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Lemierre's Syndrome Masking Metastatic Non- Small Cell Lung Cancer In a Diabetic Female : A case report

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Abstract:- We report a case of **a** 48 years old female with known history of diabetes mellitus for 4 years, presented to ER of Prince Digna Tertiary care teaching hospital in Port Sudan, Eastern Sudan. with sore throat ,mild fever and general body weakness for 3 weeks ,later on she developed painful neck swelling mainly on left site ,SOB, productive cough and anorexia, as well as left arm swelling and pain. OE, there was painful tender swelling on left side of the neck, and left arm Neck doppler US showed Left Internal jugular , Left subclavian and brachiocephalic venous thrombosis),giving characteristic clinical pictures **of** Lemierre syndrome.

Keywords: Lemierre syndrome, *Fusobacterium necrophorum* , suppurative thrombophelebitis, septic emboli.

I. Introduction

Lemierre syndrome is a rare disease. it results from oropharyngeal infections in young, otherwise healthy adults, male to female predominance 2:1 with an incidence rate about 0.8–3.6/million per year[(1)].The oropharyngeal infection (most commonly caused by Fusobacterium necrophorum *and* Fusobacterium nucleatum slow growing ,strictly anerobic, gram-negative pleomorphic bacilli. Fusobacterium necrophorum the most common pathogen ,other pathogens that may be associated with Lemierre syndrome include Streptococci, Klebsiella pneumonia, Bacteroides species, and Staphylococcus aureus, MRSA ,gram negative) .[(2,3)] Infection extended into lateral pharyngeal space of the neck ,or formation of a peritonsiler abscess , abscess wall ruptures internally in an anaerobic growth allow bacteria to invade near tissue and the drainage carrying bacteria find gateway to internal jugular vein ,the inflammation swelling of the area surrounding the vein causes compression of internal jugular vein, this lead to blood clot formation, thrombosis , septic thrombophlebitis, and septic emboli to other organ , lung (most common site and can lead to effusion ,cavitation ,abscess or consolidation) , heart (pericarditis) and joints(abscess,osteomylitis ,arthritis) , brain(cavernous sinus thrombosis ,meningitis , brain abscess) ,also can affect other organs like eyes, liver ,spleen and kidneys and can lead to septicaemia and death.[(4,5)] The characteristic symptoms started initially with non specific symptoms of an acute infection as seen in tonsillitis or pharyngitis, hence the most common symptoms are sore throat, which may be accompanied by fever, as the condition progress to internal jugular vein thrombophlebitis, patient may present with sepsis or septic shock, and unilateral neck pain and tenderness, pleuritic chest pain, Dyspnea , and cough Abdominal pain, Bone or joint pain. Splenomegally,hepato megally or jaundice also may be present[(2,4)]. It is imperative to recognize these symptoms and signs early as a prompt initiation of treatment is crucial in preventing the progression of infection. Sepsis following this throat infection was first described by Hugo Schottmuller in 1918[(3)] , French physician Andre Lemierre who ,in 1936 reported of 20 cases of anaerobic septicemia originating from oropharyngeal infections of whom 18 died[(6)].however there are unusual other form of this disorder have been rarely reported[(7)]. Lemierre syndrome is highly curable if appropriate therapy is administered on timely basis. In the pre antibiotic era, LS was acommon complication of pharyngitis with poor prognosis, resulting in 90-100% mortality[(8,9)].

