Case Conference

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2012/10/24

Patient Data

Case 1:

- 60 y/o, male
- Day1 , 00:41
- E4V5M6
- TPR: 36.6 /111/18 BP:176/84 mmHg
- SpO2: 98%
- 檢傷主訴：全身肢體無力，家屬11PM起覺有口齒不清，怪異行為
- Triage: **1**

History

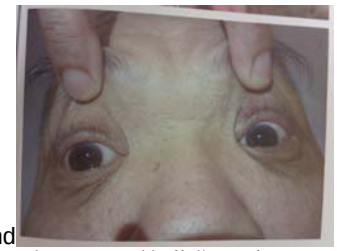
- Chief Complaint: Delirium-like behavior since 10 PM
- 走路搖來搖去
- 會講錯東西
- 大舌頭

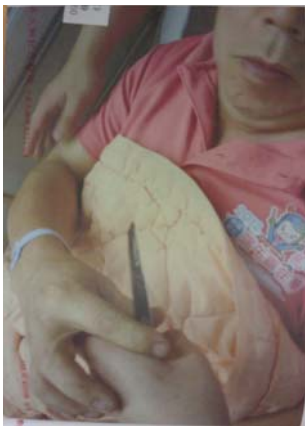
Past History

- Allergy: NKA
- HTN (took medication before but stopped for long time, SBP 130+mmHg), Hyperglycemia (200+ without medications)
- Occupation: 鐵工（焊接油漆工）

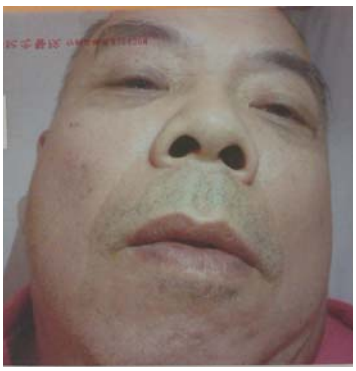
Physical Examination

- Cons: clear
- Appearance:怪怪的
- Neurological exams:
  - Pupil: 4- / 4-
- Neck: LAP(-)
- Chest: clear BS
- Heart: RHB
- Abdomen: soft
  - Hypoactive bowel sound
- Extremity: no drift sign , 有picking的動作，走路要扶





Picking movement



Facial flushing

Impression

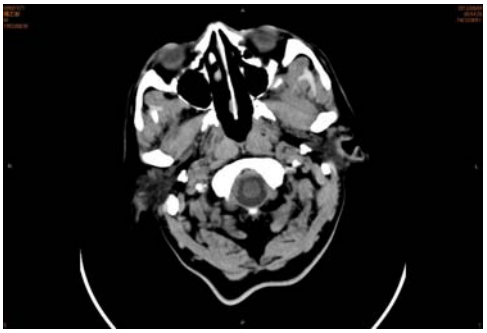
- Delirium ?
- r/o stroke ?

Initial management

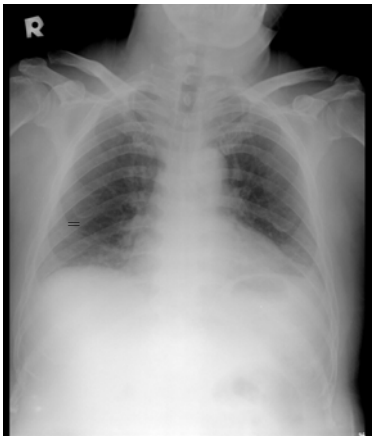
Day1 00:44

- **啟動 t-PA, cosult Neuro**
- Check CBC/PLT, PT/aPTT, GOT, BUN/Cr, Ammonia, CO, VBG(G6), F/S: 134
- 12-lead ECG, CXR, **Brain CT**
- IV: N/S 60ml/hr

