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PARENTERAL PARAQUAT POISONING : A FATAL CASE REPORT AND PATHOLOGICAL FINDINGS REVIEW

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รายงานผู้ป่วยเสียชีวิตจากพิษของพาราควอท โดยวิธีฉีด และทบทวนพยาธิสภาพ

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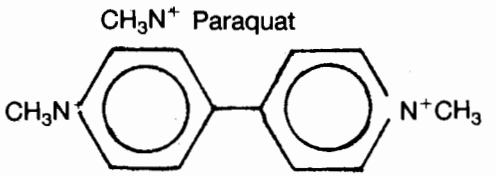
พาราควอท เป็นสารฆ่าหญ้าที่นิยมใช้กันแพร่หลายในหลาย ๆ ประเทศทั่วโลก มีรายงานเกี่ยวกับการเกิดพิษของพาราควอทจำนวนมากในประเทศไทย โดยได้รับทางกิน หายใจ หรือดูดซึมผ่านทางผิวหนัง ในรายงานนี้เป็นรายงานรายแรกของประเทศไทยที่เกิดพิษจากพาราควอทโดยวิธีฉีด โดยผู้ป่วยเป็นชายอายุ 17 ปี มีประวัติดื่มยาฆ่าหญ้า (แอมเฟตามีน) โดยวิธีฉีด ได้ฆ่าตัวตายโดยใช้พาราควอทฉีดเข้าเส้น ลักษณะอาการทางคลินิก ผลการตรวจวิเคราะห์ทางห้องปฏิบัติการ และผลการตรวจทางพยาธิวิทยาได้รายงานไว้ในที่นี้ โดยตรวจพบพาราควอทและสารประเภทฝิ่นในปัสสาวะ และพบแอมเฟตามีนในตับ ผู้ป่วยเสียชีวิตลงด้วยปอดเป็นพังผืดอย่างมาก ร่วมกับภาวะแทรกซ้อนปอดอักเสบติดเชื้อในวันที่ 11 หลังจากฉีดพาราควอทเข้าเส้น (วันที่ 5 หลังจากได้รับไว้รักษาตัวในโรงพยาบาล)

ABSTRACT

Paraquat is a popular and widely used herbicide in many countries all over the world. All cases of paraquat poisoning in Thailand had been reported to induce via oral, inhalation or per-cutaneous routes. Here we report the first case of parenteral paraquat poisoning of a 17 year old male with a problem of parenteral amphetamine addict who committed suicide by paraquat via intravenous administration. His clinical and laboratory investigations including autopsy were performed. Paraquat and opiated compound were detected in his urine and amphetamine was detected in liver. The death ensured from progressive diffuse cellular intraalveolar and intravascular fibrosis (paraquat lung) with complication of pneumonia and septicemia at 11th day after administration (5 days after hospital admission)

Introduction



1,1′ Dimethye-4,4′ bipyridylium ion

Paraquat is an effective Bipyridryl herbicide and widely used in over 130 countries of the world[6]. But it is also extremely toxic for human. The well-known tradename in Thailand is Gramoxone (20% paraquat solution), product of C.I.A. co, Ltd; London. The initial deaths from paraquat occured by accident[8]. Because of the resemblance of paraquat to root beer or a cola drink, espicially when decanted into soft drink bottles left unlabeled. In recent years suicidal deaths predominate. But homicidal deaths had been reported in the United kingdom, the United States, and Japan by mixed with food, because of it's tastelessness in food. Ingestion is the most common route of toxicity. Inhalation, per-cutaneous and sub-cutaneous routes had been published. Recently, one case of parenteral route has reported in Spain[1]. Here is the first fatal case of parenteral paraquat poisoning reported in Thailand.

Case report

Thai patient, a-17-year-old male with a history of parenteral amphetamine addict committed suicide by parenteral self-administration of about 1 ml. of Gramoxone (20% Parquat) After administration he felt hot flushing and then sweating, nausea and vomit. Six days later he was admitted to Kalasin hospital with fever, cough and dyspnea. In the following day, he was refered to Srinagarind hospital for better care.

