CASE REPORT – OPEN ACCESS

International Journal of Surgery Case Reports 75 (2020) 89–93

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

Severe acute pancreatitis concurrent with lethal rupture of cerebral aneurysm: A case report and review of the literature

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ARTICLE INFO

Article history:
Received 7 May 2020
Received in revised form 11 August 2020
Accepted 12 August 2020
Available online 18 August 2020

Keywords:
Severe acute pancreatitis
Inflammation
Blood-brain barrier
Cerebral aneurysm rupture
Case report

ABSTRACT

INTRODUCTION: With high incidence and mortality, severe acute pancreatitis (SAP) is an inflammatory disease of pancreas. When concurrent with systemic inflammatory response syndrome (SIRS), multiple organ failure syndrome (MODS) or pancreatic encephalopathy (PE), it will significantly augment the mortal rate. Herein, we report the first SAP case complicated with fatal rupture of cerebral aneurysm and pre-existing cerebral arteriovenous malformation; meanwhile, numerous examinations indicated the occurrence of SIRS and MODS.

CASE PRESENTATION: A 34-year-old male was admitted for these complaints of fixed and continuous epigastric distending pain, nausea and vomiting for nearly 6 h after his greasy lunch. Imaging and experimental examinations indicated SAP concurrent with SIRS and MODS in this patient. Conventional therapies stabled him, but he developed unconscious for fatal rupture of cerebral aneurysm based on cerebral magnetic resonance imaging results. Subsequent treatments failed and this patient died from lethal systemic complications.

DISCUSSION: After reviewed relevant literature in detail, we unveil the potential mechanisms in this case that systemic inflammation initiated by necrotic tissues of pancreas will disrupt blood-brain barrier (BBB), increase BBB permeability, trigger neuroinflammation and eventually damage cerebral vascular.

CONCLUSION: Therefore, to prevent lethal complications of PE or cerebral hemorrhage (CM) in severe pancreatitis, more attentions are recommended to be paid on identifying inflammation-induced brain dysfunction and applying prompt anti-inflammatory therapies.

1. Introduction

Severe acute pancreatitis (SAP), possessing the highest mortality in pancreatitis, is an ordinary and exceedingly challenging disease in hepatopancreatobiliary surgery, for its miserable suffering and intractable systemic complications [1]. The secondary infection induced by pancreatic or peripancreatic necrotic tissues triggers release of inflammation mediators, and initiates systemic inflammatory response syndrome (SIRS) subsequently, single or multiple organ failure syndrome (MODS), even death in SAP [2]. To our knowledge, blood-brain barrier (BBB) was impaired and BBB permeability was increased in murine models with SAP [3], which resulted in neuroinflammation or pancreatic encephalopathy (PE) [4]. Furthermore, previous articles have reported that systemic inflammation could induce cerebral microhemorrhage in LPS-treated murine model [5]. Although a similar article published an acute pancreatitis (AP) case with PE and cerebral hemorrhage (CM) [6], clinical evidences on whether extensive inflammation in SAP could lead to damage of BBB and rupture of cerebral aneurysm are rare. Herein, we firstly report a 34-year-old patient who suffered SAP with fatal ruptured cerebral aneurysm, resulted from heavy SIRS-induced neuroinflammation after BBB permeability was destructed in this literature.

2. Case presentation

With these complaints of fixed and continuous epigastric distending pain, nausea and vomiting for nearly 6 h after his greasy lunch, a 34-year-old male was immediately admitted to the emergency department of our hospital. His vital signs were measured and presented as follow: heart rate is 150 per min, blood pressure 120/65 mmHg, body temperature 38.3°C, respiratory rate 30 per min and SPO_2 98%. There was no abnormity in physical examination

Abbreviations: SAP, severe acute pancreatitis; SIRS, systemic inflammatory response syndrome; MODS, multiple organ failure syndrome; PE, pancreatic encephalopathy; BBB, blood-brain barrier; CM, cerebral hemorrhage; CT, computer tomography; MRI, magnetic resonance imaging.

