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Atypical Presentation of Bronchial Adenocarcinoma

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***Abstract**:*
Unknown Primary Tumour (UPT) corresponds to the presence of one or more metastasis in the body without an identified primary tumor. In some cases, the primary cancer is never found.
Lung cancers are more often characterized by pulmonary, bone, brain, adrenal and liver growth. However, abnormal localizations may be possible and sometimes reveal the primary site of origin.
The case of a 77-year-old patient who suffered from a left cervical adenopathy mass is reported. After different examinations, it was impossible to identify the tumour process involved or the primary site of origin. During the etiological research, an adenectomy and the histological analysis were performed which reported that a lymph node site of an adenocarcinoma whose immunohistochemical pattern was in favour of a bronchopulmonary origin.
In this paper, we shall describe our diagnostic and treatment approach to this rare situation as well as the monitoring procedure established for our patient.
***Keywords**: unknown primary tumor (UPT), cervical lymphadenopathy, bronchial adenocarcinoma, immunoistochemical marking, surgical treatement.*

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I. Introduction

The lymph nodes are organs of the lymphatic system spread throughout the body and they function as sensors for the immune system. Adenopathy which is an increase in the volume of the lymph node is often found in cases of infectious diseases but also in cases of autoimmune, metabolic, or cancerous diseases.

Thus, cervical adenopathy is a very frequent reason for consultation in neck and head surgery and its treatment requires the adoption of a well-coded strategy. **[1]**

Carcinoma of unknown primary origin (UPT) is defined by the presence of metastatic disease without an identification of the primary tumor. They represent 5% of all diagnoses in oncology. These rare situations imply the need for specific diagnostic and therapeutic approaches. **[2]**

Our report is based on a rare case of isolated cervical lymph node growth that was not found after different analysis. The condition is
resulting from the presence of the adenocarcinoma of the lungs

II. Case Presentation

A 77-year-old male patient came in for consultations after noticing a swelling on the left cervical region that was progressively increasing in size. The patient is a former smoker with a 50-pack-year history, who stopped smoking 7 years ago and has no notable pathological history. The protrusion was soft, painless, non-bleeding with a slight cutaneous infiltration at a glance and movable in relation to the surface area. The tone of voice was preserved and there was no sign of dysphagia or anorexia. However, our patient reported a weight loss of about 6 kg in 5 months.

Figure 1: cervical region swelling

When the ENT stomatology, cephalic as well as the nasofibroscopy examinations were conducted, nothing was revealed.

In the first place, a cervico-maxillofacial and thoraco-abdominal-pelvic CT scan were performed after which, a magma of left lateral cervical adenopathy was noted at the cervical level. The largest Magma measured 28 mm and 21 mm in average diameter with infiltration of the skin. There were no significant abnormalities in the brain parenchyma along the facial mass and the thoracic-pelvic region.

The PET scan showed hypermetabolism (SUVmax= 15.7) of left posterior superior spinal adenopathy, the largest one measured 39 mm X 36 mm, and a focal hypermetabolic left colonic focus (SUVmax= 3.8).

