The Role of Virtual Autopsy in Uncertain Clinical Scenarios

Taha R. Mallick, MD* Muneera J. Alhammadi, MB BCH BAO*
Mohamed Elbahr, MBBCH, MSc, EDIC** Wael Ebrahim, MD, PhD***
Dalal Alromaihi, MD**** Eamon Tierney FFARCSI, FJFICMI*****

We present a case of a patient who was transferred from the general ward to the ICU in an unstable condition and passed away within approximately twenty-four hours without having had full investigations due to her unstable clinical condition. In the absence of necessary investigations, a virtual autopsy to search for a medical cause of her rapid deterioration was performed. The virtual autopsy revealed cardio-respiratory failure. Post-mortem computed tomography (PMCT) scans were performed, which revealed that the immediate cause of her deterioration was most likely to have been a myocardial infarction associated with pneumonia.

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A virtual autopsy employs CT and MRI to replace a traditional autopsy to investigate the cause of death. Blood analyses, biopsies and needle aspiration of tissues might be a part of the virtual autopsy. It has been argued that virtual autopsy provides better delineation of pathology within a smaller time frame, while at the same time, respects various cultures and beliefs and reduces the risks of infection associated with a traditional autopsy[1]. It has also gained value in the practice of forensic medicine[2].

In many patients, it is not possible to arrive at a definite clinical diagnosis. This is often due to the inability to perform suitable investigations because of time restraints or because the patient is too unstable to transfer to the Radiology Department. Determining the cause of death is important for many reasons: it is an educational and quality improvement process for the attending medical team; it helps to satisfy the team that its differential diagnoses and investigations were appropriate; the family needs to be informed about the cause of death, issues of hereditary illness that may require follow-up amongst family members, in suspected case of medical malpractice; at a national level, each country needs to keep statistics on the causes of death to plan public health programs and appropriate research.

The aim of this presentation is to evaluate virtual autopsy in patients on whom meaningful investigations could not be performed.

THE CASE

A seventy-nine-year-old female was seen in the emergency department with a two-day history of vomiting and diarrhea. There was no associated history of gastrointestinal bleeding, abdominal pain or distention. A review of systems did not reveal any significant positive finding. She received the first treatment of methotrexate a week prior to admission.

The patient had a complex past medical history: hypertension treated with perindopril, chronic obstructive pulmonary disease managed with salbutamol/ipratropium bromide nebulization and fluticasone propionate inhalation, left-sided hemiparesis, rheumatoid arthritis treated with subcutaneous methotrexate injection once weekly, hyperuricemia managed with daily allopurinol, chronic deep venous thrombosis of the left lower limb involving the femoral and iliac veins confirmed by Doppler scan. The patient was bedridden due to both stroke and joint disease, the patient was known to have bilateral fixed breast masses and was awaiting an appointment with a breast surgeon.

On examination, the patient was not in obvious distress and was vitally stable and afebrile. She was able to maintain an adequate oxygen saturation on room air and was alert, awake and oriented. Her peripheries were well-perfused with palpable pulses in all four limbs.

Chest auscultation was normal except right-lower lobe crepitations. The abdomen was soft and lax with no tenderness, guarding or rigidity. Both lower limbs were grossly swollen. A residual left-sided hemiparesis was evident. Initial investigations showed a microcytic hypochromic anemia with a hemoglobin level of 7g/dl. The white blood cell and platelet count were unremarkable ($6.4x10^6$/L and $702x10^9$/L respectively).

* Senior House Officer
** Registrar
Intensive Care Unit
*** Head of Department
Department of Radiology
**** Consultant Internal Medicine and Endocrinology
***** Director of Intensive Care
Department of Intensive Care
King Hamad University Hospital
The Kingdom of Bahrain
Associate Professor of Critical Care, RCSI-MUB
E-mail: taha.mallick@khuh.org.bh, estjmt@gmail.com

Renal function parameters were suggestive of acute kidney injury possibly secondary to fluid loss due to diarrhea and vomiting. The creatinine level was 163.44 umol/L and urea level was 11.9 mmol/L.