Physical examination revealed dyspneic and cyanosed young man with good consciousness. Blood pressure 100/60 mmHg. Pulse rate and respiratory rate were 104/min and 44/min respectively. Body temperature showed mild fever (38℃). Heart inspection only showed sinus tachycardia without murmur. The physical examination was otherwise within normal limits.

He received supportive treatment until died on the 5th day of hospital admission from pulmonary failure.

Laboratory analyses and radiography

Table 1 Showed biochemical parameters determined between the patient's admission and death. The blood creatinine and urea level increased that represented progressive impairment of renal function. In liver function test; the rise of serum transaminase (SGPT, SGOT) reflected liver cell damage.

Table 1 Biochemical parameters

Day x (y) / (Normal range values)	1(8)	2(9)	3(10)	4(11)
Glucose(70-100 mg%)	103			
Urea (5.8-19.1 mg%)	49.2			
Creatinine (0.8-2.3mg%)	2.9		3.6	
Na (130-147)	135		140	
K (3.4-4.7)	3.5		4.2	
HCO_3 (20.6-28.2)	21.9		19.4	
Cl (96-107)	101		105	
Total protein (6.5-8.8)	8.0		7.3	
Albumin (3.8-5.4)	4.0		3.3	
Globurin (2.6-3.4)	4.0		4.0	
Total bilirubin(0.25-1.50)	0.71		1.03	
Direct bilirubin(0-0.25)	0.24		0.40	
SGPT (4-36)	34		579	604
SGOT (12-22)	53		1392	832
Alk phos (37-147)	78		116	

Note : X = Day of admission, Y = Day after parenteral administration

Table 2 Gasometric parameters

Day x(y) / (Normal range values)	1(8)	2(9)	3(10)	4(11)
PO_2 (mmHg) (80-100)	46.3	70.9	89.2	93.2
PCO_2 (mmHg) (35-45)	24.1	32.2	46.2	41.1
pH (7.35-7.45)	7.479	7.468	7.269	7.332
BE (0±2mmol/L)	-2.2	1.1	-5.8	-4.2
HCO_3 (22-26)	17.2	22.4	20.1	21.1
SO_2 (%) (96-97)	81.8	94.3	93.4	96.4
Fio_2 (L/min)	Room air	7 Lpm	.60	.60

Table 3 Radiography (Figure 1)

Day x(y)	findings
1(8)	Interstitial infiltration (Reticular) both lungs
2(9)	infiltration ↑, with Subcutaneous emphysema
3(10)	infiltration ↑↑
4(11)	

Gasometric parameters

Table 2 showed arterial blood gas. In the first and second days of admission, it showed hypoxemia with respiratory alkalosis and the last two days of admission, it showed respiratory acidosis.

Ante-mortem Toxicological reports

During admission, plasma and urine were sent for detecting amphetamine and paraquat by thin layer chromatography method (at Department of toxicology, Faculty of Pharmaceutical Sciences) No quantitative test was done. The report showed positive both of amphetamine and paraquat in urine, but negative in plasma.

