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CASE REPORT

Food/farmed animals

Chronic arsenic poisoning in pigs associated with groundwater contamination

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Abstract

Arsenic is a heavy metal ubiquitous in soil, rocks and water. Both acute and chronic toxicity are reported in various species of animal, including humans, although publications specifically related to pigs are uncommon. This article describes a case of chronic arsenic poisoning in a pig finishing unit associated with the use of contaminated water being used to produce liquid meals and as source of water. Food safety was also considered. Mortality linked to clinical signs (lack of coordination, flaccid limb paralysis, collapse) was 2.8%. Resolution of the clinical case was reached by replacing 50% of the water used for producing the meals with dairy whey thereby lowering the exposure dose. In conclusion, the presence of inorganic arsenic at the dose of 300 μg/L in drinking water administered for more than 6 weeks in 30–60 kg weight pigs might determine a chronic intoxication.

KEYWORDS
arsenic, drinking water, intoxication, pigs, water quality

BACKGROUND

Arsenic is a heavy metal, its name derived from the Greek word *arsenikon*, meaning potent.[1] It is an ubiquitous element found in soil, rocks, atmosphere, water and organisms. It is mobilised by a combination of natural processes, such as thermal reactions, biological activity and volcanic emissions, as well as sometimes by human activity. Of the different sources of arsenic in the environment, water is certainly the one that creates the greatest problems for human and animal health. While surface waters are those most exposed to contamination, groundwater can reach very high concentrations of arsenic regardless of man-made events.[2]

Elemental arsenic is a metalloid that exists in nature in different oxidation states, and can form both organic and inorganic compounds in the environment and within the human body. In combination with other elements such as oxygen, sulphur and chlorine, it is referred to as inorganic arsenic, and when combined with hydrogen and carbon, it is referred to as organic arsenic, the former being characterised by a greater capacity to induce toxicity than the latter.[3] Moreover, arsenic can form gaseous compounds as arsine gas that is considered one of the most toxic forms.[4] As most arsenic compounds lack colour and smell, the presence of arsenic is not immediately obvious in food, water or air, thus presenting a serious human health hazard given the toxic nature of the element.[5] Indeed, the name arsenic is often associated to poisons, in consequence of its long and nefarious history.[6] Acute arsenic poisoning in humans is associated initially with nausea, vomiting, abdominal pain and severe diarrhoea. Encephalopathy and peripheral neuropathy are reported. Chronic arsenic toxicity results in multisystem disease, including various types of cancer, cardiovascular disease, neurological disorders, dermal effects and gastroenteric effects.[5]

Groundwater contamination by arsenic and other metals has severely affected the health of populations in various regions in the world, in particular Bangladesh, China, Mexico, United States and West Bengal (in India).[7] To place this in perspective, the WHO-recommended limit for arsenic in human drinking water is 10 μg/L.[8]

In arsenic-affected areas, livestock are also exposed to toxic concentrations of arsenic very similar to human beings, and some cases of arsenicosis in field conditions has been reported in cattle[9] and horses.[10] Very few cases of acute arsenic poisoning have been reported in pigs,[11] probably due to the relative resistance to inorganic arsenic of this species. Guidelines published by the Canadian Council of Ministers of the Environment (CCME, 2009)[12] for arsenic in water used for livestock have set the maximum level at 25 μg/L, even if guidelines from other countries are lacking. Moreover, as the principal route of exposure to arsenic in human occurs by food ingestion, food safety related to meat consumption from food-producing animals exposed to arsenic might represent a human health hazard.[13] The aim of the work was to describe a case suggesting chronic arsenic poisoning in an Italian farm rearing finishing pigs associated with the use of arsenic-contaminated water being used to produce liquid meals and also as the source of water.

LEARNING POINTS/TAKE HOME MESSAGES

- The daily ingestion of about 2700 μg of inorganic arsenic (>5000 μg of total arsenic) in pigs weighing 60 kg for a period of 6 weeks might cause chronic intoxication.
- Water quality analysis is an important part of an on-farm disease investigation, both for infectious and toxicological agents.
- Meat products from food-producing animals exposed to arsenic might represent a human health hazard, and food safety must be evaluated.
- The provision of a high-quality feed to food-producing animals is mandatory by an animal welfare point of view, and arsenic removal techniques are strongly recommended.