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https://doi.org/10.1016/j.ijscr.2020.08.016

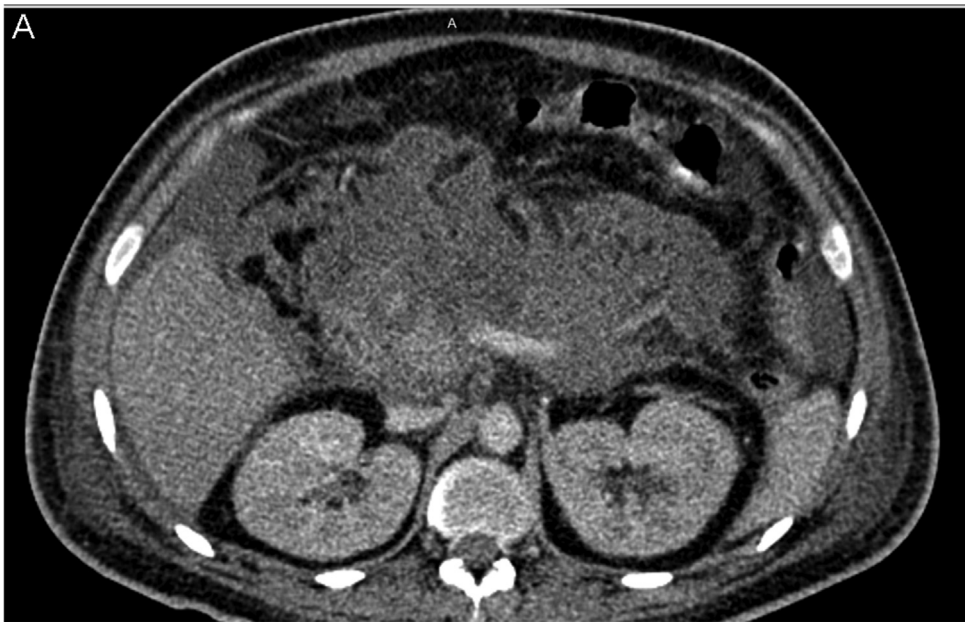

Fig. 1. Computer tomography (CT) scan of pancreas. (A) Representative image of severe pancreatic necrosis and excessive peripancreatic fluid collection.

excerpt for tenderness in epigastrium and percussed pain in hepatic area. The aberrant laboratory test results included elevated white blood cell (WBC) count of 11.39×10^9/mL, in which neutrophil accounts for 83.7%, increased amylase count of 643U/L, extremely high total cholesterol of 12.79 mmol/L, triglyceride of 9.39 mmol/L, creatinine of 312umol/L, procalcitonin of 8.95 ng/mL as well as reduced platelet of 37×10^9/L and triple prolonged prothrombin time (PT). Besides, his abdominal computer tomography (CT) scan showed severe necrosis of pancreas and excessive peripancreatic seepage (shown in Fig. 1), which indicated severe pancreatitis in this patient.

According to the aforementioned symptoms, clinical and laboratory evidences, diagnosis of SAP with hyperlipemia, multiple organ failure (MOF) and SIRS was confirmed. Then this patient was subjected to conventional treatments including antibiotics, protease and gastric acid inhibitors, gastrointestinal decompression and intravenous infusion. However, these therapies failed 2 days after his admission, and further he developed dysphoric and anhelation with SPO_2 decreased to 95%. After his blood gas analysis hinted metabolic acidosis, he was urgently transferred to intensive care unit (ICU) to receive more comprehensive therapies including reducing phlegm, preventing shock, controlling glucose homeostasis, decreasing inflammatory factors and supplementing calcium. Gratefully, he turned to stable during 10 days' intensive treatment in ICU and was sent back to surgical ward.