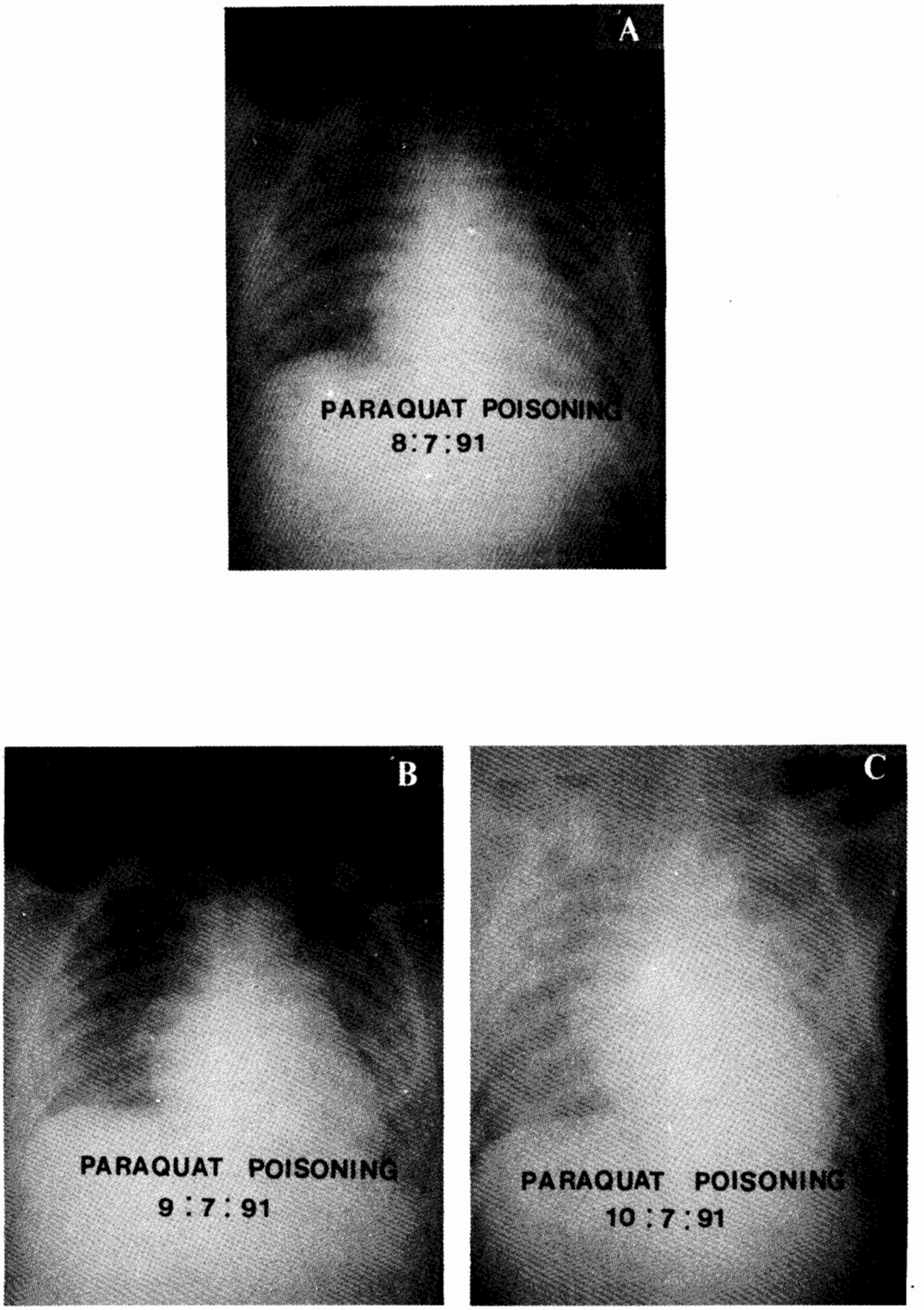


Figure 1 : Three chest films (A,B,C) show progession of pulmonary infiltration and pulmonary edema

Post-mortem findings

Gross examination revealed a deceased young Thai male who weighed 55 kilograms and his height was 162 centimeters. No abnormalities were found

Internal findings are summarized in Table 4

Table 4 Internal findings

organs	weight (grams)	Macroscopic	Microscopic
Brain	1500	Congestion,Moderated edema with bilateral tonsillar herniation(Figure 2)	Edema,Gliosis
Heart	320	Marked congestion	Focal myocardial necrosis
Lungs	655 (R) 570 (L)	Greenish mucopurulent in tracheobronchial trees, firm consistency with diffuse scattered white patch infiltration (Figure 3A)	Diffuse cellular intra-alveolar and intravascular fibrosis with pulmonary edema (Figure 3B,3C,3D)
Liver	1400	congestion (Figure 4A)	Centrilobular necrosis (Figure 4B)
Kidney	155 (R) 150 (L)	congestion	Cortical tubular necrosis (Figure 5)

