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Case Report

A young lady with adenocarcinoma of unknown primary presenting with right upper limb deep vein thrombosis and pulmonary embolism: A case report

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Introduction

Carcinoma of unknown primary (CUP) is defined as a histologically proven metastatic cancer in the absence of a clinically detectable, anatomically defined primary tumour site, after an adequate diagnostic evaluation [1, 2]. In 1865, French physician Dr. Armand Trousseau described an association between thrombosis and cancer, which was later named 'Trousseau Syndrome" as he diagnosed it on himself and died of it in 1867, although it had been reported earlier in 1823 by Jean Baptiste Bouillaud [3, 4]. Around 20% - 30% of first venous thromboembolic events are associated with cancer [5]. We present a case of a fit young woman admitted with venous thrombosis and pulmonary embolism, later diagnosed with carcinoma of unknown primary.

Case Presentation

In December 2015, a 39 year old woman presented with a history of progressive exertional breathlessness of more than two weeks and right upper limb swelling of 24 hour duration. Her past history was unremarkable, except that she had intermittent bilateral lower limb swelling mainly over the calves one month back, which was not painful and resolved spontaneously. Two weeks later she developed a gradual onset shortness of breath on mild exertion for two weeks associated with dry a cough, pleuritic type chest pain and painful swelling of the right upper limb extending to the right shoulder and neck. Later she developed haemoptysis, but there was no fever, night sweats, weight loss or loss of appetite. She had a strong family history of carcinomata, namely carcinoma of the colon in her father, thyroid in two of her cousins and breast in her maternal aunt.

Physical examination revealed a BMI of 26, tachypnoea and tachycardia. There was no organomegaly or lymphadenopathy. Thyroid and breast examination was normal. There was no bone tenderness. Her right upper limb was swollen up to the supraclavicular region with fullness, tenderness and warmth. Distal pulse was palpable and oxygen saturation was 94% in the right arm Auscultation revealed bilateral coarse crepitations

and scattered rhonchi mainly over middle and lower zones. Her abdomen was soft and per vaginal, rectal examinations were normal.

Initial laboratory investigations revealed a haemoglobin of 11.6g/DL, high leucocyte count of $21X10^9$/L with 82% neutrophils and platelet count of $138X10^9$/L. Inflammatory markers were normal. ECG showed sinus tachycardia of 128 beats per minute and 2D echocardiogram suggested possibility of segmental or minor degree pulmonary embolism. Arterial blood gases were compatible with type 1 respiratory failure. Chest X-Ray (CXR) revealed miliary shadows suggestive of lymphangitis carcinomatosis. Bilateral lung fields showed diffuse small nodules, patchy consolidation and ground glass appearance with mediastinal and bilateral hilar necrotic lymphadenopathy (figure 1). Venous duplex scan confirmed a right upper limb DVT extending up to the right axillary vein.

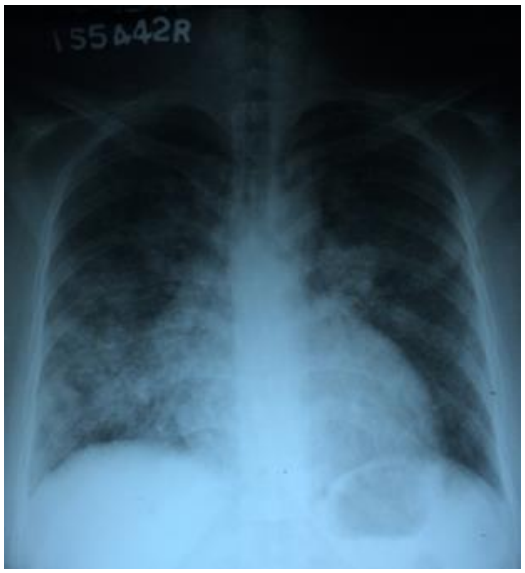

Figure 1: CXR - AP shows bilateral miliary mottling, ground glass appearance

Computed tomography pulmonary angiogram (CTPA) confirmed bilateral pulmonary embolism in descending pulmonary arteries causing partial obstruction (figure 2).

In addition, thrombosis of the right internal jugular vein, innominate vein and superior vena cava up to the origin were noted.

We performed a contrast enhanced computed tomography (CECT) which showed multiple hypo echoic focal lesions in liver segments II, III, VIII compatible with metastases (figure 3).