Nevertheless, he suddenly developed unconsciousness and irresponsive one day after his transfer. Thereafter, Neurological examination was performed, and discovered positive bilateral Babinski sign and abnormalities in dual pupils including different diameters, irregular shape and disappearance of light reflex in left pupil, contracted pupil and bluntness of light reflex in the right. Additionally, head CT and magnetic resonance imaging (MRI) results simultaneously presented a massive intracranial hemorrhage with extensive periphery edema located in the left temporo-parietal lobe and remarkable right-skewed midline (shown in Fig. 2). Furthermore, high blood pressure or coagulation disorder induced hemorrhage were denied because of the normality in relevant tests. Whereas, according to the clinical manifestations of brain dysfunction, suspicious diagnosis of concurrent PE wasn't denied, until his cerebral CT and MRI imaging results illustrated huge hemorrhage.

Consequently, he was subjected to hematoma evacuation and following vascular malformation excision when disorganized blood vessels and a ruptured cerebral aneurysm were found. Total volume of the hematoma reached up to 100 mL. The surgery was a success, but unfortunately this patient died in a week postoperatively. Pathological H&E examination of hemorrhagic brain tissue showed extensive infiltration of inflammatory cells in the brain, which indicated heavy neuroinflammation and cerebral edema (shown in Fig. 3).

3. Discussion

Zhong and Gong reported an AP patient with PE and intracerebral hemorrhage, which was blamed to vascular injury of central nervous system possibly by phospholipase A2 (PLA2) activation [6]. Unlike the aforementioned case, clinical evidences revealed that this patient suffered SAP, subsequently SIRS and MODS. After treated conservatively, he almost turned stable, but suddenly unconscious for the rupture of cerebral aneurysm; besides, cerebral arteriovenous malformation was found and then removed during surgery. Pitifully, this patient didn't survive because of fatal complications and reattack of SIRS after intracerebral hemorrhage. Thus, different symptoms and disease progress implies entirely distinctive relevant mechanism of this patient from Zhong's case.

Hypertriglyceridemia, gradually being recognized as the third etiology of AP behind gallstone and alcohol, together with these clinical manifestations validate our diagnosis [7], and the score from multifactorial scoring systems [8] implicate the severity. PE, characterized by abnormal cerebral functions, such as spatial disorientation, trance and hallucination, usually occurs in the early stage of SAP and heralds a poor prognosis [9]. Whereas, head CT or MRI is not yet a routine examination to identify any abnormality in the brain after admission for AP. This case was initially considered as concurrent PE when displayed numerous neurological symptoms, which confused our diagnosis of cerebral hemorrhage and directly lead to adverse clinical outcome.

The acute inflammatory process of SAP is initiated by self-digestive pancreatic necrotic tissues, followed by extra-pancreatic infections, which increase the mortality of SAP and function as a prediction of local complications [10,11]. In this case, an obvious pancreatic and peripancreatic necrotic region shown in