The Stomach showed congestion, hemorrhagic gastritis (Figure 6) and the rest of internal organs were congestion

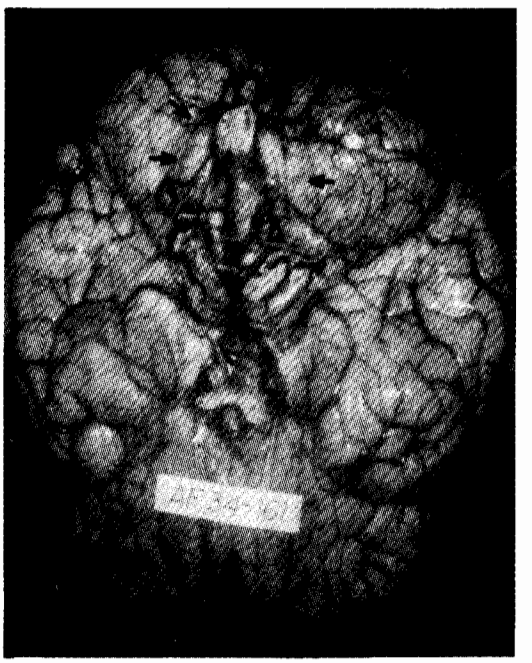


Figure 2 Brain showed congestion and edema with bilateral tonsillar herniation (arrow)

