Sudden death of neuromyelitis optica: 
A case report of clinical missed diagnosis

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Abstract: Deaths of clinical miss-diagnosed diseases are caused by various reasons. Similar symptoms shared by different diseases and the recent medical history could affect the judgement of clinicians sometimes, especially when the disease is unusually found. We present a case of sudden death in hospital. Patient was admitted with sudden visual loss and quadriplegia. He died suddenly without certain pathogenesis next day. The medical history showed he had head injury recently. The autopsy revealed scattered inflammatory demyelination in optic nerves and spinal cord. Postmortem serological testing showed positive result of neuromyelitis optica-IgG. Therefore, the cause of death is severe respiratory distress due to acute neuromyelitis optica.

Key Words: neuromyelitis optica; autopsy; sudden death; forensic pathology.

Sudden deaths due to unrecognized disease in hospital are not infrequent and always concerned by forensic pathologists. Clinically missed diagnoses of disease are attributed to various reasons. The unusual diseases, different entities that share the same manifestations or the recent medical history of injury may affect the accurate diagnosis. We report a case of sudden death during hospitalization due to clinically unrecognized disease. The forensic examination revealed the cause of death was acute neuromyelitis optica, which is seldom reported in the field of forensic medicine.

CASE REPORT

A 52-year-old male was sent to hospital with sudden onset of visual loss and loss of strength of lower extremities. He reported a history of head injury due to a fight nearly one month ago but denied any headache, nausea or seizure at this time. Physical examinations showed vital signs within the normal range(temperature: 35.8°C, pulse rate: 58 beats per minute, respiratory: 14 breaths per minute, blood pressure: 113/67mmHg), stiff neck, lower extremity weakness, urinary retention, and sensory impairment under T12 level.

Computerized tomography (CT) scan of the brain was unremarkable. In the next day, the patient suddenly appeared cyanosis and was admitted to the intensive care unit with respiratory failure. Despite resuscitation efforts with intubation were performed immediately, he progressed to unconsciousness and ensuing death. Clinical diagnosis was undetermined. Therefore, a medicolegal examination was required for investigating the cause of death.

AUTOPSY FINDINGS

The body was thawed and absence of rigor. External examination of body revealed a well-developed and medium-nourished male. The body length was 169cm.
Livor mortis were distributed in the posterior dependent portions of the body. Obvious cyanosis of lips and finger nails were found. A 4 cm long remote scar was found to the right side of the occipital scalp with haemorrhage. No skull fracture was seen. The rest of body revealed no injuries or other abnormalities. Internally, all the other organs were normally situated and unremarkable. No liquid was found in the pleural or peritoneal cavity.

The brain weighed 1433g. Serial sectioning of the brain revealed no gross neuropathologic abnormality. Slides from brain, optic nerves, optic chiasma and spinal cord were formalin-fixed and paraffin embedded and then stained by hematoxylin & eosin (H&E) and Luxol fast blue (LFB). Microscopically, the cerebral showed mild oedema, and demyelinating lesions were found mainly affecting posterior columns from the cervical to thoracic level of the spinal cord (Figure 1). Perivascular inflammation associated with neuron damages were noted in the brain, which were identified as scattered lymphocytes and plasma cells (Figure 2). Active demyelinating lesions associated with microglia cells increasing significantly were noted in the optic nerves and chiasma opticum bilaterally (Figure 3). The post-mortem serological testing showed positive result of NMO-IgG. Comprehensive toxicological screening using gas chromatography and mass spectrometry was negative.
DISCUSSION

Here, we discuss the sudden death of a 52-year-old male who has been suffering from serious central nervous system symptoms prior to his death. Main pathologic findings consisted of scattered demyelinating lesions involved the brain, cervical and thoracic cord and optic nerves. Laboratory testing showed seropositivity for NMO-IgG in the blood and excluded other poisonous. Hence, the cause of death was determined as acute neuromyelitis optica (NMO).

