

# Always track the etiology of thromboembolism in younger adults : brain tumor revealed by recurrent pulmonary embolism in a young man

Mazou Temgoua<sup>1</sup>, Alfousseyni Keita<sup>2</sup>, Mekidian Diallo<sup>2</sup>, Alice Ossa<sup>3</sup>, Kieu Nguyen<sup>2</sup>, hilic Enver<sup>2</sup>, Nouhoun Diallo<sup>2</sup>, Gislain Endamena<sup>2</sup>, Sami Assi<sup>2</sup>, Lise Camus<sup>2</sup>, and Sylvain Chanseume<sup>2</sup>

<sup>1</sup>University of Yaounde I

<sup>2</sup>Hospital Centre Montlucon

<sup>3</sup>Universite de Yaounde I

May 7, 2021

## Abstract

Pulmonary embolism is a major cause of death worldwide. Recurrences are mainly observed in patients with coagulation disorders or cancers. We describe the case of a brain tumor (Glioblastoma) revealed by behavioral disorder in a young patient admitted for a recurrent pulmonary embolism

## Introduction

Pulmonary embolism (PE) is a major cause of death worldwide (1). The risk factors are well described and classified by the European Society of Cardiology (ESC) in three categories : Strong, moderate and weak risk factors (2). The strong risk factors included generally : trauma of the lower limb or spinal cord, hip or knee replacement, hospitalization for heart failure or atrial fibrillation/flutter, myocardial infarction within previous three months and previous venous thromboembolism (2). Even if pulmonary embolism is rare in young adult, the causes are the same as in the adults (3). The recurrence of thromboembolism is generally associated to malignancy or thrombophilia (4). The most frequent occult malignancies during PE involved the lung, gastrointestinal tract, breast, and uterus (5). This is the reason why the screening of these cancers is systematic in the management of pulmonary embolism (2). Association between brain tumors and pulmonary embolism is rare. Some cases have been described mainly in perioperative period for craniectomy and the risk factors included : older age, motor deficit, high grade gliomas (6,7). We describe a rare case of recurrent pulmonary embolism in a young man with occult brain tumor. This case is important because it reinforces the need of critical and multidisciplinary assessment of thromboembolism in young patients before considering it as idiopathic.

## Case presentation

A 44 year-old policeman was admitted in the emergency room of the Hospital Center of Montlucon for pre-syncope with mild dyspnea, without chest pain. Past-history revealed that the patient was followed in psychiatry for mental depression since 5 months and treated by paroxetine 20mg daily. He also was diagnosed of pulmonary embolism at the age of 13 several days after a knee trauma. He had no recent history of trauma, surgery or immobilization. Upon arrival, the patient had a satisfactory general and hemodynamic state, he was eupneic with a clear cardiovascular examination. 12-Limbs electrocardiogram was normal with regular sinus rhythm at 66 bpm, transthoracic echocardiography showed non dilated cavities with

normal bi-ventricular systolic functions and normal pulmonary pressure. A CT-Pulmonary Angiography found a bilateral segmental and subsegmental pulmonary embolism without any signs of gravity (Figure 1). Biological workups found a normal full blood count, Troponin T level at 13 pg/ml (normal range <14 pg/ml) NT pro NBP at 14 pg/ml (normal range <125 pg/ml). We concluded to a recurrent pulmonary embolism in a young man. He was therefore hospitalized for investigation of the etiology and we started anticoagulation with Apixaban 10 mg twice daily. During hospitalisation in the cardiology unit, the patient presented typical frontal release signs with desinhibition, euphorism, grasping and sucking. The Cerebral CT-Scan found a large heterogenous hypervascularized multi-lobular tumor with a large peripheric oedema located in the frontal region associated with sub-falcorial herniation suggesting high grade Glioblastoma (Figure 2). Work-up for thrombophilia (antithrombin III, protein C, protein S, Factor V mutation, anticardiolipin, anti-Beta2-GP1), tumoral biomarkers (CA 19-9, CEA, AFP, Cyfra 21-1, NSE, PSA), HIV serology, abdominal and pelvic scan were unremarkable. We started treatment with Methylprednisolone 120 mg intravenously and the patient was transferred to the neurosurgical team for better management.