II. *Case presentation*

Female of 48 years old, diabetic for last 4 years on Glimepiride 3 mg ,presented ER with history of sore throat ,mild fever and general body weakness for 3 weeks ,after 6 days of the beginning of her symptoms patient

sought medical advice at health centre , she was evaluated by a primary physician and prescribed 7 days course of amoxicillin 500mg . but she did not improved ,fever got worse spiked with rigor. Worsening sore throat , fatigue and she started to develop chest pain, mild SOB and increase work of breathing, painful cough productive with brown sputum .Patient went to rural hospital and reported being diagnosed with chest infection, received another course of antibiotics and screening of tuberculosis which was negative , 3 days before the admission , the condition deteriorated, symptoms worsen more and patient developed left sided neck pain and swelling, and left supra clavicular swelling , swelling was painful and associated with left arm swelling and pain ,there was, anorexia and episode of mild abdominal pain with three time of GIT motion, then patient referred to Emergency Department of our hospital .No symptoms of cardiac, OR urinary systems involvement. Patient known diabetic for 4 years on oral hypoglycemic drug. She was otherwise had no past history of neck trauma, neck cannulation ,surgical operation , hypertension or malignancy ,and no history of chronic medication .

III. Examination

At the time of presentation ,the patient looked unwell , tachypnic not jaundice or pale ,HR 108b/min , RR 28cycle/min , Bp 130 /75 ,O2 saturation 88% on room air ,Temp. 38,2 C. No neck stiffness and no focal neurological deficit.

chest:- there is decrease in air entry in left lower chest with dullness on percussion on left lung area, bilateral coarse crackles, no wheezes .

cardiovascular and abdomen and nervous system:- Un remarkable.

Head and Neck:- Non- tender thyroid nodule was felt on left side of the neck. There was diffuse swelling on anterior part of the neck mainly on left side and left supraclavicular region ,swelling was warm and tender with pitting pattern, both carotid and subclavian pulses were felt well, also there was left arm pain and mild pitting edema, with normal distal neurovascular assesment, **Figure (1)**

Mouth:- There is significant for redness of posterior pharynx with mild exudates, swollen both tonsils and tender cervical lymphoadenopathy. **IDL** examination not reveals pharynx or larynx tumour.

Her other examination were normal.

The diagnosis of Lemierre syndrome as most probable diagnosis is based on clinical suspicion of a classical medical history and course of the illness and clinical findings in the examination .



Figure (1) Photo shown swelling in the neck on left side and left supraclavicular region.

IV. Investigation

Diagnosis and investigation studies ordered depend on the patient history, signs and symptoms.
Blood tests showed CRP 250mg/l , ESR 80 ,TWBC was 13,300 mainly neutrophil , PLT 557000 , HB 9.5g/dL , RFT + electrolytes were normal ,LFT was normal ,TFT was normal ,RBG (300mg/dl) ,UG clear
PT 20, INR 1,6 and raised D-dimer. Covid test negative, HIV and sputum for AFB were negative
blood culture detect grew Fuso bacterium necrophorum .
Neck US(Left thyroid lobe showed small solitary solid nodule measured 7.1x10 mm , **Neck Doppler US** Left Internal jugular vein, Left subclavian and brachiocephalic venous thrombosis) **Figure (3)**.
Chest Xray showed bilateral nodular lesions ,left central cavitary lesion with hailer lymphadenopathy as well as left middle and lower zone soft tissue mass. **Figure (2)**
FNAC of thyroid nodule showed benign colloid nodule.
ECG. Echocardiography were clear .