NMO (or Devic Syndrome) is an unusual central nerve system lesion with high mortality. Severe respiratory failure caused by the impairments of upper spinal cord leads to sudden death[1]. A recent population-based study indicates Asians and females are more likely to develop NMO[2]. NMO is also known as an autoimmune inflammatory neurological disease characterized by optic neuritis and transverse myelitis[3]. Clinical manifestations are exceedingly variable due to different range and extent of lesions[4]. The patients with NMO typically present visual loss, decreased coordination, paraplegia and sensory impairment [5-7].

Irreversible loss of bowel and bladder control may also occur[6]. Magnetic resonance imaging of brain usually shows unremarkable in the early stage of NMO[5].

NMO is histologically characterized by neuroglia increased, perivascular inflammatory infiltration[8, 9], and demyelination involved brain and spinal cord. Demyelination lesion usually affects 3 or more contiguous spinal cord segments in length[2]. The histopathological changes in the early stage are often accompanied by widespread activation of macrophages and microglial cells resulting in axonal damage[2,6]. The differential diagnosis from other neurological disorders, especially for multiple sclerosis (MS), plays an important role in identifying NMO. MS is another common disseminated demyelinating disorder which has the similar manifestations of transverse myelitis and recurrent optic neuritis with the NMO[11]. Recent studies demonstrate the NMO-IgG in NMO patients is a reliable biomarker with high sensitivity and specificity[12].

It is useful in establishing the diagnosis of NMO as well as distinguishing from MS[13-15]. NMO-IgG which expressed mainly in astroglial foot processes can activate the inflammatory demyelination and widespread necrosis by targeting of aquaporin-4 (AQP4) in the central nerve system[4, 10,16,17]. However, the pathogenic mechanism is still unclear. In our case, the typical histopathological findings of scattered demyelinated inflammation in upper spinal cord and optic nerves

![Figure 3. Marked increased microglia cells and scattered demyelination inflammation in the optic nerves showed in part A (H&E stain, original magnification x10) and part B (Luxol Fast Blue stain, original magnification x4) respectively. Part C and D showed the patches of demyelination and gliosis in the chiasma opticum as well (C, Luxol Fast Blue stain, original magnification x4; D, H&E stain, original magnification x10).](image-url)
by specific stain and the positive serological results of NMO-IgG strongly demonstrated the conclusion of NMO according to the latest diagnostic criteria[7,13].

Clinical features of this case were noteworthy, including typical bilateral visual loss, quadriplegia and bladder dysfunction, unremarkable premonitory symptoms, negative radiographical findings of the brain, rapid deterioration to severe respiratory failure and death. According to the investigation of the medical history, a record of 17 days hospitalization due to injuries caused by street fight was documented prior to his last admission in hospital. Treatment for the scalp laceration and rib fractures were performed. Neither intracranial haemorrhage nor central nerve system abnormalities were found at that time. When he was re-admitted with the arising of visual and spinal cord symptoms, clinicians reviewed the records of injuries and considered about the complications of the previous head injury. They tried to relieve the symptoms but finally failed. The pathogenesis was not yet determined till the patient died.

Clinically missed diagnosis of disease may be attributed to various reasons. In this present case, the recent history of head injury interfered with the clinicians’ judgement of the symptoms. Neurological manifestations from traumatic lesions vary and they are easily confused with other central nerve system disorders. Delayed deaths or symptoms after minor head injury without unconsciousness were infrequently reported. Auer and his colleagues[18] had ever described a case that the victim died unexpectedly seven weeks after the minor head injury due to the vertebral artery injury and haemorrhagic infarction. In such cases of delayed death after head injury, the major pathological findings included infarction, thrombi and haemorrhage in cerebra[19]. In the present case, no significant findings revealing recent traumatic lesions of the central nerve system were seen both grossly and microscopically.

NMO can pose a diagnostic challenge to both clinicians and forensic pathologists when dealing with such case because myriad of disorders could show similar symptoms of NMO, including the multiple sclerosis and neuropathological disorders following head trauma[4]. It is not that common to have such a case that the NMO happened to occur after a head injury. In most cases, an accurate diagnosis of NMO can be made based on a thorough medical history investigation followed by a complete neuropathological examination and serological testing[20]. The present case illustrates the death may occur a considerable time after the injury due to autoimmune diseases which could have nothing to do with the previous injuries. Complete forensic examination should be performed to find out the accurate cause of death.

References