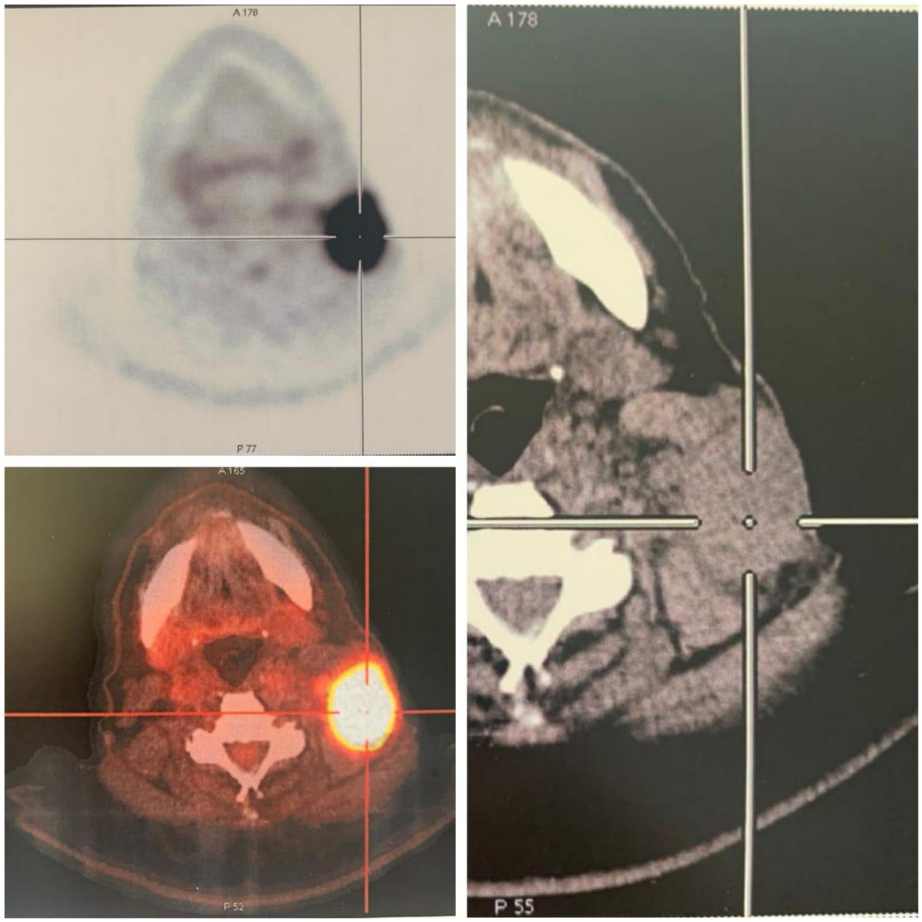

Figure 2: PET scan pictures

We therefore decided to perform an excisional biopsy of the entire mass to have a precise etiological orientation. The procedure included a single block carcinological excision, with a skin paddle circumscribing the area of infiltration.

Figure 3: per operative pictures (infiltration and excision)

The resulting loss of substance after surgery was covered by a musculocutaneous flap of the left pectoralis major and the postoperative recovery was good.