CASE PRESENTATION

The case described was found in a finishing pig farm in the province of Brescia (Lombardy, Italy). The farm, consisting of two identical barns with concrete-slatted floor and natural ventilation, housed a total of 2500 growing animals. On arrival at the finishing unit in April, the pigs weighted 30 kg and slaughter was planned for 5 months later. The average mortality calculated in the last four finishing cycles was 2.7%. The animals were fed three daily liquid meals, with a ratio of flour:water of 1:4. Water supply for drinking and liquid meals was obtained from the groundwater. The animals, of Danish breed and origin, were treated at the beginning of the growing cycle in Italy with flumechin 50% (2.4 g/100 kg of bodyweight for 5 days) by oral administration due to slight clinical diarrhoea attributed to *Escherichia coli* (bacteriology performed on faeces, data orally reported by the owner). No analysis on virulence factors for *E. coli* was available at the time of the first visit. Before arrival in Italy, the animals had been vaccinated against *Mycoplasma hyopneumoniae* and porcine circovirus type 2 (no data available for vaccination calendar), while in Italy they had undergone prophylactic vaccination for Aujeszky's disease following the required legislation. Clinical signs were first observed about 6 weeks after arrival when the average weight was approximately 60 kg. Initially, only one case per day was observed, but this escalated to three new cases daily for the subsequent 10 weeks. Initially, clinical signs were of apathy, with anorexia and sporadic diarrhoea. There was pronounced deterioration within a few hours of onset, accompanied by lack of coordination, convulsions, flaccid limb paralysis and collapse (Figure 1). Death occurred in all clinical cases within approximately 24–36 hours. The total mortality was 2.8% (Figure 2).

DIFFERENTIAL DIAGNOSIS

Postmortem examination was performed on eight pigs, with all cases showing serious gastritis and haemorrhagic intestinal content (Figure 3). Differential diagnoses considered and investigated: (a) *Streptococcosis* (*Streptococcus suis*); (b) oedema disease (*E. coli*); (c) Aujeszky's disease (pseudorabies virus [PRV]); (d) *Salmonella*; (e) porcine circovirus type 2 (Drolet et al.[14] identified the virus in an outbreak of sudden death and acute nervous signs); (f) *Listeria monocytogenes* (rare, but sudden death in piglets, septicaemia, fever 42°C and nervous signs have all been recorded by Lopez and Bildfell[15]); and (g) intoxication. An eighth point should be astrovirus type 3, but no investigation was performed.

INVESTIGATIONS

Tissue matrices (brain, meninges, spleen, liver, lymph nodes, blood and intestines) were sent to the laboratories of Istituto Zooprofilattico Sperimentale della Lombardia e dell'Emilia Romagna for investigations aimed at identifying the correct diagnosis (Table 1, first visit). Following a negative bacteriology and RT-PCR negativity for Aujeszky's disease virus, the involvement of a likely infectious agent could be excluded. The hypothesis of intoxication was then considered. Feed could be excluded in the pathogenesis, because it was consumed by animals at other farms without any clinical problems. Therefore, an analysis of the water (Chelab laboratories, Italy) was carried out. In addition to more classical analytical parameters (pH, hardness, electrical conductivity, etc.), chemical and biological parameters of potability and pollutants were evaluated (Table 1, second visit).