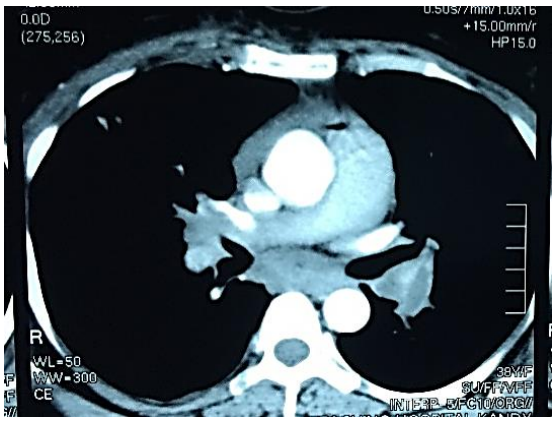

Figure 2: CTPA shows evidence of cut off sign in bilateral pulmonary arteries

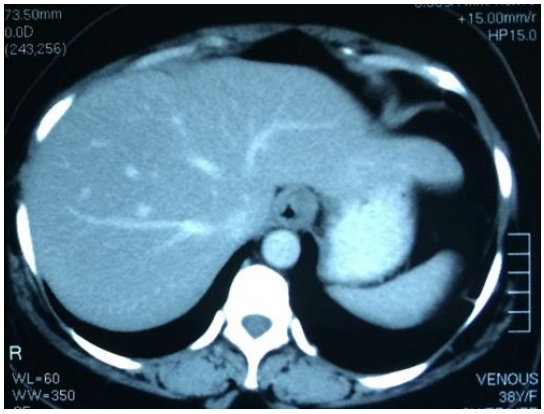

Figure 3: CECT abdomen shows liver metastatic lesions

Ultrasonography of the neck showed multiple bilateral deep cervical lymphadenopathy. Fine needle aspiration cytology of a deep cervical lymph node confirmed deposits of well differentiated adenocarcinoma. An extensive investigation panel was made to identify the primary, including mammogram, endoscopic procedures and bone marrow examination but all turned out to be negative. Although carcino embryonic antigen (CEA) was negative her CA125 was slightly elevated. However, as the CT abdomen did not reveal an ovarian pathology, it was attributed as a false positive [6].

Ultimately, a diagnosis of carcinoma of unknown primary was made and she was started on an initial course of chemotherapy as her general condition was deteriorating rapidly. Unfortunately the patient was not able to survive beyond her initial chemotherapy.

Discussion

The exact number of cases of cancer of unknown primary is unknown. However the American Cancer Society estimates that about 33,770 cases of cancer of unknown primary will be diagnosed in 2017 in the United States [7]. About 3% of all cancer patients suffer from cancer of unknown primary origin [8, 9]. The initial evaluation should include a detailed history and physical examination, including head and neck, rectal, testicular, pelvic and breast examinations.

Once a biopsy proven diagnosis is made an extensive evaluation with specific pathologic investigations (immunohistochemistry, molecular diagnosis), laboratory workup with tumor markers [CEA), CA 125, CA 19.9, PSA (in men), alpha fetoprotein, beta human chorionic gonadotropin] and modern imaging technology (computed tomography, mammography, positron emission tomography) are necessary to identify possible primary sites. However most tumour markers are nonspecific and cannot be used to establish a definitive diagnosis. Even after exhaustive evaluation, the primary site remains unknown in most patients, even on autopsy. It has been recognized that the most frequently detected primary carcinomas are hidden in the lung or pancreas [8].

Following extensive diagnostic evaluation in this patient, palliative chemotherapy was directed towards the most likely diagnosis of adenocarcinoma of lung, considering the features suggestive of lymphangitis carcinomatosis in the chest x-ray.

When considering venous thromboembolism risk in carcinomata, primaries from pancreas, brain, lung, and ovaries are reported to pose highest risk. In addition the thrombotic risk is high for lymphomas, myeloma, and kidney, stomach and bone cancer [10].

Patients with cancer and venous thrombosis have a poorer prognosis due to thrombotic events which are the second leading cause of death in cancer patients [11]. Prophylactic anticoagulant treatment for the prevention of venous thrombotic events in cancer patients is thought to improve prognosis and quality of life but the disadvantage is an increased risk of bleeding [12].

The median survival for carcinoma of unknown primary for non-adenocarcinomas with less than two organ metastasis without involving liver, bone, adrenals or pleura is 40 months and for other histologic types with liver metastasis is 5 months.