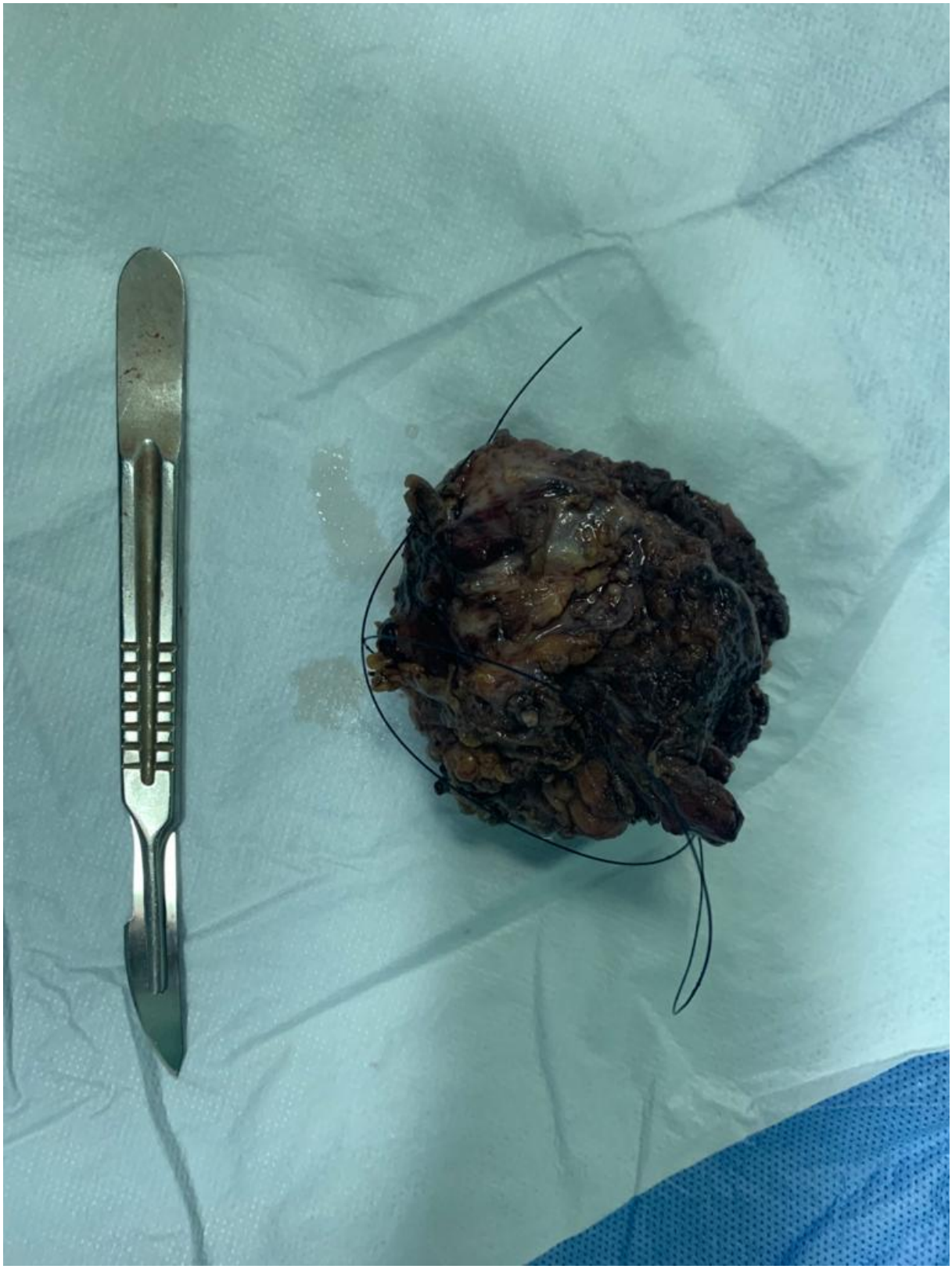

Figure 4: specimen sent to the laboratory for pathological examination

Pathological examination shows a lymph node location of an adenocarcinoma whose immunohistochemical profile supports the bronchopulmonary origin.

In fact, the histological section taken to the laboratory from the specimen showed lymph node tissue which was massively infected by a cancerous-looking proliferated tumour consisting of large tract cells. These are sometimes crushed and they show prominent cytonuclear atypia.

This proliferation infiltrated the fibrofatty and striated muscle tissues around the lymph nodes. We observed an absence of glandular tissue, mitosis, corneous maturation, orintravascular tumor embolisms.
The tumor cells were carcinomatous in nature, they express cytokeratins AE1/AE3, cytokeratin 7 but not cytokeratin 20. These cells also showed TTF1, Nepsin A however, the anti-CD 56 antibody was negative.
The postoperative recovery was simple, and the patient benefited from adjuvant radiotherapy. Clinical and radiological follow-up after 6 months, 1 year and 2 years were satisfactory.