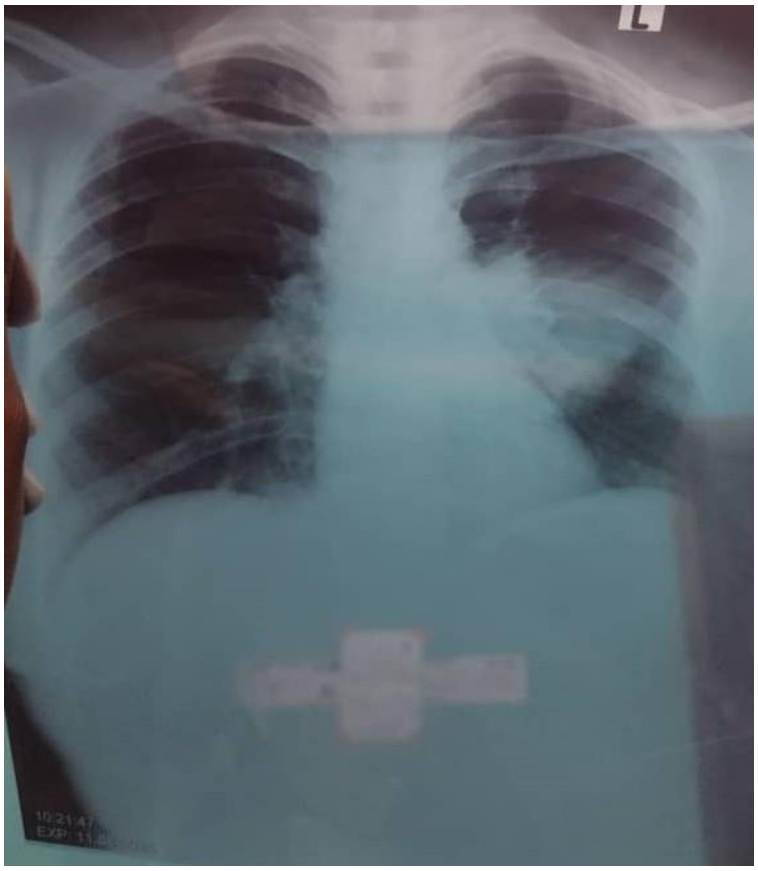


Figure (2) AP chest X-ray demonstrating showed bilateral nodular lesion ,left central cavitary lesion with hailer lymphadenopathy as well as left middle and lower zone soft tissue mass .