For convenience patients are grouped according to their histologic diagnosis and nearly 60 per cent of CUP is adenocarcinoma [13]. Most patients with cancer of unknown primary benefit only from supportive treatment. However, a few patients benefit from palliative treatment. Although the prognosis for most patients remains poor, several subgroups who are amenable to treatment have been recognized [9, 14].

Conclusion

It is recommended to evaluate the patients with CUP thoroughly for possible detection of the primary tumour and to identify the recognized, treatable subgroups.

References

1. Blom JW, Doggen CJ, Osanto S, Rosendaal FR. Malignancies, prothrombotic mutations, and the risk of venous thrombosis. Jama. 2005 Feb 9;293(6):715-22. https://doi.org/10.1001/jama.293.6.715 PMid:15701913
2. Stella GM, Senetta R, Cassenti A, Ronco M, Cassoni P. Cancers of unknown primary origin: current perspectives and future therapeutic strategies. Journal of translational medicine. 2012 Jan 24;10(1):12. https://doi.org/10.1186/1479-5876-10-12 PMid:22272606 PMCid:PMC3315427
3. Bouillaud S, Bouillaud J. De l'Obliteration des veines et de son influence sur la formation des hydropisies partielles: consideration sur la hydropisies passive et general. Arch Gen Med. 1823;1:188-204.
4. Buller HR, Van Doormaal FF, Van Sluis GL, Kamphuisen PW. Cancer and thrombosis: from molecular mechanisms to clinical presentations. Journal of Thrombosis and Haemostasis. 2007 Jul 1;5(s1):246-54. https://doi.org/10.1111/j.1538-7836.2007.02497.x
5. Brækkan SK, Borch KH, Mathiesen EB, Njølstad I, Wilsgaard T, Hansen JB. Body Height and Risk of Venous Thromboembolism-The Tromsø Study. American journal

of epidemiology. 2010 May 15;171(10):1109-15. https://doi.org/10.1093/aje/kwq066 PMid:20418276
6. Moss EL, Hollingworth J, Reynolds TM. The role of CA125 in clinical practice. Journal of clinical pathology. 2005 Mar 1;58(3):308-12. https://doi.org/10.1136/jcp.2004.018077 PMid:15735166 PMCid:PMC1770590
7. American Cancer Society. Cancer Facts and Figures 2017. Atlanta, Ga: American Cancer Society; 2017. www.cancer.org/cancer/cancer-unknown-primary/about/key-statistics.html Accessed: June 19, 2017
8. Pavlidis N, Briasoulis E, Hainsworth J, Greco FA. Diagnostic and therapeutic management of cancer of an unknown primary. European Journal of Cancer. 2003 Sep 30;39(14):1990-2005. https://doi.org/10.1016/S0959-8049(03)00547-1
9. Briasoulis E, Pavlidis N. Cancer of unknown primary origin. The Oncologist. 1997 Jun 1;2(3):142-52. PMid:10388044
10. Cronin-Fenton DP, Søndergaard F, Pedersen LA, Fryzek JP, Cetin K, Acquavella J, Baron JA, Sørensen HT. Hospitalisation for venous thromboembolism in cancer patients and the general population: a population-based cohort study in Denmark, 1997–2006. British Journal of Cancer. 2010 Sep 28;103(7):947-53. https://doi.org/10.1038/sj.bjc.6605883
11. Khorana AA, Francis CW, Culakova E, Kuderer NM, Lyman GH. Thromboembolism is a leading cause of death in cancer patients receiving outpatient chemotherapy. Journal of Thrombosis and Haemostasis. 2007 Mar 1;5(3):632-4. https://doi.org/10.1111/j.1538-7836.2007.02374.x PMid:17319909
12. Prandoni P, Lensing AW, Piccioli A, Bernardi E, Simioni P, Girolami B, Marchiori A, Sabbion P, Prins MH, Noventa F, Girolami A. Recurrent venous thromboembolism and bleeding complications during anticoagulant treatment in patients with cancer and venous thrombosis. Blood. 2002 Nov 15;100(10):3484-8. https://doi.org/10.1182/blood-2002-01-0108 PMid:12393647
13. Hainsworth JD, Greco FA. Treatment of patients with cancer of an unknown primary site. New England Journal of Medicine. 1993 Jul 22;329(4):257-63. https://doi.org/10.1056/NEJM199307223290407 PMid:8316270
14. Hess KR, Abbruzzese MC, Lenzi R, Raber MN, Abbruzzese JL. Classification and regression tree analysis of 1000 consecutive patients with unknown primary carcinoma. Clinical Cancer Research. 1999 Nov 1;5(11):3403-10. PMid:10589751