CT 00:51



CXR 00:53



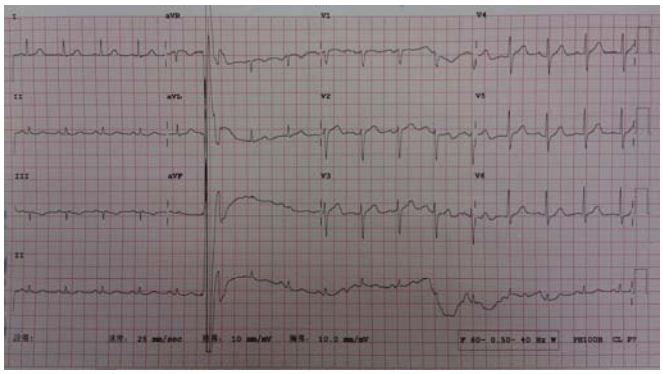
Lab Data 01:20

CBC/DC		PT/aPTT		Biochemistry	
WBC (x10³/uL)	11400	PT	12.2	GOT (U/L)	21
RBC (x10⁶/uL)	4.13	PT (INR)	1.17	BUN (mg/dL)	19
Hb (g/dL)	12.4	APTT	33.5	Cr (mg/dL)	0.8
HCT (%)	36.8			Ammonia	48
MCV (fl)	89.1				
MCH (Pg)	30.0				
MCHC (%)	33.7				
PLT (x10³/uL)	284k				

Lab Data 01:20

VBG(G6)		AVOXimeter 4000	
pH	7.445	Measured	
PaCO2 (mmHg)	35.6	tHb	10.9 g/dl
PO2 (mmHg)	65	O2Hb	92.2%
BE	0	COHb	1.8% *(0-3%)*
HCO3	24.4	MetHb	0.3%
TCO2	26	Calculated	
SO2	93%	O2Ct	14.0 mL/dL
Na	139		
K	3.5		

ECG 01:35



Neuro consultation

4days ago　　1day ago

吃中藥粉
back pain
(trauma)

17:30 吃中藥粉
21:30 吃另一種中藥粉 (unknown content, 熬煮)
22:30 general weakness, gait disturbance, disorientation
23:00 dysarthria, bilateral hands 空中揮舞, numbling, disorientation, delusion

Conscious: confusion (E4V4M5), illusion (牆上的紅點是蟑螂)
Mentality: poor judgement, poor attention and memory
Cranial nerve: pupil4.5+/4.5+, no facial palsy, no EOM limitation, positive corneal reflex, no obvious dysarthria
Muscle power: full, DTR: intact 2+
Gait: not fast (ataxia?)

Impression: adrenergic/ anticholinergic effects
r/o drugs/ toxin exposure
r/o non-convulsive seizure (complex partial seizure)

ER course

Day1 01:46

- Bedside echo: acute urinary retention
  - R/O anticholinergic intoxication
- IV hydration
- On monitor
- F/U Conscious level
- Check toxic screen, BZD, alcohol
- Arrange EEG

ER course

Day1 02:00

Biochemistry	
BZD	<3
Ethyl alcohol	undetectable

ER course

Day1 06:55

- S: Feel better
- O: conscious clear, E4V5M6
  pupil: 3+/3+, MP: full

ER course

Day1 12:20

- EEG
  - Non specific slow wave
  - No seizure like

ER course

Day1 15:20

- 走路都正常了，自覺沒事，pupil: 4+/4+ ➔ MBD

CVA 重要性>acute delirium

- Time is brain !!!
- 症狀有overlap時要優先處理會死的 會被告的

CVA symptoms

Traditional symptoms	Sudden numbness or weakness of face, arm, or leg—especially unilateral
	Sudden **confusion or aphasia**
	Sudden memory deficit or spatial orientation or perception difficulties
	Sudden visual deficit or diplopia
	Sudden dizziness, **gait disturbance, or ataxia**
	Sudden severe headache with no known cause
Nontraditional symptoms	Loss of consciousness or syncope
	Shortness of breath
	Sudden pain in the face, chest, arms, or legs
	Seizure
	Falls or accidents
	Sudden hiccups
	Sudden nausea
	Sudden fatigue
	Sudden palpitations
	Altered mental status

Discussion

Anticholinergic intoxication

INTRODUCTION

- Anticholinergic intoxication is commonly encountered, and familiarity with the management of this syndrome is essential for the emergency clinician