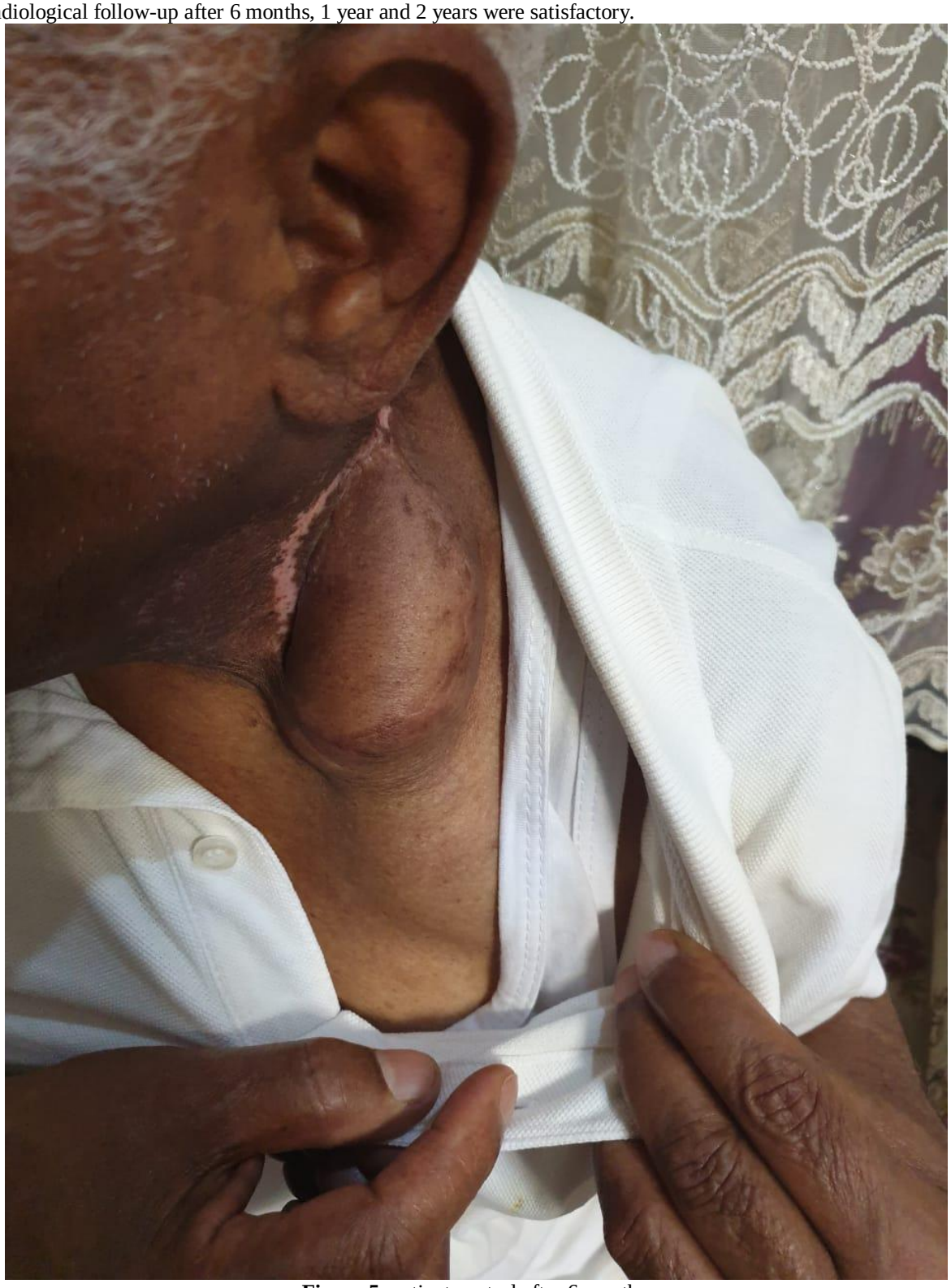

Figure 5: patient control after 6 months

III. Discussion

An unknown primary tumor (UPT) is defined by the presence of one or more metastasis without a known primary site of origin. They represent 5% of diagnoses made in oncology and are epithelial tumours. **[1,2]**

Lymph Nodes which make up 40% of all cases, is the most reported initial presentation followed by liver, lung, bone, brain, and skin metastasis in the order of the number of cases. In most of the cases when the primary tumor site is found, it is usually cases of bronchial or pancreatic origin followed by renal, colorectal, adrenal, thyroid, and prostate causes. It is important to note that pancreatic adenocarcinomas are the main source of PTCs, although they account for only 4% of cancers in the population. **[1,3]**

Clinically, these are tumours that usually do not show any signs of the initial site of origin, hence the scientific term UPT (unknow primary tumor). This is typically our patient case who didn't have any respiratory signs that could alert to a possible bronchopulmonary involvement. In most cases, the first clinical examination and paraclinical explorations allow us to find the primary tumours at the origin of the cervical lymph nodes. **[4,5]** A good etiological investigation is therefore essential in cases of isolated cervical lymph nodes. During the guided interrogation, we will look for medical and surgical history, alcohol or tobacco consumption, dietary habits, and check if the patient is from South-East Asian or North African origin. The analysis should be completed by an ENT examination, a facial and scalp examination, and an exploration of the salivary glands and the thyroid. Also, it is important to pay attention to the characteristics of the adenopathy. It should be noted that in the context of the untraceable primary site of origin, high cervical adenopathy more often points to cancers of the ENT sphere, while low cervical or supra-clavicular adenopathy raise suspicion of bronchial origin. **[4,6]**

Radiographic assessment is always needed in the presence of any cervical adenopathy and four techniques are most often used: Doppler ultrasound, CT scan, magnetic resonance imaging and positron emission tomography coupled with the CT scan. **[7]** The indications for the examinations to be conducted will depend on the clinical context. In terms of sensitivity, specificity, and diagnostic power, 18 FDG-PET is the best test for cervical adenopathy with no obvious origin. The combination of all mentioned scans does not significantly increase the efficiency of the diagnosis. **[8,9]**

Biologically, in the presence of cervical adenopathy, a blood count and a sedimentation rate should be requested as a first step. HIV serology will also be prescribed to the patient and further tests, including tumour markers, will be requested depending on the context and clinical orientation. **[4,10]**

As soon as the lymph node is considered pathological, a microscopic examination will be necessary. A sample will be taken either by an aspiration puncture, a trocar biopsy, or simply an excisional biopsy depending on the characteristic of the adenopathy and the suspected etiology. **[10]**

On the anatomopathological level, it should be noted that histological examination guides us towards the potential origin of the tumour. There are four types of histological analysis:

- Well or moderately differentiated adenocarcinomas
- Undifferentiated carcinoma
- Squamous cell carcinoma
- Neuroendocrine differentiated carcinomas

Adenocarcinoma is the most common histological subtype of bronchopulmonary cancer and tumour metastasis of pulmonary origin are in the brain, liver, bone and adrenal glands. However, a pulmonary origin can be suspected in the presence of metastatic cervical adenopathy, but this still is one of the most unlikely suggestions in our etiological investigation. The tumour cells seen expressed cytokeratin 7 and not 20 which more or less orient us towards a pancreatic origin, especially by its occurrence in the cases of CUP. Besides, the positive immunohistochemical marking to TTF1 and nepsin A allow us to confirm the pulmonary origin. **[4,11]** Therefore, histological analysis based on cell morphology provides a diagnostic orientation in most cases which will be confirmed thanks to immunohistochemical labelling. **[11,12]**

When a histology of squamous cell carcinoma or adenocarcinoma is confirmed on cervical adenopathy, a certain etiological diagnostic strategy should be adopted. An ENT examination aided by panendoscopy would be carried out if the chest X-ray is normal. This exam is to rule out cancer of the ENT sphere which will then be completed by a cervical-maxillofacial CT scan. Several conflicting studies on the ability of PET scans to find the primary site of origin have been published in recent years. The diagnostic yield varies only between 7 and 24% when PET is used for cervical adenopathy. **[10,13,14]**

In our patient's case, none of the radiological examinations detected the tumour cause of the adenopathy. Ongoing studies are still trying to explain the reasons for the appearance of tumour metastasis without identifiable primary tumor at presentation. Some hypotheses suggested that:

- The presence of an occult carries, with infra clinical and infra radiological origin
- Progressive development of the primary tumour due to a defect in angiogenesis
- Destruction of the primary tumour by the immune system
- Host specificity favouring the metastatic process. **[1,10]**

Surgical intervention becomes a necessity in the presence of cervical adenopathy when all the available techniques have proven ineffectiveness and hence, histological evidence is now looked for. In this case, an exploratory cervicectomy with an extemporaneous test will be performed for diagnostic purposes, which will be completed by a larger cervical cut in certain cases and serves in for treatment purposes. The therapeutic follow-up will depend on the results of the anatomopathological examination. A radiotherapy protocol will be adopted in cases of proven cancer. It is particularly important that a delay of at most 6 weeks between surgery and radiotherapy is observed unless there is an absolute contraindication to the initiation of radiotherapy, hence the need for good coordination between the different medical team. **[4,15,16,17]**

The therapeutic protocol in the management of UPT depends on the medical team and schools. The GEFCAPI score (French research group on carcinomas of unknown origin) defines two groups of patients through two main criteria: WHO performance status (PS) and LDH level.

Favourable	WHO 0-1 and normal LDH or no liver metastasis if LDH unknown
Unfavourable	OMS > 1 or High LDH

Figure 6: GEFCAPI (French Research group on carcinomas of unknown origin) Prognostical evaluation score.

Patients with a favorable prognosis will be treated as metastasis with known origin. A multidisciplinary consultation appointment will decide on surgery or radiotherapy depending on the tumour site. **[12,18]**

For those with an unfavourable prognosis, a "doublet chemotherapy" combining a platinum salt with gemcitabine or taxanes is performed in the first line. If no standard treatment exists, a combination of oxaliplatin and capecitabine is still the best option for patients with a good general condition. To date, targeted therapies have not yet provided satisfactory evidence of success. **[18,19]**

Remote monitoring of patients is crucial in the therapeutic process, which varies according to the type of cancer and the origin site. For metastatic cervical adenopathy without a pulmonary origin, monitoring in patients until complete remission includes clinical examination and nasofibroscopy every 3 months for 2 years and then every 6 months for 3 years, biannual oral surveillance in cases of irradiation, thoracic radiography, cervical-facial and thoracic-abdominal CT annually. **[17,19,20]**

IV. Conclusion

UPTs are disseminated cancers whose primary cannot be found either by clinical, pathological, or radiological features. They represent a diagnostic and therapeutic challenge because of their aggressive tumour pathologies whose diagnosis is based on histological analysis.

We reported an exceptional case of lung adenocarcinoma revealed by a cervical lymph node location, and the differential diagnosis was possible thanks to immunohistochemistry labelling techniques.

Treatment depends on the primary site of origin that was retained after various investigations and approximately 25% will be linked to a specific potential cause.

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