

Suicide by Skull Stab Wounds

A Case of Drug-Induced Psychosis

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Abstract: Suicide by stabbing to the head and/or driving sharp objects into the skull is of extreme rarity. This article reports the case of a 27-year-old man, who committed suicide by multiple knife stabs and cuts to the head, the torso, one shoulder and the forearms. Autopsy showed a perforating wound of the skull and the 10-cm long broken blade of the knife being still embedded in the right temporal lobe of the brain. The deceased had no history of psychiatric illness but was currently treated by mefloquine, a quinine derivative associated with a high rate of psychiatric adverse effects. Toxicological examination confirmed a recent intake of mefloquine together with chloroquine, another antimalarial drug. To our knowledge, this is the first report of a completed suicide with very strong evidence of mefloquine implication. Discussion focuses upon mefloquine-induced psychiatric disorders and highlights the importance of performing toxicological investigations in cases of unusual suicides.

Key Words: mefloquine, adverse effects, psychosis, suicide, sharp force
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Mefloquine ((R*, S*)-(±)-α-2-piperidinyl-2,8-bis (trifluoromethyl)-4-quinolinemethanol hydrochloride; molecular weight, 414.78), a 2-aryl substituted analog of quinine, has been in widespread use since 1982 under the trade name Lariam (Roche Pharmaceuticals, Neuilly-sur-Seine, France) for the prophylaxis and the treatment of malaria caused by chloroquine-resistant *Plasmodium falciparum* or *Plasmodium vivax* in geographical areas. In adults, the dose regimen for prophylaxis is one 250-mg tablet once weekly. Higher doses (eg, 1250 mg as a single oral intake or 1500 mg distributed for 12–16 hours) are required for curative purposes. From 1987 onward, a number of studies have highlighted the risk of psychiatric adverse effects, sometimes serious, prone to occur in patients undergoing this therapy.

This article presents an exceptional case of suicide by sharp force in a patient without previous history of mental illness, in which the triggering role of an intercurrent treatment by mefloquine was highly presumable.

CASE REPORT

A 27-year-old man was found dead at home, lying on his bed. Doors were locked from the inside, and there was no evidence of violence in the flat. The deceased was completely

naked, with abundant bloodstains on the whole body surface. The 10-cm long handle of a kitchen knife, also stained with blood, was present near the corpse with the blade broken at approximately 1 cm from the guard. The rest of the blade was apparently missing. According to cadaveric signs and police findings, death was likely to have occurred the day before.

Postmortem Examination

At autopsy, general examination of the skin surface found 8 wounds, all presumably caused by a sharp, cutting instrument, that were distributed as follows:

- Two superficial cuts at the lower, anterior part of the neck
- Two stab wounds, 0.5 cm long for the anterior and 1.5 cm long for the posterior, in the right temple
- One 1-cm-long stab wound in the precordium area
- One 3-cm-long cut at the top of right shoulder near the acromion
- One 4-cm-long cut at the anterior side of the right forearm
- One deep, 10 cm in length and 6 cm in width, complex cross-shaped incised wound at the anterior side of the left forearm and wrist (Figs. 1 and 2).

All stabs and cuts had clean margins, and none were associated with tentative wounds. Dissection of the head showed a perforating wound of the right temporalis muscle and greater wing of sphenoid bone near the pterion, aligned with the posterior stab of the right temple (Fig. 3). Opening the skull allowed to retrieve the missing part of the knife (a 10-cm-long distal fragment of a single-edged blade) with a wound path oriented from right to left and slightly backward transecting the right temporal lobe and the point of the blade found embedded in a notch at the right side of the pituitary fossa (Figs. 4 and 5). Autopsy findings were otherwise unremarkable, except for a 320-mL hemothorax of the left pleural cavity without penetrating wounds of the lung or the pericardium.

Further investigations revealed that the deceased was just back from a visit in Africa, during which he took mefloquine for malaria prophylaxis. He had no history of medical or psychiatric illness and never displayed signs of depression or suicidal ideation. According to the medical examiner, death was attributed to craniocerebral injuries caused by sharp force, with a high degree of violence being necessary to make the blade penetrate the victim's skull (Fig. 6). Although unexpected and quite exceptional in its circumstances, the manner of death was ruled suicidal.

Toxicological Analyses

Toxicological analyses were performed on postmortem fluids using colorimetry (meprobamate in blood), fluorescence polarization immunoassay (benzodiazepines, barbiturates, and tricyclics in blood; usual drugs of abuse in urine), gas chromatography (ethanol), and liquid chromatography with diode-array detection (general-unknown screening for pharmaceuticals, toxicants, and abused drugs in blood). Mefloquine was the only drug

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FIGURE 1. Body in the flat.



FIGURE 3. Stab wounds in the right temple.

identified (heart blood concentration, 8 µg/mL; gastric content, 6 µg/mL), together with chloroquine, another antimalarial agent (heart blood, 6 µg/mL; gastric content, 3.5 µg/mL). Owing to extensive postmortem redistribution affecting both mefloquine and chloroquine,^{1,2} these results are difficult to interpret but seem not suggestive of a recent, massive intake of either drug (gastric levels in the same order of magnitude than blood levels). Drug screening was otherwise quite negative.