Chest X-ray was suggestive of right-lower lobe atelectasis and fibrotic changes. The patient was treated with supportive measures including intravenous fluid therapy. The patient was admitted to a general ward with a provisional diagnosis of gastroenteritis with secondary acute kidney injury and anemia. The patient continued on a normal saline infusion. Ciprofloxacin 500mg twice daily and Metronidazole 500mg three times daily were commenced. During her admission, her second dose of methotrexate was given. In addition, ondansetron and loperamide were prescribed. The patient's diarrhea initially resolved and then recurred after methotrexate. In addition, the patient developed mucosal ulcers in the mouth and swelling of lower lip. A repeat FBC revealed hemoglobin 4.5 g/dl, WBC 0.57 x 10^9/L and platelet count of 21x10^9/L. Because of the severe anemia, a unit of packed RBCs over five hours was given. Following the blood transfusion, the patient developed hypotension, and her consciousness deteriorated. The patient was transferred to the ICU, where she was intubated and started on mechanical ventilation and inotropic support.

The patient was started on imipenem, amikacin, vancomycin and caspofungin. Blood culture showed Pseudomonas aeruginosa sensitive to meropenem, amikacin, cefepime and piperacillin/tazobactam. Echocardiography showed that right-side cardiac function was normal, decreasing the likelihood of a pulmonary embolism.

Arterial blood gas analysis showed severe high anion gap metabolic acidosis with a pH of 6.9, pCO2 of 23 mmHg and HCO3 of 5 mmol/L. The lactate level was 12.5 mmol/L. Intravenous sodium bicarbonate was used to correct the acidosis and dialysis was considered but could not be done due to severe hypotension despite inotropic support.

The family expressed dissatisfaction and associated her deterioration with the blood transfusion. The patient passed 26 hours after her ICU admission. Because of her clinical instability, it had not been possible to perform CT or MRI scans to evaluate her cardiovascular collapse.

A virtual autopsy was requested. CT scan of the brain, chest, abdomen, and pelvis were performed after obtaining consent from the family. The CT brain showed no evidence of intra-cerebral hemorrhage, but there was a left parietooccipital sub-acute infarction, see figure 1 (A to D). The lungs revealed bilateral pulmonary consolidation more in the lower lobes suggestive of a diffuse inflammatory process. In addition, there were bilateral pleural effusions more evident on the left side, no evidence of pulmonary edema was found. The CT heart revealed a focal hypodense area in the left ventricle which was indicative of myocardial infarction, see figure 2 (A to D). This led us to believe that the immediate cause of her deterioration was a myocardial infarction associated with a background of pneumonia.

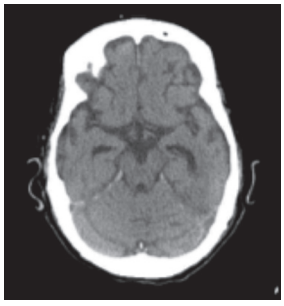

Figure 1 (A)

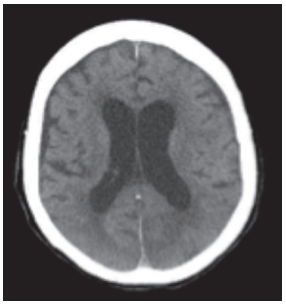

Figure 1 (B)

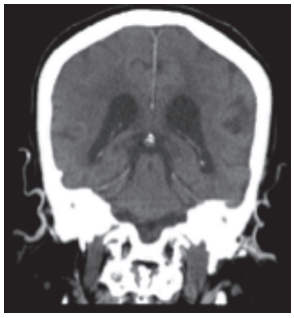

Figure 1 (C)

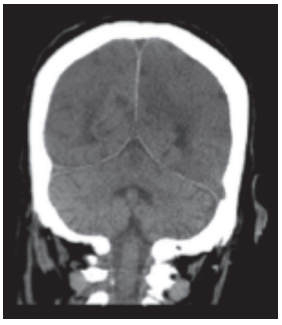

Figure 1 (D)

Figure 1 (A to D): CT Brain Showing No Obvious Pathology

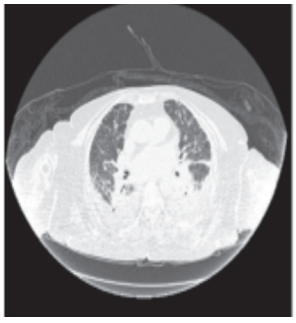

Figure 2 (A)

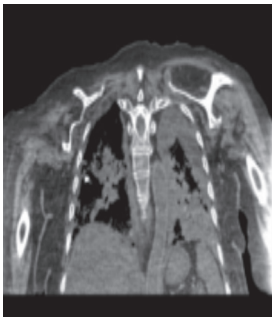

Figure 2 (B)

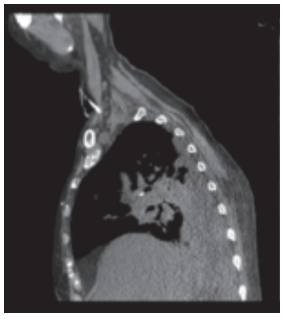

Figure 2 (C)

