A CASE OF CANTHARIDIN POISONING

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Cantharidin is a substance which can be extracted from the bodies of some species of beetles of which the Spanish fly (Cantharis vesicatoria) is probably the best known. It is the anhydride of cantharic acid with a chemical formula as follows: 3:6-epoxy-1:2-dimethylcyclohexane-1:2-dicarboxylic anhydride. It occurs in the form of odourless and colourless crystals which are relatively insoluble in water but soluble in chloroform, acetone, ether and fixed oils.

Hippocrates recommended cantharides for the treatment of dropsy more than 2,000 years ago. It had been used mainly as a counter-irritant and lesicant to relieve pain in conditions such as pleurisy and pericarditis. Vinegar of cantharidin and solution of cantharidin had also been used in hair lotion for their rubefacient action. Cantharides and cantharidin are highly toxic, deaths have been produced by 1.5 to 3 G. and less than 60 mg. respectively.

Cantharidin poisoning can occur as a result of overdosage of cantharides used as a counter-irritant (Avery, 1908) or accidentally when using it as a bait in fishing (Lecutier, 1954). Criminal poisoning with cantharidin was much in vogue at one time (Leschke, 1934). In 1847, Brunet compiled from criminal statistics in France as many as 20 murders or attempted murders occurring within a few years in which cantharides powder had been mixed as a spice in the soup of the intended victims.

Cantharidin has the unfortunate reputation of being an effective aphrodisiac and abortifacient, but the dose required for such effect is usually toxic. A case of death due to taking Spanish fly as an aphrodisiac was described (1951). The man took 1.5 grains of the substance, developed abdominal pain and vomiting soon after and died the same evening. Nickolls and Teare (1954) reported the post-mortem findings on two young women dying of cantharidin poisoning following ingestion of coconut ice to which crystalline cantharidin had been added with aphrodisiac intent. Symptoms appeared 5-10 minutes after eating the sweet, death occurring 16 and 24 hours later. Autopsies showed excoriation of the mucosa of the gastrointestinal tract, intense engorgement of the genitourinary tract with frank blood in the renal pelvis, ureters, bladder and ovaries, peripelvic and periureteric haemorrhages, petechial haemorrhages on surface of heart and subendocardium of interventricular septum, intense injection of whole of the bronchial tree with fine frothy blood-stained mucus in the air passages, gross oedema of the lungs and fatty chages in the liver. Here the fatal dose is believed to be less than one grain. Polycythaemia and marked leucocytosis were present in one of the two victims (Craven and Polak, 1954). The causes of death in these cases were peripheral circulatory and acute renal failure respectively.

A young Dutch seaman aged 22 years was recently admitted with history of abdominal pain, haematuria and oliguria. No history of ingesting any form of aphrodisiac was obtainable but urine analysis showed presence of cantharidin. The following is a summary of his case history.

He was admitted on 19.5.61, complaining of dull ache over the left loin for six days. Four days before admission, he had a severe attack of abdominal pain mainly over the left side and the suprapubic region followed by passage of frank blood and strangury. Since then he had passed very little urine and had not passed any on day of admission. There was no history of vomiting, diarrhoea, fever, sore-throat or swelling. He had never had similar pain or haematuria before. He denied emphatically taking any form of aphrodisiac. He was referred as a case of 'acute nephritis'.

On examination: Temp. 99°F. No puffiness of face; no oedema of legs. No glands felt. Cardiovascular system: neck veins not engorged; pulse: 100, regular; B.P. 160/100; heart: not enlarged clinically, soft systolic murmur all over, dual rhythm; fundi: N.A.D. Respiratory and central nervous systems: N.A.D. Gastro-intestinal tract: tongue clean, no blister; throat: markedly injected; no excoriation seen in oral cavity. Abdomen: marked tenderness with guarding over the left side of the abdomen and left renal angle; liver, spleen and kidneys were not palpable. Rectal examination: tenderness in front, no melaena.

By the next morning, tenderness and guarding had spread to the rest of the abdomen

particularly over both loins and suprapubic area. Oliguria was present.

Laboratory Investigations: Hb. 88%. Total white count: 10,000 per c.mm. P 83%, L 10%, M 6%, E 1%; platelet 130,000 per c.mm. Bleeding time: 1¼ min., clotting time: 2¼ min., prothrombin time: 20 sec. (control: 16 sec.). Urine: alb. ++, w.b.c. 10-12, r.b.c. 60-70, no cast, no epithelial cells; culture: no growth. Blood urea: 137 mg.%. B.S.R. 45 mm. (1st hour). Culture of throat swab: normal flora.

X-Ray Chest: Markings appear to be generally heavy — cannot exclude pulmonary congestion; heart size top normal with prominent left ventricle. X-Ray abdomen: no calcified stone seen.

Because of the high blood urea and oliguria, he was managed as a case of acute tubular necrosis, being given limited fluid intake and no protein and fat in his diet. Pethidine and atropine were given for his pain.

A cystoscopy was done on 23.5.61 by Mr. Harrison-Levy and showed intensive trigonitis and some general cystitis; ureteric orifices and efflux were normal.

As his general condition improved and urine output increased, a 24 hour specimen of urine was collected and this after extraction showed presence of cantharidin.

The tenderness of his abdomen completely subsided on 25.5.61, i.e., on the 7th day after admission. Urine was free from red cells on 2.6.61 and from white cells from 5.6.61. Only a trace of albumen was detected since the same date. Blood urea came down rapidly with recovery and on 26.5.61 it was 47 mg.%. On 6.6.61, three days before discharge, the blood urea was 23 mg.%.

An I.V.P. done on 9.6.61 was normal and B.P. before discharge was 130/80. He was discharged on 10.6.61 completely free from symptoms and went back to Holland soon after.

The unusual features of this case are firstly, the repeated denial of voluntary ingestion of the drug in any form. It is conceivable that it might have been mixed up in food or drink by another party with the usual intent to produce sex stimulation, or that it was accidentally taken by the patient. However no one else in the crew suffered similar symptoms. Again there was no sign of blistering of the mouth or lips so characteristic of the cases reported, although in the analysis of the urine the Government chemist reported blistering effect of the final extract on the skin of three members of his staff — this was in fact one of the methods of detection of cantharidin used in the cases reported by Nickolls and Teare (1954). Whether a similar effect could be produced by another agent is doubtful although it might have been better to use X-Ray diffraction method by the same authors. Lastly, the absence of overt gastrointestinal bleeding is difficult to explain in the absence of direct evidence of absorption through other routes. This case was reported because of the clinical presentation as a case of acute tubular necrosis, howbeit with obvious involvement of the major portions of the urinary tract. The diagnosis was suggested by the severity of symptoms, the abrupt onset in a healthy young man with no previous history of kidney disease and lastly by a high 'suspicion-index' with reference to the hazards offered to unwary seamen stranded in big seaports.

The pathological picture in these cases is believed to be due to the direct toxic effect of cantharidin on the various organs. There is no specific antidote to cantharidin. A demulcent is recommended (Lecutier, 1954). Treatment is mainly symptomatic, directing at the peripheral circulatory failure if present and the acute renal failure. The ultimate prognosis is good as regards renal function if the patient survives the acute phase.

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