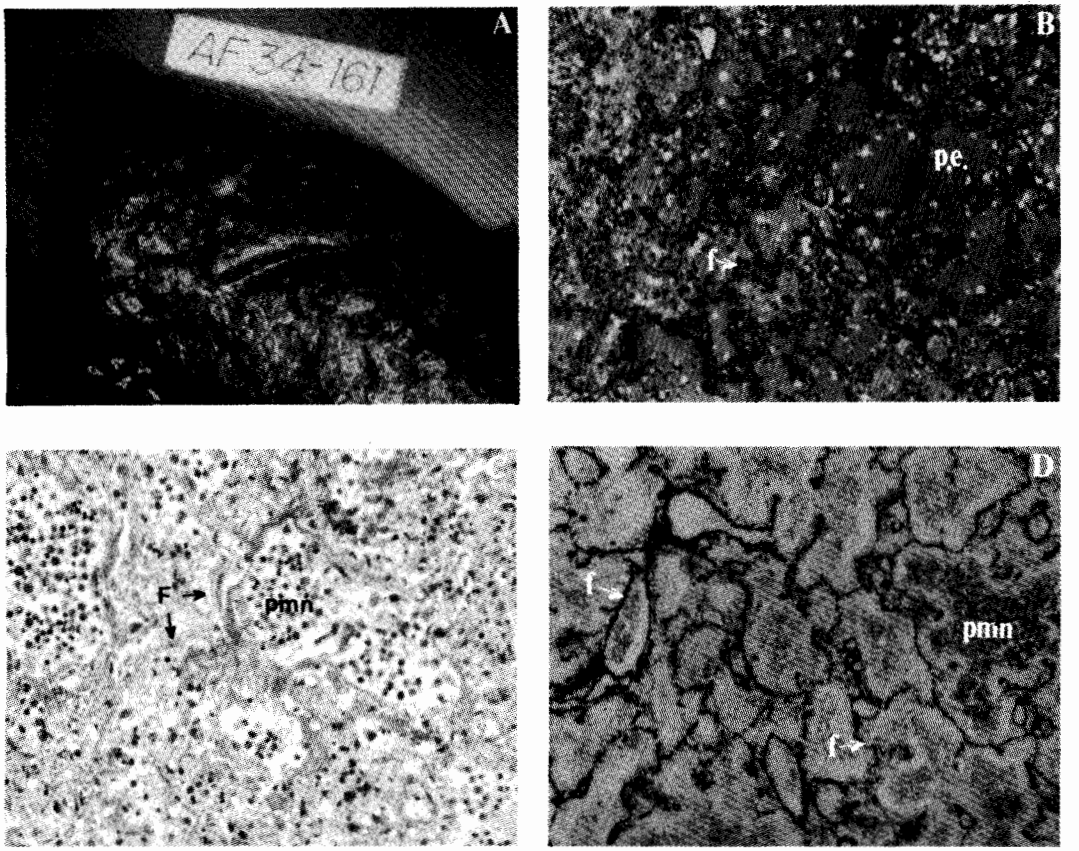


Figure 3 (A) coronal section of the lungs show diffuse scattered white patch nifiltration, represent pneumonia

(B) Pulmonary fibrosis (f) and pulmonary edema (p.e.) (H&Ex40)

(C) Pulmonary fibrosis (F) and polymorphonuclear leukocytes (pmn) infiltrate. (Masson x 100)

(D) like 3. (C) (Reticulin x 40)

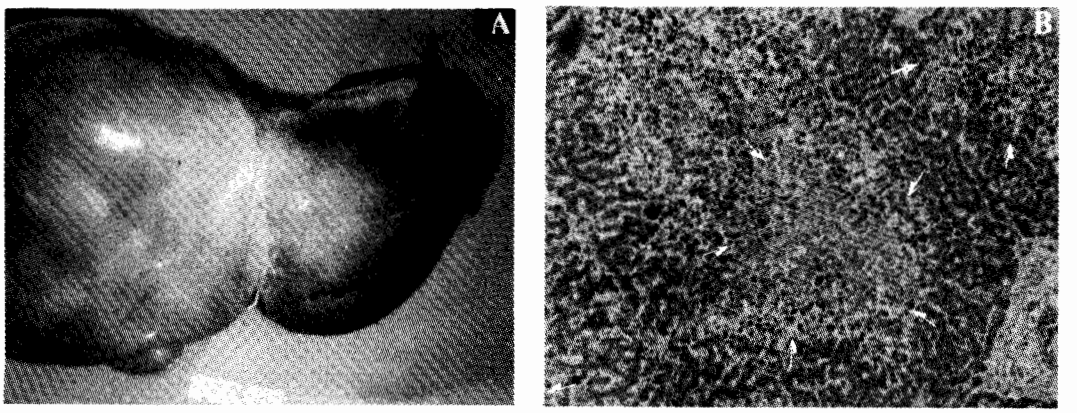


Figure 4 (A) Congested Liver. (B) Centrilobular necrosis area (arrow) of Liver (Masson x 40)

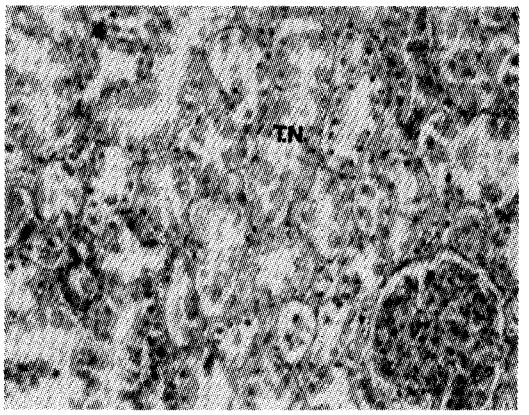


Figure 5 Cortical tublar necrosis (T.N.) of renal tubules (H & E x 100)

Figure 6 Congested and hemorrhagic gastritis.

Post-mortem toxicological & bacterial culture reports

After autopsy, many biological specimens (lung, liver, kidney, bile and urine) were sent to toxicological laboratory, Faculty of Pharmaceutical Sciences for toxico- medicinal compounds analysis. The urine showed positive both of paraquat and opiate compound and amphetamine was found in liver by thin layer chromatography. Quantitative test and the rest specimens (lung, kidney, bile) were not analysed. include liver for paraquat and opiate compound. Bacterial isolated showed in Table 5