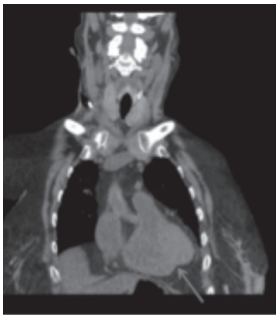

Figure 2 (D)

Figure 2 (A to D): CT Chest Showing Presence of Bilateral Plural Effusions and Pulmonary Infiltrates (A to C) and Focal Hypodense Area in the Left Ventricle (D)

DISCUSSION

A post-mortem examination was appropriate; however, due to cultural reasons, it was not feasible. Therefore, consent for Virtual Autopsy was obtained.

The relationship of the patient's clinical deterioration and the blood transfusion raised the possibility of various types of transfusion reactions contributing to the patient's demise. The indication for transfusion was clear that is Hb of 4.5g/dl. The packed RBCs had been grouped, cross-matched and subsequently cross-checked in accordance with standard hospital practice.

Transfusion of packed RBCs particularly in an elderly patient with multiple comorbidities raises the possibility of fluid overload but only one unit of red cell concentrate, about 300 mL, was transfused. In addition, the unit of packed RBCs was transfused slowly to minimize the risk of volume overload. There was no evidence of fluid overload on the CT scan of the thorax.

The probability of an infective process was supported by an ESR of 140 mm/hour, CRP of 165 mg/L and a procalcitonin of 8.3 ng/ml. Bilateral pneumonia was confirmed by the findings on the post-mortem CT scan.

The possible cause of the pancytopenia in this patient was iatrogenic. The patient had been on methotrexate orally on a long-term basis, but had recently been started on methotrexate injection and had received three injections prior to her collapse. Therefore, methotrexate through injection could have contributed to and caused the pancytopenia in this patient. In addition, sepsis in itself may induce myelosuppression.

As sequelae to anemia and sepsis, myocardial perfusion was compromised and led to myocardial infarction since the cardiac enzymes continued to rise during ICU admission. Troponin-I readings increased from 0.257 ng/ml to 2.57 ng/ml while CK-MB readings increased from 1.87 ug/L to 34.1 ug/L. Although there were no ischemic ECG changes, the patient had a previous history of stroke; therefore, a non-ST elevation myocardial infarction (N-STEMI) could not be discounted. The post-mortem CT scan revealed a hypodense area in the left ventricle, supporting a non-ST elevation myocardial infarction.

A previous history of chronic proximal deep venous thrombosis and the sudden onset of hemodynamic instability raised a suspicion of a pulmonary embolism. The D-dimer level was elevated at 13.42 ng/ml. However, no supporting evidence was found on transthoracic echocardiography.

Several studies have compared the value of virtual autopsy with a traditional autopsy and suggested that virtual autopsy could reveal internal injuries which may be missed by a traditional autopsy[3,4,5]. Studies have shown that postmortem CT scans could provide valuable information in the evaluation of victims who succumbed to a variety of fatal events, including gunshot wounds, blunt trauma, airplane accidents and drowning[6,7,8].

Postmortem angiography and a programmable biopsy could be included in virtual autopsy[2,9]. Postmortem evaluation of the heart using MRI, CT scan, and CT angiography has shown potential for staging myocardial infarction, evaluating myocardial lesions and detecting atherosclerotic changes in the coronary arteries[10,11,12]. It must be argued that a traditional autopsy is superior in providing direct visualization and histologic analysis. One study argues that several etiologies of sudden death are not picked up by virtual autopsy[13]. Some consider virtual autopsy best placed as an adjunct to traditional autopsy or as a viable alternative when a traditional autopsy could not be performed, especially in trauma cases[3,14]. Data from virtual autopsies may also be used to generate epidemiologic data for evaluation of morbidity and mortality in the general population[15,16].

CONCLUSION

While most studies have focused on the role of virtual autopsy in trauma cases, we used the same modality in a non-trauma scenario which allowed us to provide an explanation for the patient's sudden deterioration, and we were also able to discount a transfusion reaction as the most likely cause.

The findings of a virtual autopsy could add valuable information in situations where there is not enough evidence to determine the cause of death. The virtual autopsy provides the family with the probable cause of the demise of their loved one.

The information from a virtual autopsy may seem inferior to that obtained from a traditional autopsy. The traditional autopsy provides direct visualization as well as the opportunity for histologic evaluation.

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