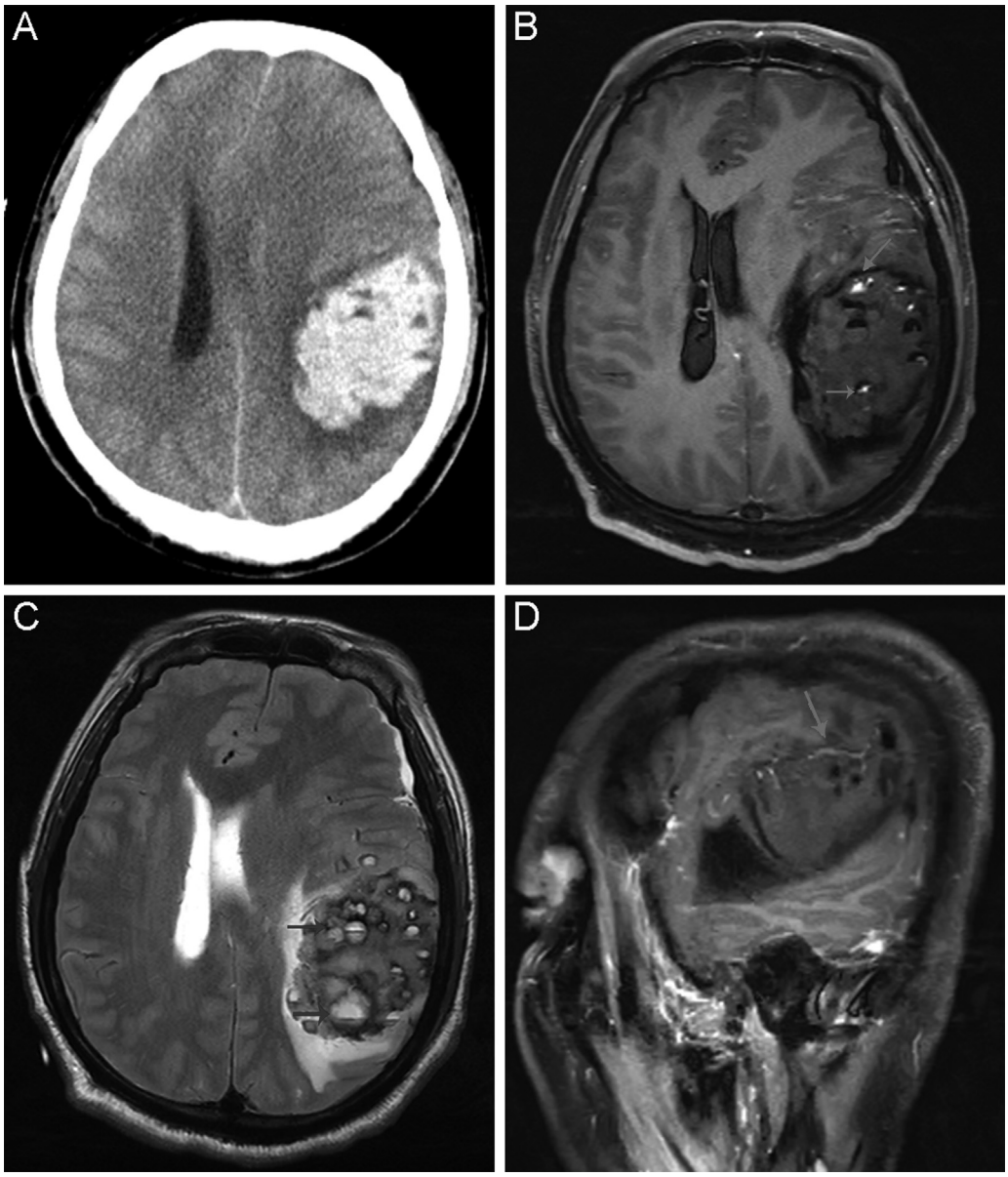

Fig. 2. Representative images showing cerebral hemorrhage (CM) and cerebral arteriovenous malformation in the left temporo-parietal lobe.
(A) Horizontal CT scan imaging showes a 63 mm × 40 mm high-density hematoma in the left temporal-parietal lobe, which results in oppressed left cerebral ventricle and remarkable right-skewed midline.
(B, C) Representative horizontal magnetic resonance imaging (MRI) photographs of CM and cerebrovascular malformation. Apparent edema surrounding hemorrhagic tissues was shown (B) mass of hypointense in T1WI. (C) mass with inhomogenous intensity in T2WI.
(D) Vertical MRI scan of cerebrovascular malformation. The red arrow shows contrasted malformed cerebral vascular, the blue hemorrhagic and inflammatory necrotic brain tissues.

CT image, combined with elevated WBC count and neutrophil percentage during his hospitalization jointly indicated necrotic tissues-induced SIRS. Meanwhile, a clinical trial points out that inhibiting the inflammatory cascade in predicted SAP is of cost-effectiveness to strikingly reduce concurrence and promote the prognosis of SAP [12].