Table 5 Post - mortem bacterial cultures

Specimens	Bacteria
heart Blood	- Enterobactor Species - Citobactor freudii
lungs	- E. coli - Klebsiella Pneumonia - Acinetobacter vas anitratus - Enterobactor hemolytic type

Discussion and conclusion

The most important prognostic indicator of paraquat toxicity is the quantity of paraquat absorbed, as shown by the plasma paraquat concentration[15]. The published cases, which subcutaneous and parenteral administration showed more than severity, especially in lungs pathology. Paraquat is very poorly absorbed though intact skin. But its caustic properties can produce the wound that will permit greater systemic absorption. The lowest known concentration of paraquat to result in fatal cutaneous case in 5 g/l[16]. Inhalation route occured by spraying without protective mask, which can produce irritant in respiratory tract, conjunctivitis and epitaxis. Spraying inhalation is less systemic toxicity because of its low vapor pressure and large spray droplets. Smoking inhalation had been reported in Mexico[11] by contaminated with marijuana. No fatal case has been reported both of spraying and smoking inhalation. The other signification prognostic indicators were volume of paraquat administrated, concentration, serum creatinine (Cr), potassium (K^+), arterial blood bicarbonate and base excess levels, arterial blood pH, the strength of urinary paraquat qualitative test (Sodium dithionate; blue colour reaction), respiratory index ($RI=A\text{-}aDo_2/PO_2$; survivors $RI<1.5$ and non-survivor $RI>1.5$ at any time point after ingestion), RI-time (defined as the time taken from ingestion for the RI to be greather than 1.5[2])

The fatal dose for human has been estimated to be as small as 4 mg/kg[12]. In this case, although he received only about 1 ml of 20% paraquat solution (3.64 mg/kg). But parenteral route can be direct systemic absorption and he died 11 days after admistration. Fernandez P. et al. reported[11] parenteral admistration of about 4 ml of 20% paraquat, death occured 15 days after hospital admission. However the severity of pathological finding showed more severe than in basically oral route, especially in lungs pathology.

Paraquat poisoning pathologic findings review can be conclude as

skin & mucosa[8,12]

: Erythema, mild reactive hyperkeratosis, blistering and pustular formation, cracked nails.

: Ulceration lips, tongue, pharynx and esophagus. Pseudomembrane reminiscent of diphtheria.

Brain[5]

: Neuronal depletion (probably secondary to anoxia) and particularly the brain around the lateral and third ventricle. Examination of the brain by electron microscopy showed edema and destruction of myelin with abundant myelin breakdown products, and astrocytic fibrous gliosis

Heart[6,8,11]

: Epicardial hemorrhage, Myocartitis and focal myocardial necrosis.

Lungs[3,4,12]

: The target organ is the lungs because of it is high oxygen tension organ. Oxygen must be use in oxidative reaction, which can produce superoxide radical. There are two stages of lungs injury. In the early stage, the alveolar epithelium degenerates but the epithelial basement membrane remain intact. In the late stage, the epithelial basement membrane is focal disrupted, the mesenchymal cells grow into the alveolar space, and intra-alveolar fibrosis appears. Intra-alveolar fibrosis may follow as consequence of damage to the epithelium without severe damage to the underlying basement membrane[3]. Lungs pathology showed progessive diffuse cellular intra-alveolar and intravascular fibrosis, pulmonary hemorrhage and edema, atelectasis and hyaline membranes formation[12]. Complication, spontaneous pneumothorax can occur in acute or chronic phase[4].

Stomach

: Stomach showed hemorrhagic gastritis

Liver[14]

: It may be show mild liver dysfunction without jaundice, nonspecific reactive changes with intact bile ducts and ductules. Or dilatation of bile canaliculi with decrease of microvilli and thickening of pericanalicular ectoplasm in the hepatocytes. Centrilobular cholestasis with extensive bile duct loss. Or centrilobular necrosis that found in this case

Kidney

: Acute tubulo-interstitial nephritis, Renal tubular necrosis.

Adrenal glands[12]

: Necrosis of the adrenal cortex (mostly in fasciculata and reticularis)

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