## Discussion

Pulmonary embolism (PE) is a major cardiovascular disease which could be potentially life-threatening (1). Pre-existing malignancy is one of the most common etiology in recurrent forms. (4). The most frequent occult malignancies during PE involved the lung, gastrointestinal tract, breast, and uterus (5). These malignancies are generally diagnosed at the advanced stage of the disease (8). The pathophysiology of malignancy associated with thromboembolism include : hypercoagulable state due to many factors including release of inflammatory cytokines, activation of the clotting system, expression of hemostatic proteins on tumor cells, inhibition of natural anticoagulants, and impaired fibrinolysis (9). Brain tumors like ovary and pancreatic cancers even if rare in terms of prevalence are strongly associated with thromboembolic events (10). This is illustrated by the fact that 11-20% of patients with brain tumors have pulmonary embolism and the median time to develop the disease in generally 6.5 years after the diagnosis of the tumor (11). Our patient was followed for a depression since 5 months before the diagnosis of the second episode of pulmonary embolism. We think that the first episode of pulmonary embolism during childhood could be due to a provoked cause (knee trauma). Glioblastoma is known as the main brain tumor and the most associated with pulmonary embolism (11). The radiological presentation of the mass evoked this diagnosis, even if the final diagnosis is done by histopathologic studies. At the early stage of the disease, MRI of the brain is the most sensitive tool for the diagnostic of Glioblastoma isointensity to hypointensity on T1WI, hyperintense ill-defined lesions on T2WI, little or no mass edema, and no contrast enhancement (12). CT-Scan could evoked hypervascularised brain tumor, but the difference between primitive lymphoma or glioblastoma is difficult by imaging (13). Knowing that the patient was immunocompetent and the lesion was polylobular and heterogenous contrary to lymphoma we have retained the diagnosis of glioblastoma. But this diagnosis will be well investigated by the neurosurgical team. The presence of signs of herniation signify that the tumor was advanced. This case suggest that the physician should be more aware and thoroughly examine young patients with pulmonary embolism in order to exclude potential life-threatening conditions like malignancy.

## Conclusion :

Brain tumor is a potentially life-threatening cause of pulmonary embolism even in young. A good clinical assessment associated with extensive paraclinical workups should be made before concluding on an idiopathic cause especially in case of recurrence.

## Abbreviations

AFP: Alpha foetoprotein

CEA: Carcino-embryonic Antigen

CT: Computed Tomography

ESC: European Society of Cardiology

HIV: Human Immunodeficiency Virus

NSE: Neuron Specific Enolase

PE: Pulmonary Embolism

PSA: Prostate Specific Antigen

## Diclosures

**Approval of the research protocol:** Formal ethical approval from the University Research Ethics Board was not required for the completion of this study.

**Informed consent:** Written informed consent for publication of this case report was obtained from the patient.

**Data Availability Statement :** The data that support the findings of this study are available from the corresponding author upon reasonable request.

**Registry and registration no. of the study :** N/A.

**Animal studies:** N/A.

**Conflict of interest:** None

**Funding:** None

## Author Contribution :

Management of the case : All the authors

Manuscript writing : MNT

Critical revision : AO

Supervision : SC

## References

1. Goldhaber SZ. Pulmonary embolism. *The Lancet*. 17 avr 2004;363(9417):1295-305.
2. Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing G-J, Harjola V-P, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). *Eur Heart J*. 21 janv 2020;41(4):543-603.
3. Rosendaal FR. Thrombosis in the young: epidemiology and risk factors. A focus on venous thrombosis. *Thromb Haemost*. juill 1997;78(1):1-6.
4. Galioto NJ, Danley DL, Maanen RJV. Recurrent Venous Thromboembolism. *Am Fam Physician*. 1 févr 2011;83(3):293-300.
5. Gore JM, Appelbaum JS, Greene HL, Dexter L, Dalen JE. Occult cancer in patients with acute pulmonary embolism. *Ann Intern Med*. mai 1982;96(5):556-60.
6. Chaichana KL, Pendleton C, Jackson C, Martinez-Gutierrez JC, Diaz-Stransky A, Aguayo J, et al. Deep venous thrombosis and pulmonary embolisms in adult patients undergoing craniotomy for brain tumors. *Neurol Res*. mars 2013;35(2):206-11.
7. Rinaldo L, Brown DA, Bhargav AG, Rusheen AE, Naylor RM, Gilder HE, et al. Venous thromboembolic events in patients undergoing craniotomy for tumor resection: incidence, predictors, and review of literature. *J Neurosurg*. 4 janv 2019;132(1):10-21.

8. White RH, Chew HK, Zhou H, Parikh-Patel A, Harris D, Harvey D, et al. Incidence of venous thromboembolism in the year before the diagnosis of cancer in 528,693 adults. *Arch Intern Med.* 8 aout 2005;165(15):1782-7.
9. Rodrigues CA, Ferrarotto R, Kalil Filho R, Novis YAS, Hoff PMG. Venous thromboembolism and cancer: a systematic review. *J Thromb Thrombolysis.* juill 2010;30(1):67-78.
10. Lee AYY, Levine MN. Venous thromboembolism and cancer: risks and outcomes. *Circulation.* 17 juin 2003;107(23 Suppl 1):I17-21.
11. Yust-Katz S, Mandel JJ, Wu J, Yuan Y, Webre C, Pawar TA, et al. Venous thromboembolism (VTE) and glioblastoma. *J Neurooncol.* aout 2015;124(1):87-94.
12. Wang H, Liu Z, Zhang Y, Hou F, Fu W, Lin J, et al. Additional Diagnostic Value of Unenhanced Computed Tomography plus Diffusion-Weighted Imaging Combined with Routine Magnetic Resonance Imaging Findings of Early-Stage Gliblastoma. *BioMed Res Int [Internet].* 18 fevr 2020 [cite 1 mai 2021];2020. Disponible sur: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7049329/>
13. Schramm P, Xyda A, Klotz E, Tronnier V, Knauth M, Hartmann M. Dynamic CT perfusion imaging of intra-axial brain tumours: differentiation of high-grade gliomas from primary CNS lymphomas. *Eur Radiol.* 2010;20(10):2482-90.