Table 196-1 Major Groups of Substances with Anticholinergic Activity

Class and Subclass	Prototypical Agent(s)
Antidepressants	
Cyclics	Amitriptyline hydrochloride, imipramine hydrochloride, doxepin hydrochloride
Selective serotonin reuptake inhibitors	Fluoxetine, paroxetine, sertraline
Specific serotoninergic antidepressants	Mirtazapine
★ Antihistamines	
Ethanolamines	Diphenhydramine, dimenhydrinate
Ethylenediamines	Tripelennamine
Alkylamines	Chlorpheniramine
Piperazines	Loratadine, meclizine, cetirizine
Phenothiazines	Prochlorperazine, promethazine
Antiparkinson drugs	
Tropanes	Benztropine mesylate
Piperidines	Trihexyphenidyl
Antipsychotics	
Phenothiazines	Chlorpromazine, thioridazine, perphenazine
Nonphenothiazines	Clozapine, olanzapine, molindone, loxapine
Antispasmodics	
Cyclohexanecarboxylic acids	Dicyclomine
Quaternary ammonium	Methantheline bromide
Belladonna alkaloids	
Tropanes	Atropine, homatropine, scopolamine hydrobromide
Pyrrolidines	Glycopyrrolate
Mydriatics	
Phenylacetates	Cyclopentolate hydrochloride
Pyridines	Tropicamide
Skeletal muscle relaxants	
Tricyclics	Cyclobenzaprine hydrochloride
Ethylamines	Orphenadrine citrate
Plants	
Datura species	*D. stramonium* (Jimson weed), *D. candida* (angel's trumpet)
Mandragora species	*M. officinarum* (mandrake)
Brugmansia species	*B. suaveolens* (angel's tear, maikoa, or white angel's trumpet), *B. versicolor* (angel's tear or angel's trumpet)
Amanita species	*A. muscaria, A. pantherina*

SPECIAL CONSIDERATION

- **Most common**
  ➔*antihistamine*
- **Children**
  ➔*anti-spasmotics, diphenhydramine salves*
- **Elderly**
  ➔*additional effect, oph instillation*
- **Taiwan**
  ➔ *Single-plant exposure; Belladonna alkaloids*
  （顛茄生物鹼）

KINETICS

- Onset: usually occurs ***within one to two hours of oral ingestion***
  - Atropine: achieves peak plasma concentrations within two hours
  - May delay

PHARMACOLOGY AND CELLULAR TOXICOLOGY

- “Antimuscarinic effect“
- **Peripheral effect**
  - Parasympathetic nervous system
  - Tachycardia, flushing, dry mouth, ileus, urinary retention
- **Central effect**
  - Fever, agitation, delirium, coma

Table 196-2 Muscarinic and Antimuscarinic Effects

Organ	Stimulation or Muscarinic Effect	Antagonism or Antimuscarinic Effect
Brain	Complex interactions, possible improvement in memory	Complex interactions, impairs memory, produces agitation, delirium, hallucinations, and fever
Eye	Constricts pupil (miosis), decreases intraocular pressure, increases tear production	Dilates pupil (mydriasis), loss of accommodation (blurred vision), increases intraocular pressure
Mouth	Increases saliva production	Decreases saliva production, dry mucous membranes
Lungs	Bronchospasm, increases bronchial secretions	Bronchodilation
Heart	Bradycardia, slows atrioventricular condition	Tachycardia, enhances atrioventricular conduction
Peripheral vasculature	Vasodilation (modest)	Vasoconstriction (very modest)
GI	Increases motility, increases gastric acid production, produces emesis	Decreases motility, decreases gastric acid production
Urinary	Stimulates bladder contraction and expulsion of urine	Decreases bladder activity, promotes urinary retention
Skin	Increases sweat production	Decreases sweat production (dry skin), cutaneous vasodilation (flushed appearance)

CLINICAL FEATURES

- **"Dry as a bone" (anhidrosis)**
- **"Hot as a hare" (anhydrotic hyperthermia)**
- **"Red as a beet" (cutaneous vasodilation)**
- **"Blind as a bat" (nonreactive mydriasis)**
- **"Full as a flask" (urinary retention)**
- **"Mad as a hatter"**
  - Anxiety, agitation, confusion, disorientation,, delirium, coma
  - Dysarthria
  - Psychosis (paranoia), visual or auditory hallucinations
  - Repetitive picking at the bed clothes or imaginary objects
  - Jerking movement and seizures
- **Others:** decreased or absent bowel sounds

Anticholinergic v.s. sympathomimetic

Diaphoresis?

