocytes are concurrent to decimated β- oxidation and lipolysis within the mitochondria [5,6].

Malfunction of lipid metabolism is observed. A significantly enhanced activity of lipoprotein lipase within the adipose tissue, plasma hyper-alpha-lipoproteinaemia along with a particular defect within adrenergic- stimulated lipolysis occurring within the lipomatous tissue is observed. Berkovic., *et al*. proposed a theory of deterioration of mitochondrial deoxyribonucleic acid (DNA) which suggests that mitochondrial dysfunction may repress the lipolytic pathway [5,6].

Clinical elucidation

Multiple symmetric lipomatosis demonstrates a symmetric accumulation of adipose tissue appearing as a palpable tumefaction within subcutaneous tissue of the face, neck, shoulder, trunk, upper extremities, upper dorsal region, tongue and occiput. Cogent clinical symptoms are cosmetic deformities, restricted neck mobility, compression of trachea or oesophagus and an infrequent infiltration of laryngeal tissues with associated dyspnoea, dysphagia or dysphonia. Surgical intervention is adopted in roughly 40% instances of exceptionally infiltrated larynx [5,6].

Multiple symmetric lipomatosis is associated with a typical physical appearance which can be established by physical examination. Majority of instances depict a singular cosmetic deformity. Additionally, dysphonia, dysphagia or dyspnoea may arise due to direct compression of soft tissue or the infrequently infiltrated larynx [5,6].

On examination, massive enlargement of the neck or incriminated sites is observed although palpable, tender tumefaction may be absent. Lipomatous lesions may be situated upon superficial soft tissues and cartilage with extension into adjacent crevices [6,7].

Schiltz., *et al*. divided multiple symmetric lipomatosis into three distinct subcategories contingent to morphological features of implicated sites. Precise direction of adipose tissue dissemination remains obscure. Frequently, the disorder is associated with lipomas circumscribing the neck. Pertaining to tumour localization, the condition is denominated as "horse collar" of the cervical vertebra, a "buffalo hump" of the posterior neck or a "hamster cheek" abutting the parotid region [6,7].

The condition is associated is specific features of combined motor, sensory or autonomic neuropathy and myopathy. The disease is devoid of psychiatric manifestations [6,7].

Histological elucidation

On gross examination, tumefaction appears to incriminate subcutaneous and deep-seated soft tissue. The neoplasm manifests as a diffuse, non-encapsulated adipose tissue aggregate. On microscopy, enlarged, dystrophic adipocytes constitute the neoplasm. Unencapsulated aggregates of mature adipose tissue are discerned. Sarcoma-like alterations are usually absent [6,7].

Histologically, the enlarged, vacuolated adipocytes depict dystrophic morphology, in contrast to normal adipocytes. However, sarcomatous change or occurrence of multiple symmetric lipomatosis associated liposarcoma remains to be ascertained.

Tumefaction may be associated with anomalies of mitochondrial deoxyribonucleic acid (DNA) [7,8].

Investigative assay

On ultrasonography, tumefaction depicts the characteristics of a lipoma [7].

Appropriate investigations as computerized tomography (CT) and magnetic resonance imaging (MRI) can be performed to identify neoplasms circumscribing the trachea or oesophagus which

engender dysphagia or dyspnoea. Multiple lipomas encompassing the neck and shoulder may or may not compress trachea and oesophagus, as denominated by cogent computerized tomography and magnetic resonance imaging [7,8].

Computerized tomography (CT) and magnetic resonance imaging (MRI) can be beneficially adopted to evaluate depth and distribution of tumefaction. Computerized tomography depicts a declining calibre of lumen of trachea or oesophagus. Massive adipose tissue infiltration of soft tissue abutting the incriminated sites is exemplified [7,8].

CT and MRI are beneficial in discerning airway obstruction as engendered with adjunctive diseases and identifying the zone of adipose tissue infiltration for cogent surgical intervention. However, imaging assay may fail to differentiate the condition from diverse malignant disorders [7,8]. Fine needle aspiration cytology (FNAC) is not a recommended diagnostic procedure [8].

Therapeutic options

As lipomas are infiltrative, the condition is associated with enhanced localized reoccurrence, cosmetic deformities and physical discomfort, surgical excision of the tumefaction is an efficacious therapeutic manoeuvre and is performed to obtain symptomatic relief. Also, suction assisted lipectomy is an optimal treatment methodology. Aim of surgical intervention is to decimate the lipomas without complete eradication [9,10].

Tumefaction can be subjected to partial surgical extermination. Additionally, a comprehensive surgical eradication can be adopted. Localized tumour reoccurrence or significant enlargement of remnant tumefaction is absent [9,10].

Surgical manoeuvres such as lumpectomy and exploration of neck may be adopted. Superficial adipose tissue can be excised along with examination of deep-seated structures [9,10].

Manoeuvres such as lipectomy and liposuction may be adopted. Lipectomy is an efficacious, predominantly adopted procedure as it mandates a comprehensive tumour eradication and is associated with minimal possible detriment to adjacent peripheral nerves and vascular articulations. Nevertheless, surgical complications such as postoperative infection, haemorrhage, configuration of a haematoma or a lymphatic fistula may arise [9,10].

