Oberhausbergen, 15 June 2015

Ref: case Vladimir Kara-Murza

15A494

Report about the examination of hair, blood and urine

On 30 May 2015, I have received in my office in Oberhausbergen, a set of human samples, attributed to Vladimir Kara-Murza.

These specimens included: blood, urine, hair and nail (no label on the tubes)

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The request was to analyse these specimens for a large screening of drugs.

Analyses

Pharmaceuticals, drugs of abuse, chemicals, solvents, volatile substances, cyanides, pesticides were screened by GC/MS, LC/DAD, HS-GC/MSLC-MS/MS and LC/MS-time of flight in blood and urine.

Metals and elements were screened by ICP-MS in hair

Results

The following results were obtained:

Blood

Cyanides at normal range (< 80 ng/ml)

Presence of fluconazole, propofol and lidocaine

Omeprazole: 3,9 mg/l

Escitalopram: 74 ng/ml

Citalopram: 105 ng/ml

Urines

Presence of 4-heptanone, cyclohexanone, propofol

Absence of drugs of abuse

Lidocaine: 1,3 mg/l

Escitalopram: 3,7 mg/l

Citalopram: 3,9 mg/l

Presence of dobutamine, ketamine and norketamine, and oseltamivir

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<u>Calculation of the dosage of citalopram</u>

Citalopram has been used as an antidepressant since 2014.

It exists has a racemic drug, or as the S-enantiomer, escitalopram. After administration of citalopram, a portion of escitalopram is circulating in the body.

The half-life of the drug is about 33 hours (24 to 40 hours), irrespective of enantiomer. The volume of distribution is about 12-16 L/kg

In the blood sample from 29 May 2015, at 10 pm, the total citalopram was 179 ng/ml. This can be considered as a therapeutic concentration (therapeutic range 50 - 200 ng/ml) if the last exposure occured on the same day as the day of blood collection. However, one can anticipate that citalopram was not administrated after the symptoms have started (this point must be verified).

It is indicated that the clinical symptoms started on 26 May 2015, at around 3.30 pm.

Therefore, for pharmacological calculations, one can estimate that the last administration of citalopram was in the morning on 26 May 2015 (a delay of about 82 hours is therefore calculated between the last exposure and the time of blood collection).

Maximal blood concentration is given by:

$Cmax = C \times 2^{nb\ of\ half-lives}$, with C, the measured concentration (179 ng/ml) and the number of half-lives (82 / 33 = about 2.5), and $Cmax = 179 \times 2^{2.5} = 1013$ ng/ml.

The total dosage can be calculated by: dose (in μg) = Cmax x Vd x P, with Vd volume of distribution (Vd about 14 L/kg) and P the weight of the subject (85 kg)

Dose = 1013 x 14 x 85 = 1205470 μg, that corresponds to about 1,20 g

This can be 30 tablets of 40 mg of the drug

Numerous factors can influence this interpretation. In particular, the calculation is only valid in case there is no defect in metabolism (liver failure) or elimination (kidney failure). This must be discussed in relation with the clinical records.

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Analysis for elements

Hair specimen was strongly decontaminated using acetone (5 mL, 2 min) with horizontal shaking.

After weighing, hair (10 mg) was mineralized in polypropylene tubes with 250 µL of Suprapur 65% nitric acid at 70°C for 60 min.

Before testing, the residue was diluted 1:40 with 0.1% nitric acid and 0.01% Triton X-100. Rhodium (Sigma, Saint Quentin Fallavier, France) at 1 ng/mL was added as an internal standard.

Arsenic and other elements were quantitated in hair sample by ICP-MS on a Thermo Electron X7 (Waltham, MA) apparatus.

The RF generator power was 1.4 kW. The plasma gas flow rate of argon was as follows: nebulization, 0.95 L/min, plasmagen 13 L/min, and auxiliary 0.90 L/min.

The following results were obtained:

Element	Limit of detection (μg/L)	Concentration (ng/mg hair)	Normal values (5ème 95ème percentiles)
Lithium	0,1	0,099	0,003-0,042
Beryllium	0,1	Not detected	0,003-0,012
Magnesium	5	121,2	127-153 (IAEA)
Vanadium	0,1	0,02	0,001-0,051
Chromium	0,1	0,16	0,11-0,52
Manganese	0,1	33.9	0,016-0,570
Iron	50	0,68	13-177
Cobalt	0,1	0,02	0,004-0,14
Copper	1	112	9,0-61,3
Zinc	20	473	129-209
Arsenic	0,1	0,15	0,03-0,08
Selenium	1	2,43	0,37-1,37
Strontium	0,1	2,44	0,17-4,63
Molybdenum	0,1	0,17	0,010-0,028
Rhodium	0,01	0,01	-
Palladium	1	0,89	0,004-0,049
Cadmium	0,1	Not detected	0,004-0,17

Tin	0,1	0,21	0,007-0,34
Antimony	0,1	0,13	0,003-0,13
Baryum	0,1	0,85	0,05-1,58
Cerium	0,01	0,015	-
Tungsten	0,01	0,064	0,0001-0,007
Platinum	0,01	0,003	0,00035-0,0008
Mercury	0,1	2,01	0,31-1,66
Thallium	0,01	0,002	0,0001-0,0004
Lead	1	2,02	0,13-4,57
Bismuth	0,1	0,010	0,0004-0,14
Thorium	1	0,002	-
Uranium	0,01	0,067	0,002-0,03

From the results, it appears that 4 elements are at higher dosages than the normal population. This includes manganese, zinc, copper and mercury.
On the opposite, the concentration of iron appears too low.

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