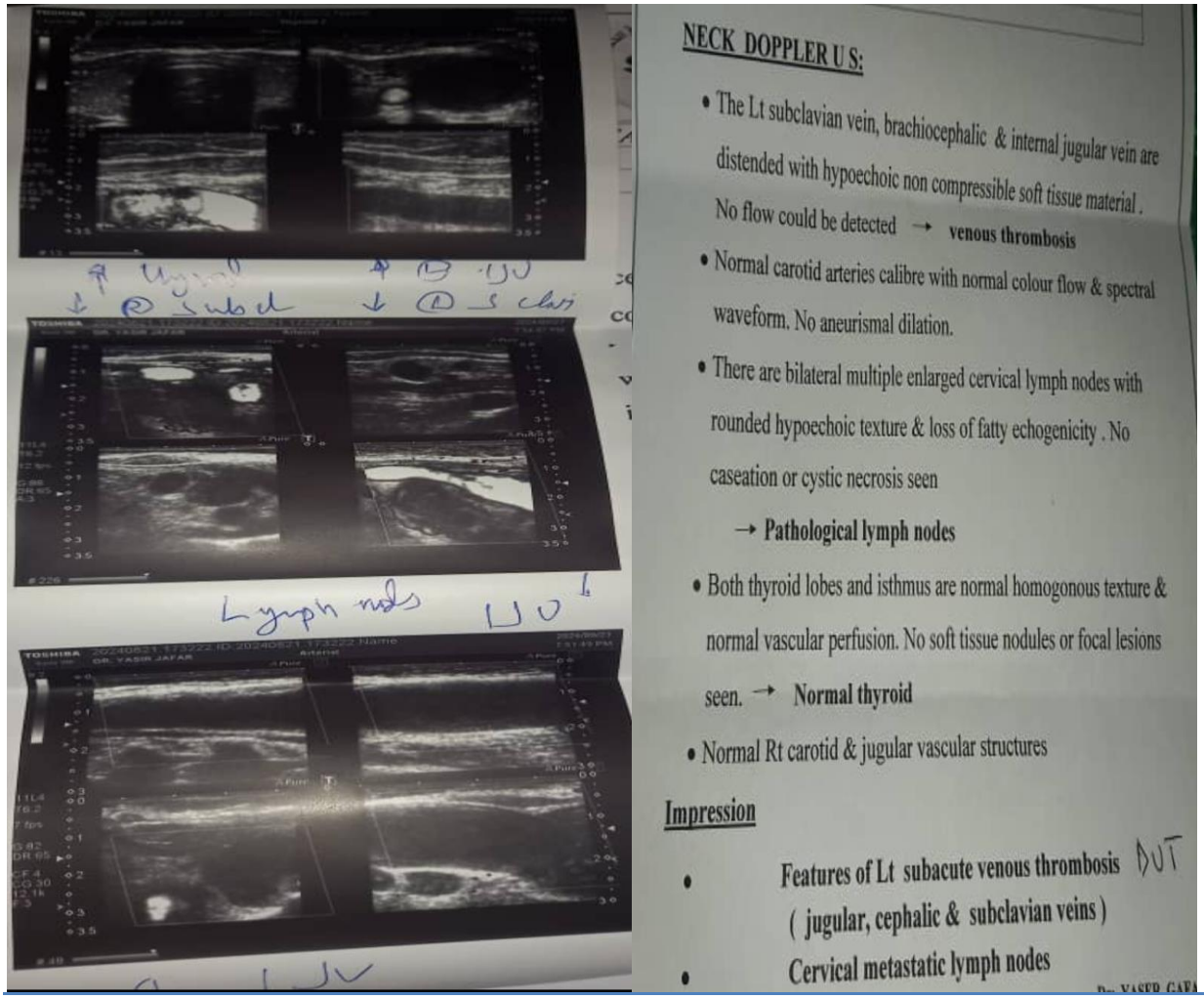


Figure (3) neck Doppler US Left Internal jugular vein, Left subclavian and brachiocephalic venous thrombosis).

High resolution contrast enhanced CT chest shown large lobulated mass occupying most of left lower lobe connected to the hilum , measuring (9,5×6,5 cm) with multiple bilateral lung nodules scattered at both lungs .and multiple mediastinal lymph nodes and minimal left side pleural effusion. with impression of primary left lower lobe bronchogenic carcinoma with lymphatic spread and lymphangitis carcinomatosa and lung metastasis **Figure (4**).

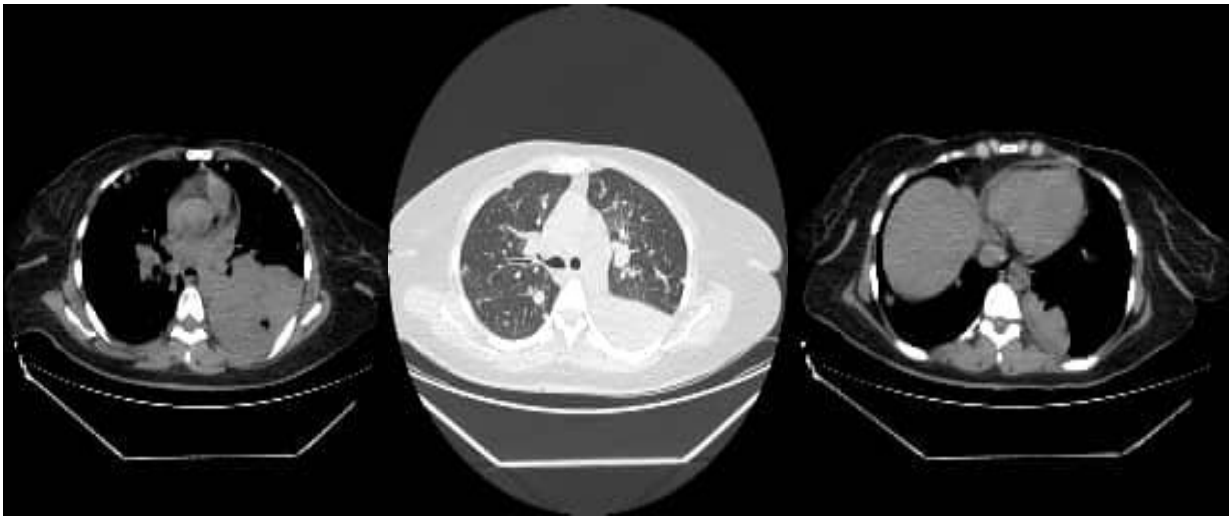


Figure (4) CT chest shown large lobulated mass occupying most of left lower lobe connected to the hilum , impression of primary left lower lobe bronchogenic carcinoma with lymphatic spread and lymphangitis carcinomatosa and lung metastasis.

