

CASE REPORT

Toxic liver disease after intentional paracetamol abuse for a suicide attempt in a 15-year-old girl

Anna Mania¹, Katarzyna Jowik², Katarzyna Mazur-Melewska¹, Paweł Kemnitz¹,
Wojciech Służewski¹, Magdalena Figlerowicz¹

¹Department of Infectious Diseases and Child Neurology, Poznan University of Medical Sciences, Poznan, Poland

²Students' Scientific Association of the Department of Infectious Diseases and Child Neurology, Poznan University of Medical Sciences, Poznan, Poland

ABSTRACT

We present a case of a 15-year-old girl who was admitted to hospital due to vomiting, diarrhoea, jaundice, and fever, which were observed for about a week. Liver dysfunction was found in laboratory tests, and the diagnostic process suggested autoimmune hepatitis. Anamnesis and new information from the patient's family members led to the diagnosis of toxic liver disease after intentional paracetamol abuse for a suicide attempt. There were some essential risk factors: teenage, female sex, serious family troubles. The use of paracetamol for the purpose of suicide is a frequent phenomenon. Because of the increasing number of suicides in teenagers in Poland, it seems to be important to remind to paediatricians about their reasons and risk groups, as well as about clinical and laboratory symptoms of paracetamol poisoning.

KEY WORDS:

children, hepatitis, paracetamol, toxic liver disease.

INTRODUCTION

An increasing number of suicides has been noticed in recent years among children and teenagers. In 2013 suicide was the cause of death in nearly 20% of people between 15 and 19 years of age [1]. Intentional poisoning is found more frequently in girls (90%) and children from urban areas (over 70%) Moreover, family (including alcohol abuse by the parents) and school conflicts are the main causing factors [2].

Substances used most frequently in suicide attempts are psychotropic substances, non-steroid anti-inflammatory drugs, and painkillers. Paracetamol is a medical substance of antipyretic and painkilling potential available without a prescription – over-the-counter (OTC). It is one of the most frequently bought and

overused drugs, not only in Poland but also all over the world [2–4].

CASE REPORT

A 15-year-old girl was admitted to hospital due to severe vomiting, diarrhoea, and raised body temperature (around 38°C) lasting for about a week. The symptoms were present despite symptomatic treatment and Nifuroxazide, introduced by a general practitioner. History analysis revealed dyspeptic symptoms for around three months and yellow discoloration of the sclerae for about a month before admission to hospital. The patient had psoriasis. The mother of the patient died because of pneumonia and sepsis in the course of acquired immunodeficiency syndrome (AIDS). According to available clinical data of the

ADDRESS FOR CORRESPONDENCE:

Magdalena Figlerowicz, Department of Infectious Diseases and Child Neurology, Poznan University of Medical Sciences, 27/33 Szpitalna St., 60-572 Poznan, Poland, e-mail: mfiglerowicz@gmail.com

girl, tests for the presence of human immunodeficiency virus (HIV) were negative – anti-HIV antibodies test was performed twice.

TABLE 1. Results of basic blood tests performed in a 15-year-old girl with a toxic liver disease after intentional paracetamol abuse

Laboratory test	Result on the 1 st day of hospital stay	Reference range
Cellular blood count:		
WBC	10.39 (10 ³ /μl)	4.00–10.00
RBC	4.37 (× 10 ⁶ /μl)	4.00–5.00
Hb	13.1 g/dl	12.0–16.0
Hct	39.4%	37.0–47.0
MCV	90.2 fl	80.0–94.0
MCH	30.0 pg	27.0–34.0
PLT	241 (× 10 ³ /μl)	150–400
CRP	0.68 mg/dl	< 0.5
ALT	1676 IU/l	< 23
AST	4264 IU/l	< 25
GGTP	12 IU/l	4–24
ALP	94 IU/l	50–162
Total bilirubin:	2.53 mg/dl	0.18–1.23
indirect	1.69 mg/dl	0.20–0.80
direct	0.84 mg/dl	< 0.20
Ammonia	83 μg/dl	< 82
Glucose	75 mg/dl	60–101
Total protein	7.0 g/dl	5.7–8.0
Albumin	4.5 g/dl	3.5–5.2
Lactate	2.40 mmol/l	0.5–2.2
Coagulation tests:		
fibrinogen	195 mg/dl	180–350
prothrombin index	64.8%	80.0–120.0
INR	1.63	0.85–1.25
APTT	40.22 s	25.9–36.6
D-dimer	1620 ng/dl	< 500
Creatinine	0.55 mg/dl	0.24–0.73