Liposuction is an advantageous and preferential modality of cosmetic surgery. Liposuction is a simple, minimally invasive procedure although proportionate localized reoccurrence is significant as a comprehensive eradication of the lipoma may be challenging [9,10].

Therapeutic intervention is usually mandated for superior cosmetic outcomes or to alleviate pertinent symptoms such as dyspnoea or dysphagia occurring secondary to tumefaction associated visceral compression [9,10].

Concurrent reduction or abstinence from alcohol is recommended as it may circumvent tumour progression, localized tumour reoccurrence and reduce the magnitude of adipose tissue aggregates. Lipoma infiltrating the larynx may engender dyspnoea and requires alleviation in order to relieve the dyspnoea [9,10].

Salbutamol ingestion is accompanied by inconsistent outcomes. Dietary restriction of lipids is ineffective. Ingestion of fibrate drugs or intra-lesional injections may be beneficial [9,10].

Somatic neuropathy and sudden death may ensue in multiple symmetric lipomatosis occurring within the mediastinal space with consequent accumulation of adipose tissue. However, proportionate mortality due to multiple symmetric lipomatosis remains inadequately defined although mortality may ensue due to sudden cardiac death, haemorrhagic shock secondary to hepatorenal syndrome and hepatocellular carcinoma. Localized tumour reoccurrence is generally absent [9,10].

Neuropathy is observed in around 85% of lesions. On account of incrimination of central nervous system, monitoring for neurological signs and symptoms is mandated [9,10].

Associated diseases such as alcoholism, hepatic cirrhosis, dyspnoea and neuropathy require evaluation. Excessive and extensive surgical procedure may require circumvention [9,10].

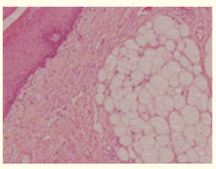

Figure 1: Multiple symmetric lipomatosis composed of aggregates of enlarged, dystrophic adipocytes encompassed by mature fibrous tissue and a superimposed epidermal layer [11].

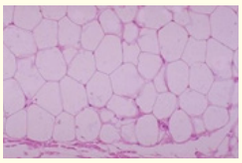

Figure 2: Multiple symmetric lipomatosis comprised of enlarged mature adipose tissue cells subdivided by mature fibrous tissue septa [12].

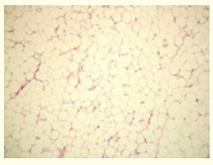

Figure 3: Multiple symmetric lipomatosis demonstrating accumulation of enlarged, dystrophic adipose tissue cells commingled with mature fibrous tissue septa [13].

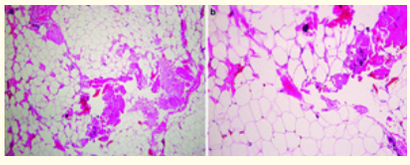

Figure 4: Multiple symmetric lipomatous delineating accumulated, enlarged mature adipose tissue cells entangled with abundant fragments of mature fibrous tissue septa [13].

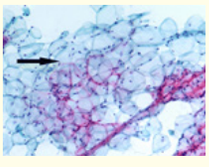

Figure 5: Fine needle aspiration cytology of multiple symmetric lipomatosis delineating aggregates of univacuolar adipose tissue cells with eccentric nuclei and dividing fibrous tissue [13].

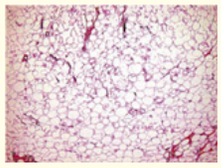

Figure 6: Multiple symmetric lipomatosis demonstrating aggregates of mature adipose tissue cells traversed with mature fibrous tissue septa [14].

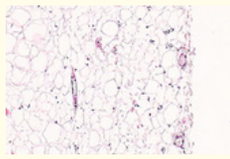

Figure 7: Multiple symmetric lipomatosis exhibiting nests of mature adipose tissue cells with entangled fibrous tissue septa [15].

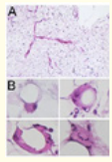

Figure 8: Multiple symmetric lipomatosis depicting yellowish nodules of mature adipose tissue. Aggregates of mature adipose tissue cells are subdivided with fibrous tissue septa [16].

Type	Incriminated zones
Type I - Ia	Neck
Ib	Neck, shoulder girdle, upper arms
Ic	Neck, shoulder girdle, upper arms, chest, abdomen, upper and lower back
Type II	Gluteal region, thighs, upper legs
Type III	General distribution excluding head, forearms, lower legs

Table: Classification of multiple symmetric lipomatosis [5].

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11. Image1 Courtesy: Science Direct.

12. Image 2 Courtesy: Orthobullets.com.

13. Image 3, 4 and 5 Courtesy: Springer Link

14. Image 6 Courtesy: Medical Journals se.

15. Image 7 Courtesy: Libre pathology.

16. Image 8 Courtesy: Diagnostic pathology-Biomed Central.