US guided biopsy of the lung mass revealed features of metastatic non- small cell carcinoma.

From above presentation and investigation, patient diagnosed as Lemierre syndrome

V. Treatment

A high index of suspicious is needed for diagnosis of Lemierre syndrome. Patient admitted in HDU ,on oxygen ,Fixed dose of soluble insulin ,IV fluid . received metronidazole infusion 8/hourly, meropenem injection 1 g Bid ,Ibuprofen infusion 400 mg 6 /hourly ,LMW anticoagulant , We demonstrate our multidisciplinary team discussion involving surgeon, Respiratory Medicine, Diagnostic Radiology, and Medical Oncology, for work-up and subsequent management of this case .Histological analysis of non small cell lung cancer .leading to transition of patient care to the oncology team for further management.

VI. Discussion

Lemierre syndrome was initially described by Andre lemierre in 1936, itis a condition characterized by suppurative thrombophelebitis of internal juguler vein following a recent oropharyngeal infection. with resulting in septicemia and metastatic septic lesion. The diagnosis of Lemierre syndrome is based mainly on classical medical history and course of the illness, microbiological and imaging findings (imaging of the neck with ultrasound ,CT or MRI), the diagnosis is often delayed, probably due in apart of relative rarity**.** This 48 years old patient presented with the following three manifestations: (i) recent pharyngeal disease within 3 weeks, (ii) metastatic septic emboli , and (iii) internal jugular vein thrombosis and detection of *Fusobacterium necrophorum* in the blood culture. The early symptoms was sore throat and mild fever which followed by SOB ,chest pain ,cough ,fatigue ,anorexia and in last days anterior and left lateral neck tender swelling and left upper arm pain and swelling , imaging revealed cavitary lesion in left lung , Left internal jugular vein (IJV), Left subclavian and Brachiocephalic DVT with small thyroid nodule which is giving the idea of A typical presentation of Lemierre syndrome .

The pathogen first invades the lateral pharyngeal tissues and internal cervical vessels, followed by haematogenous dissemination to other organ ,lung was the commonest site of metastatic septic emboli and in this patient we found significant pathological changes in the left lung (cavitary lesion).The time of onset from the initial oropharyngitis to the development of sepsis were three weeks. This patient is diabetic on treatment for last 4 years with poor sugar control, Lemierre Syndrome is rarely associated with diabetes mellitus, but particularly poorly controlled diabetes may increase the risk of severe infections like Lemierre Syndrome .Potentially leading to more severe complication like septic emboli and can associated with diabetes ketoacidosis. In some cases Lemierre Syndrome occurs due to klebsiella pneumonia has been linked to diabetes mellitus and the elderly population[9,10].

FNAC of the solitary thyroid nodule done in this patient to exclude malignant growth . Limierre's syndrome is a disseminated infection , in rare cases , no precipitating oropharyngeal infection is identified, and other head and