CLINICAL FEATURES OF OVERDOSE

- ***Tachycardia***, which is the earliest and most reliable sign of anticholinergic toxicity
  - Diphenhydramine: WCT, QT prolong
    - Sodium channel blocker effect

FATALITY !!!

- ***Severe agitation***
- ***Status epilepticus***
- ***Hyperthermia***
- ***WCT***

DIAGNOSIS AND WORK-UP

- ***The diagnosis of anticholinergic toxicity is based on clinical findings***
- For rule out and severity assessment
  - Electrocardiogram (ECG)
    - Coingestants, TCA, phenothiazines
  - CK
  - And depends

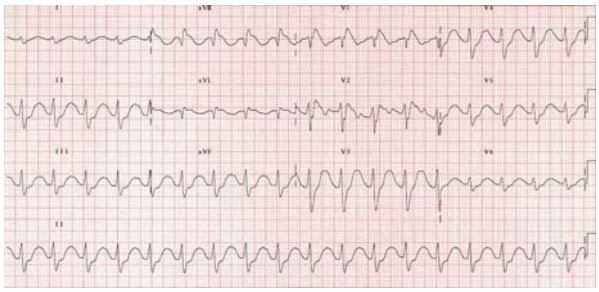
MANAGEMENT
Initial treatments

- **Stabilization of ABC**: the airway, breathing, and circulation
- IV access, oxygen, cardiac monitoring, pulse oximetry,
- ECG, toxin screen
- Evaporative cooling for hyperthermia

Control of the agitated individual

- Inadequate sedation may lead to worsening hyperthermia, rhabdomyolysis, and traumatic injuries
- **Pharmacologic sedation better then** physical restraints
- **BZD**

ECG finding and treatment



Antidote ?

Physostigmine

- ***Physostigmine can be considered in cases of severe agitation and delirium, especially in cases necessitating physical restraints and not responsive to benzodiazepines***
- Mechanism
  - Carbamate acetylcholinesterase inhibitor
- Adverse effect
  - Bradycardia, seizure, arrhythymia (few)

Antidotal therapy with physostigmine

- **Contraindication**
  - Not a purely anticholinergic poisoning is suspected (eg, TCA overdose)
  - ***QRS interval is at or above 100 msec***
  - Asthma, intestinal obstruction, epilepsy, and cardiac conduction abnormalities
- **Dose**
  - Adult: 0.5 to 2 mg, slow IV push (>5mins)
  - Pediatrics: 0.02 mg/kg IV (maximum: 0.5 mg per dose)
  - May be repeated after 20 to 30 minutes (half life: 15min)

Antidotal therapy with physostigmine

- **Setting**
  - ***Cardiac monitor, and atropine and resuscitative equipment***
  - Look for symptoms of cholinergic excess:

    DUMBELS
    - **D**iarrhea, **U**rination, **M**iosis, **B**ronchospasm/bronchorrhea, **E**mesis, **L**acrimation, **S**weating

Physostigmine臨床上不好用

- severe agitation =>先插管加 pharmacology paralysis快又安全
- 容易有coingetion
- 看走眼 ex : TCA中毒 只看出其中的 anticholinergic effect
- 打解藥還要備解藥的解藥太不實際

可否用physostigmine診斷 anticholinergic intoxication

Summary

Table 196-3 Treatment of Anticholinergic Toxicity

Action	Agent	Comments
GI decontamination AACT: <1hr	Activated charcoal (1 g/kg; maximum 50 g)	May be more effective due to the decreased GI motility.
Sedation Pharmacologic sedation is strongly recommended	Benzodiazepines Lorazepam	Decreases the risk of hyperthermia, rhabdomyolysis, and traumatic injuries.
Wide-complex tachyarrhythmias	Sodium bicarbonate	Arrhythmia due to sodium channel blockade, avoid class IA antiarrhythmics (procainamide).
Cholinesterase inhibition Controversial	Physostigmine	Use for cases of severe agitation or delirium, avoid when cardiac conduction abnormalities are present (see Treatment section).