WBC – white blood cells, RBC – red blood cells, Hb – haemoglobin, Hct – haematocrit, MCV – mean corpuscular volume, MCH – mean cell haemoglobin, PLT – platelets, CRP – C-reactive protein test, ALT – alanine aminotransferase, AST – aspartate aminotransferase, GGTP – gamma-glutamyltransferase, ALP – alkaline phosphatase, INR – international normalized ratio, APTT – activated partial thromboplastin time



FIGURE 1. Bag with white powder found in the room of 15-year-old girl with toxic liver disease after intentional paracetamol abuse

On admission, physical examination showed dehydration, yellow discoloration of the sclerae, and pain in the right upper quadrant of the abdomen on palpation. Dehydration level was assessed as moderate according to clinical dehydration scale (CDS) by dry oral mucous membranes, sunken eyes, and cold limbs. Laboratory tests revealed increased aspartate and alanine aminotransferase activity – 4264 IU/l (upper normal limit-UNL < 25 IU/l) and 1676 IU/l (UNL < 23 IU/l), respectively. Moreover, GTP and lactate were increased, and prolonged INR and low potassium level were observed. Ammonia, uric acid, and direct bilirubin slightly exceeded UNL. Remaining laboratory tests including cellular blood count with differential, urinalysis, creatinine, total protein albumins, and blood glucose were within reference values (Table 1). An abdominal ultrasound examination did not reveal any abnormalities. Differential diagnostics included serological tests for primary and secondary hepatotropic viruses – hepatitis A, B, and C viruses, Epstein-Barr virus, cytomegalovirus, and HIV, which excluded viral infections. Immunoglobulin levels in IgG, IgA, IgM class, levels of alpha-fetoprotein, carcinoembryonic antigen, ceruloplasmin, and ferritin were within reference values. Anti-nuclear antibodies (ANA) in serum were detected – 1 : 320 ratio, speckled nuclear pattern. Antibodies against LKM-1, AMA-M2, SLA/LP, LC-1, Sp100, PML, gp210, and Ro-52 were negative.

Taking into account physical findings and results of the laboratory tests autoimmune hepatitis (AIH) was strongly suspected [5]. Risk of AIH was evaluated according to the scale of the International Autoimmune Hepatitis Group (14 points), which confirmed the suspicion of the disease. Therefore, liver biopsy was scheduled to take the samples for histological evaluation.

Hepatoprotective drugs (ornithine aspartate) were used starting from the day of admission; electrolyte imbalance was corrected, lactulose was used orally. The administration of vitamin K was not needed. At the end of the first week of treatment dyspeptic symptoms disappeared, and biochemical abnormalities normalised.

On the fifth day of the hospital stay a legal guardian of the girl reported to the attending physician that a notebook suggesting strong interests in body weight reduction and anorectic behaviours was found in the girl's room along with a small bag containing white powder (Fig. 1). The substance was sent to the forensic medicine laboratory, and the test proved that the bag contained acetaminophen (paracetamol). The substance was not found in the girl's blood (the test was performed five days after admission). The girl, however, confessed to taking paracetamol on daily bases for the last couple of weeks in pills and in powder (made from pills) with the intention to commit suicide. The precise dose of paracetamol taken by the patient was impossible to determine.

According to the girl, it was a well-conceived decision, which was preceded by interests in taking her own life. The patient mentioned a difficult relationship with one

of the family members, with verbal and mental violence, which caused mood imbalance, a decline in motivation, and suicidal thoughts. She denied nutritional problems, provoking vomiting, and intentional restrictions in her intake of food.

The legal guardians were informed about the suicide attempt and the emotional problems of the girl. Psychoeducation was conducted, and family therapy was advised. A liver biopsy was not performed. After a decline in aminotransferase activity, the patient was discharged home in good general condition with the advice of hepatological and psychological follow-up.

The girl has been followed in the Hepatology Outpatient Clinic for three years after discharge (until she turned 18 years old). Aminotransferase activity stayed within reference values in control tests.