neck processes including trauma. Malignancy, and vasculitis may be implicated , and may originate at site of head and neck malignancy like laryngeal carcinoma or papillary thyroid cancer where a loss of mucosal integrity allowed for entry of the pathogen. Thrombogenesis was further promoted by the presence of an active malignancy [11,12]. Subsequent contrast -enhanced CT chest report . shown impression of primary left lower lobe bronchogenic carcinoma with lymphatic spread and lymphangitis carcinomatosa and lung metastasis. and **US** guided biopsy of the lung mass revealed features of metastatic non small cell carcinoma. Lemierre Syndrome Can sometimes be complicated by lung cancer or appear as a complication of it. Lemierre Syndrome has been observed in individual with lung cancer where typical order of events is reversed. the lung cancer might precede the infection, or the infection might be subclinical like in this case. And this is due to various factors, including weakened immune systems by the cancer impact or the presence of other infections. there have also been instance where a patient with lung cancer exhibited subclinical infections. leading to bilateral internal jugular vein thrombophlebitis and retropharyngeal collection ,effectively reversing the typical LS sequence. *Fusobacterium necrophorum* pathogen has been even discovered in broncho -alveolar lavage of some patient with lung cancer[13]. Hence Lemierre Syndrome may presents with symptoms characteristic of pulmonary cancer.[14] For that we can say up to our knowledge this is the second reported case of limierre,s syndrome masking lung cancer ,the first case was masking metastatic lung adenocarcinoma .[15].

Patient admitted in HDU, received metronidazole infusion 8/hourly,meropenem injection 1 g bd ,Ibuprofen infusion 400 mg 6 /hourly ,LMW anticoagulant ,oxygen ,Fixed dose of soluble insulin ,IV fluid . Studies have shown that delays in effective antimicrobial therapy have resulted in decreased survival rates among patients with LS , bacteria(FN) is usually sensitive to penicillin, cephalosporin, metronidazole, clindamycin and in our patient we used meropenem and metronidazole and there is noticeable improvement of patient situation in a few days . The use of anticoagulants is controversial in the management of LS. The theory of used that anticoagulation promotes the exposure of bacteria within the thrombus to high concentration of antibiotics during thrombolysis as result of that decrease in disease process and preventing spread of thrombus , in this patient her RFT and LFT and her PLT were normal and we guide with that theory of Anticoagulation and we used it for better outcome by experienced fewer thromboembolic events and fewer peripheral septic lesions.[16,17]. Patient with limierre,s syndrome were characterized by substantial risk of new thromboembolic complication and death, the risk is higher in those with initial intracranial involvement .the rate is lower in patient who received anticoagulation[18,19] Thrombectomy is a commonly performed procedure in most hospitals with an interventional radiologist . The process is minimally invasive and results in rapid to immediate symptomatic relief for the patient. A large clot burden in internal jugular vein can result in diminished blood flow in that vessel, increase septic emboli to the lungs as well as lead to increased airway edema from venous congestion, interventional percutanous thrombectomy should be considered earlier in those patients and patients refractory to antibiotics alone. And this result in decrease ICU stay, as well as hospital stay overall, and decrease the disease progression such as in the development of cavitary pulmonary septic emboli. [20,21] . Surgical excision and ligation of the IJV , is hardly necessary nowadays and is only reserved for cases with continued sepsis and septic embolization resulting in severe respiratory compromise or other repetitive embolic manifestation[22-26].

VII. conclusion

lemierre syndrome it is rare and difficult to diagnose but with delay of diagnosis it carry a high mortality rate and it is a life-threatening condition, Even with appropriate antibiotics and therapy, mortality has been reported to be between 5% and 18%.

In essence ,while lemierre syndrome typically follows an oropharyngeal infection that presents with a worsening clinical course and subsequent sepsis with evidence of metastatic septic emboli. it can occurs in individuals with lung cancer, often in an a typical manner. To our knowledge this is the second reported case of limierre,s syndrome masking non- small cell lung cancer .the first case was masking metastatic lung adenocarcinoma. while lung cancer and LS are distinct conditions, they can related in certain cases, lung cancer can increase the risk of LS due to immune suppression, and LS can complicate lung cancer treatment or lead to lung involvement. So A comperhensive approach to diagnosis and treatment is crucial in such situation,

VIII. Ethical statement

All procedure were performed in compliance with relevant laws and institutional guidelines and have been approved by the appropriate institutional committees. Informed patient consent was gained and ethical approval was not required.

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