RESULTS AND DISCUSSION

Acute psychiatric reactions, in particular depressive disorders, have been reported as an adverse effect of a wide array of medications,³⁻⁵ including nonsteroidal anti-inflammatory drugs,⁶ antihypertensive drugs,⁷ anticonvulsants,⁸ steroids,⁹ or antimalarials.^{10,11} Among this latter group, mefloquine distinguishes itself by a high prevalence of various psychiatric adverse effects, which has been pointed out as of the early postmarketing period.^{12,13} In 1989, the World Health Organization commissioned an investigation that confirmed the existence of such complications, with a prevalence estimated at 4.2/1000 treatments.¹⁴ The various effects observed were ranked in 3 categories:

- Slight complications: fatigue, loss of balance, concentration and memory difficulties, and sleep disorders
- Moderate complications: vertigo, logorrhea, vision disturbances, anxiety, depression, agitation, and confusion

- Serious complications: deep depression, suicidal ideation, panic attack, convulsions, manic behavior, acute psychosis with often paranoid delusions.

In 60% of reported cases, disorders appeared after the first intake of mefloquine. Serious complications were noticed only for curative treatments with doses equal to or greater than 1000 mg. As a result of these observations, the World Health Organization made the following recommendations¹⁵: (a) mefloquine should be contraindicated in patients with previous psychiatric history or those having tasks requiring coordination or concentration, (b) particular care should be taken with mefloquine at high, curative dosages, and (c) for prophylaxis, mefloquine administration should begin at least 1 week before arrival in an endemic area.

Further studies confirmed these initial reports and revealed the existence of predisposition factors such as intercurrent infections, previous psychiatric diseases, or a previous history of epilepsy.¹⁶⁻¹⁹ In addition, they showed that serious complications may also arise even at low-dose regimens intended for prophylaxis (risk estimated at 1/50,000 prescriptions). Such events are most often clustered around the beginning of treatment (in 90% of cases, they are observed within the first 3 weeks), but they may also supervene later and/or last long after mefloquine has been discontinued.²⁰⁻²³ Prospective trials that focused on the adverse effects of antimalarials found minor/moderate psychiatric effects



FIGURE 2. Cross-shaped incision at the anterior side of the left forearm and wrist.



FIGURE 4. Kitchen knife with blade broken.

related to mefloquine with a frequency of up to 1 of 140 patients.^{10,17,24–26} They also pointed out the risk of severe complications including acute delusional crises with disorientation and hallucinations, manic-depressive psychosis, or deep depression. Several cases of mefloquine-induced suicidal ideation have been reported^{23–27} and at least 1 suicide attempt by drowning.²⁸ Adverse events are more likely to occur in women than in men^{19,25,29,30} and have also been observed in children.³¹ No correlation seems to exist between blood levels of mefloquine and the occurrence of severe adverse effects.³⁰ Up to date, approximately 20 reports of patients with serious complications have been published in France, without prior history of psychiatric illness in half of them.²⁰

In the present observation, there is a very strong presumption that mefloquine was implicated as a causative or at least contributive factor in the victim's suicide. This statement is supported by the following:

- The extraordinary method used to commit suicide: although suicides by sharp force are rather infrequent (they account for only 2%–3% of all suicides in developed countries),^{32,33} those by stabbing to the head and/or driving sharp objects into the skull are exceedingly rare—less than 30 cases being reported in the literature since 1928.^{34–42}
- The absence of psychiatric history in the victim, whereas most suicides by sharp force to the head have been reported in mentally disturbed patients and prison populations.^{34,36,37,43}
- The close temporal relationship between suicide and mefloquine intake, as documented by the detection of the drug in postmortem samples. In the present observation, the contributive role of chloroquine coingestion is difficult to assess because psychiatric adverse effects encountered with this drug are much more infrequent than with mefloquine.^{10,11} However, it may be noteworthy that at least 1 severe reaction, including paranoia, hallucinations, and suicidal ideation, has been reported in a subject without psychiatric history and successively treated by mefloquine then by chloroquine.²³

As proven by numerous studies and isolated case reports for the past 20 years, the use of mefloquine is associated with an increased risk of psychiatric events including acute psychosis and deep depression with suicidal ideation. To the best of our knowledge, however, the present observation seems to be the first case of a completed suicide in which very strong evidence of mefloquine implication was documented on the



FIGURE 5. View of the opened skull during removal of brain: knife blade transecting the right middle cranial fossa.



FIGURE 6. Wounds in the skull.

bases of death circumstances and toxicological measurements. Although such events fortunately remain quite infrequent, forensic practitioners should keep in mind the possibility of drug-induced psychoses and depression, and toxicological analyses should be the rule in unusual suicides especially in subjects with no known psychiatric history.

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