DISCUSSION

Paracetamol (acetaminophen or N-[4-hydroxyphenyl]acetamide) is an antipyretic and pain-relieving drug with no anti-inflammatory potential. Its mechanism of action is based on the inhibition of prostaglandins through preferential inhibition of cyclooxygenase-2 (COX-2) and selective inhibition of cyclooxygenase-3 (COX-3). Absorption in the gastrointestinal system is very high, and bioavailability reaches 80%. Moreover, it binds to plasma proteins to an insufficient extent, which increases its safety [6]. The substance is metabolised mostly in the liver, where 95% is conjugated and oxidised, and finally excreted by kidneys as glucuronides and sulphates. 5–20% is metabolised by liver cytochrome P450 (isoform CYP2E1, CYP1A2, and CYP3A4). In the reaction with CYP2E1 N-acetyl-4p-benzoquinone imine (NAPQI) is formed, which displays hepatotoxic and oxidising potential.

Cellular glutathione supply, a natural source of -SH groups, is exhausted during paracetamol overuse. These groups are necessary to detoxify NAPQI. Thus, a shortage of glutathione leads to hepatocyte necrosis and the injury of myocardial, kidney, and pancreas cells [6–10].

Acetaminophen has a broad therapeutic spectrum. The maximal daily dose for an adult should not exceed 4 g in single use and 2.5 g in prolonged use. In the case of children, 10–15 mg/kg is a recommended dose 4×/day. Availability of paracetamol is widely discussed. In the United Kingdom National Poisons Information Service – a centre advising in cases of poisoning – records over 4000 questions a year from healthcare workers regarding patients who exceed the dose of this medication [11].

Single dose > 150 mg/kg or over 7.5 g in adults and > 200 mg/kg of body weight in children may cause toxic liver injury. In the case of multiple repeated supratherapeutic ingestion (RSI), hepatotoxic doses are lower: for patients < 6 years old > 200 mg/kg of body weight for one day or > 150 mg/kg daily for 48 hours or > 100 mg/kg for 72 hours. For patients > 6 years old and body weight

> 50 kg do dose is > 4 g/day and < 50 kg the dose is > 75 mg/kg/day [12].

The symptoms of paracetamol poisoning may manifest in four phases. Phase 1 (first 24 hours) is asymptomatic in the majority of patients. Nausea and vomiting may be present along with pain in the abdomen, increased sweating, pale skin, and weakness. Very severe symptoms (coma, severe lactic acidosis) are hardly present in the first day of poisoning. In phase 2 (after 24 to 72 hours) pain and tenderness in the right upper quadrant of the abdomen and jaundice develop. The symptoms are accompanied by increased aminotransferase activity and increased INR, bilirubin level, hypoglycaemia, and metabolic acidosis. Phase 3 (after 72 to 96 hours) comprises fulminant liver failure with hepatic encephalopathy and haemorrhagic diathesis (less frequent). Increased creatinine level is observed between the second and fifth day of poisoning. Phase 4 (death or regeneration of the liver) – fatal outcome of fulminant liver failure usually develops between the third and fifth day of poisoning. In some patients, liver dialysis (usually single pass albumin dialysis) or/and liver transplantation are necessary. In other patients, laboratory parameters normalise in seven to 14 days [13]. According to current data of Great Poland Centre of Occupational Medicine in Poznan, the number of patients treated because of paracetamol poisoning has shown continuous growth since 1994. Over 90% of cases are suicides [14].

The described clinical situation concerns a child with high risk of suicidal behaviours regarding multiple co-existing risk factors: age (puberty), female gender, and family situation (mother's death and surrounding circumstances, being raised by members of extended family, conflict with caregivers). Moreover, the girl had psoriasis. Chronic skin lesions in the course of the disease could cause lower self-esteem of the child.

Based on the clinical condition of the girl and the results of laboratory tests, we could diagnose phase 2 of paracetamol intoxication. Thanks to the hospital stay and medical help, the toxic liver injury was reversible. During differential diagnosis the suspicion of AIH was raised considering female gender, high aminotransferase activity without cholestasis, and exclusion of viral factors. Thus, information acquired from the caregiver and rapid decline in aminotransferase activity allowed a diagnosis of drug liver injury. The girl was followed in the Hepatologic Outpatient Clinic, but the most important advice was psychological support of the girl and the family.

CONCLUSIONS

Adolescent age seems to be the most challenging period in the psychological development of a human being. Severe psychological and somatic problems are observed in this period of life. Due to the increasing number of suicides among teenagers in Poland, paediatricians and

general practitioners taking care of patients in that age group should be very sensitive to be able to notice to this phenomenon. Children lacking proper support in their families require particular attention. Paracetamol, which is available without prescription, can be taken by children as a suicide attempt. The overdose of this drug may result in severe toxic liver failure.

DISCLOSURE

The authors declare no conflict of interest.

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