DISPOSITION

- Severe symptomatic / physostigmine use → ***admission for continued observation***
- Mild symptoms & asymptomatic in 6 hours → ***discharge***
- Moderate symptomatic → ***admission for at least 24 hr***

Two instances of chinese herbal medicine poisoning in Singapore

Phua D H, Cham G, Seow E

Singapore Med J 2008; 49(5) : e131

Case 1# 42 y/o Chinese woman

30mins — Chinese herbal medicine

2 hrs — Giddiness
Eyes rolled upwards
Upper limbs stiffened

TPR: 36.8/144/19 BP:142/85 SpO2:100%
Disoriented, empty eyes,
E4V1M5 Pupil: 6-/6-
Non-purposeful movements of four limbs
Absence of sweating
No facial flushing
Absent bowel sounds

CBC, Cr, e-: WNL
EKG: ST
CT: normal

4 hrs — Recovered

Discharged the following day

Case 2# 59 y/o Chinese man

30mins — Chinese herbal medicine

1hrs 30mins — Unwell
Blurred vision, lower limbs weakness

TPR: 36.8/81/18 BP:147/64 SpO2:97%
Disoriented
E4V1M? Pupil: 5-/5-
Non-purposeful movements of upper limbs
Absence of sweating
No facial flushing
Sluggish bowel sounds

CBC, Cr, e-, ABG: WNL
EKG: normal
CT: normal

8 hrs — Recovered

Discharged 2 days later

Summary of the two cases

- Presented as anticholinergic toxidrome
- Onset: 30 minutes
- No antidote was given
- Resolved: few hours

What is the causative agents?

- **Datura Metel L.**

Fig. 1 Photograph shows the remnant sample of *Datura metel L.*

Fig. 2 Close-up photograph of the remnant sample of *Datura metel L.*

Datura (曼陀羅)

- 科: 茄科 (Solanaceae)
- 屬: 曼陀羅屬 (Datura)
- 種
  1) 大花曼陀羅 (Datura suaveolens Humb.& Bonpl.ex Willd)
  2) 曼陀羅花 (Datura metel Linn.)
  3) 紫花曼陀羅 (Datura tatula Linn.)
  4) 毛曼陀羅 (Datura innoxia mill)
  5) 歐曼陀羅 (Datura stramonium L.)
  6) 無刺曼陀羅 (Datura inermis Jacq.)
  7) 重瓣曼陀羅 (Datura fastuosa L.)

Datura (曼陀羅)

- **別名:** 喇叭花、洋金花、醉心花、狗核桃、醉仙桃、瘋茄兒
- **外型:** 曼陀羅花一般有白色、紫色或淺黃色，蘋果呈圓球形，表面有肉刺
- **功能主治：**平喘止咳，鎮痛，解痙。用於哮喘咳嗽，脘腹冷痛，風濕痺痛，小兒慢驚；外科麻醉。
- **有毒部位:** 曼陀羅花全株有毒，以果實及種子毒性最大，乾葉的毒性則比鮮葉小

- 咳嗽及氣喘 (食煮)
- 毒蛇咬傷、腫瘡及跌打損傷 (鮮葉搗汁外敷)
- 《七俠五義》中的迷魂藥，及《水滸傳》中的蒙汗藥
- 《本草綱目》記載：「相傳此花釀酒飲，引人笑、令人舞。」「熱酒，調服二錢，子頃昏昏如醉，割瘡灸火宜先服此，即不覺苦也。」; 做為麻醉藥
- 誤食 (茄子)

Case series of anticholinergic poisoning after Chinese Medicine use

Chinese Pharmaceutical Affairs 2000:14(3);173-174. (In Chinese)

- N: 7
- 1998-2000
- Contaminated **Cangshu by rootstocks containing tropane alkaloids** was the commonest cause of CHM relate anticholinergic poisoning in Hong Kong (5/7)

Back to our patient

- **Onset: within 1 hr**
- ✓ **Tachycardia, facial flushing, nonreactive mydriasis, decreased bowel sounds, urinary retention**
- ✓ **Delirium, illusion, picking movement**
- **Gradually resolved with supportive care and close monitoring in several hours**
- **Causative agents: unknown (通血路中藥)**

參考資料

- Tintinalli 7ed
- Uptodate