Brain is one of the first target organ vulnerable to SIRS, and numerous researches focus on inflammation-induced impairment of BBB. As described previously, systemic inflammation is closely associated with altered permeability of BBB, and mechanism of LPS-induced BBB disruption is well elaborated [13]. Lin et al. present that SAP results in enhanced BBB permeability and secondary brain edema in a rat model [14]. Pathological H&E staining in our case shows an extensive infiltration of inflammatory cells through BBB in the hemorrhagic brain tissue, which indicates a severe neuroinflammation. Complied with published conclusions that inflammation contributes to the development of intracerebral microhemorrhage [5], and suppressing inflammation would stimulate microglial to repair vascular damage and mitigate vessels leakage [15], we figure out the possible pathophysiological mechanism in such disease process that it is cerebral vascular injury and heavy neuroinflammation induced by SIRS in SAP that leads to the rupture of cerebral aneurysm. However, profound molecular mechanisms underlying how and to what extent inflammation lead to BBB impairment and cerebrovascular damage still require more investigations.

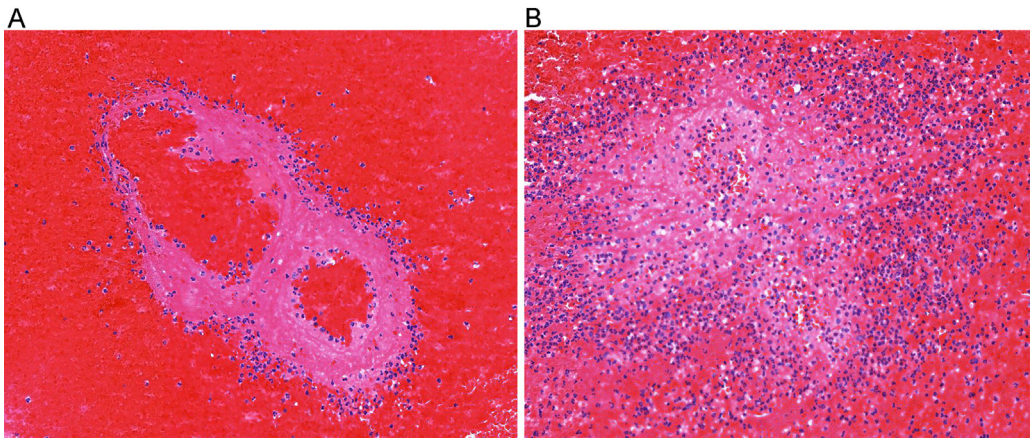

Fig. 3. Pathological H&E staining examination of hemorrhagic brain tissue.
(A) Thinness of artery vessel wall and inflammatory cells penetrating through vessels were shown.
(B) Extensive infiltration of inflammatory cells in the brain tissue. These pictures were photographed at 200× magnification.

4. Conclusion

In summary, we firstly report a SAP case with fatal ruptured cerebral aneurysm, besides, ascribe it to inflammation-induced BBB disruption and cerebrovascular injury. Occurrence of SIRS and MODS in SAP might propel disease progress and consequently raise mortal rate. Hence, we acquire a lesson from this case that once admitted, SAP patients should be promptly subjected to comprehensive nosocomial managements and anti-inflammatory treatments; furthermore, more attentions are suggested to be paid to the surveillance on the functions of each vital organ; and urgent brain CT or MRI imaging is necessary if neurological symptoms are presented.

Declaration of Competing Interest

The authors report no declarations of interest.

Sources of funding

Natural Science Research Funding; Minhang; Shanghai 2018MHZ099.

Ethics approval

This study was approved by the Ethics Committee of Minhang Hospital.

Consent

Written informed consent was obtained from the next of kin of patient for publication of this case report and accompanying images.

Author contribution

Z.Z designed the study. Y.X and J.W was major contributor in collecting patient information and writing the manuscript.

Registration of research studies

N/A.

Guarantor

Ziping Zhang.

Availability of data and materials

Not applicable.

Code availability

Not applicable.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Acknowledgements

We would show great appreciation to all medical staffs involving in the treatment of this patient. Thank you for your efforts!

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