Result from histology and immunohistochemistry were considered non-specific: (a) focal pictures of lymphoplasmacellular periarteritis in the kidney; (b) portal fibrosis in the liver; (c) congestion, intravascular coagulation and localised haemorrhage to a cortical area in the brain emerged; and (d) severe cellular damages, including marked mucosal surface erosion and inflammatory lymphocyte infiltration, were visible in the small intestine epithelium. Results of all parameters investigated in the groundwater were unremarkable except for the very high concentration of arsenic, which was 341 μg/L, more than 30 times higher than the potability limits for human drinking water imposed by European legislation (10 μg/L), and 13 times higher than limit suggested by CCME for livestock (25 μg/L). In order to confirm the data and to assess the form of arsenic, a second analysis, which included speciation by liquid chromatography system and mass spectrometry of the element, was carried out on the water as well as on muscle, kidney and liver of two deceased animals. Arsenic in inorganic form, and therefore more dangerous, was found to be the most representative share of the element (mean concentrations in water: 278 μg/L; muscle: 20 μg/kg; liver: 18 μg/kg; kidney: 31 μg/kg). A suspected hypothesis of chronic arsenic intoxication seemed likely.

FIGURE 1 Pigs with lack of coordination, convulsions, subsequent flaccid limb paralysis and collapse

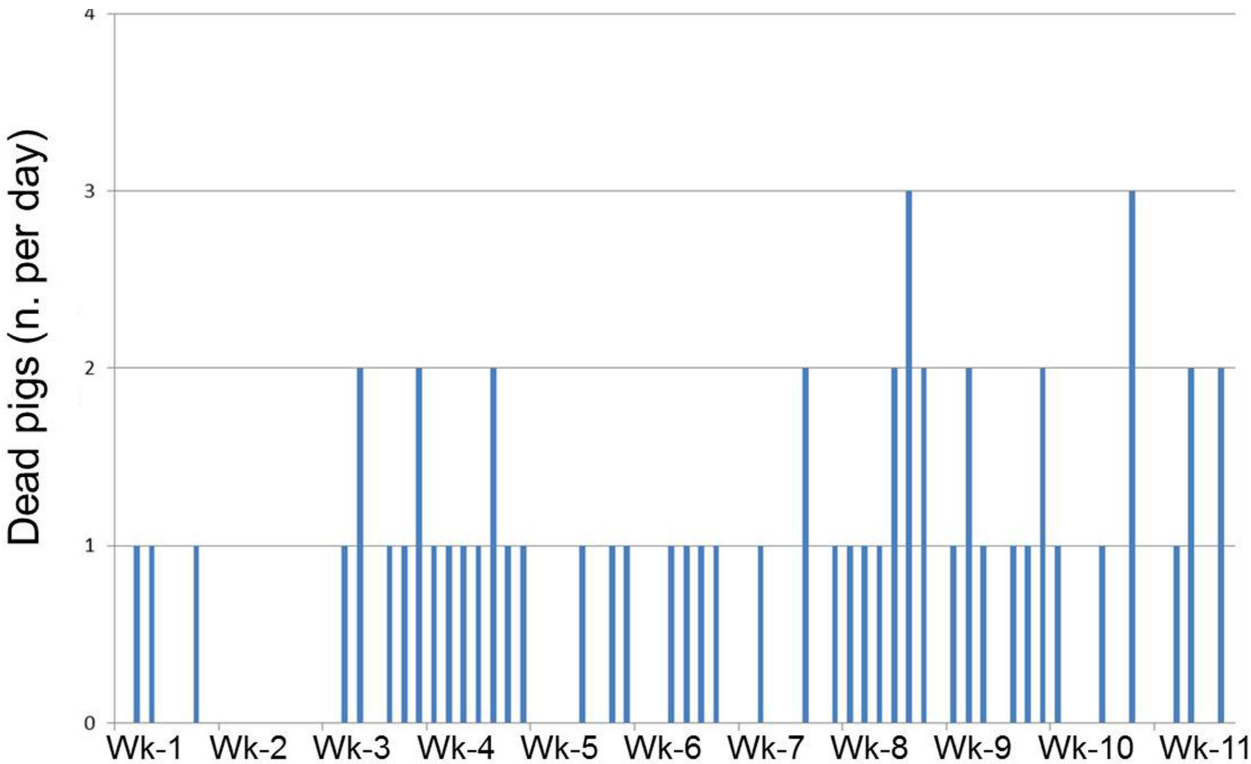

FIGURE 2 Number of dead animals per day with clinical signs referable to the clinical case

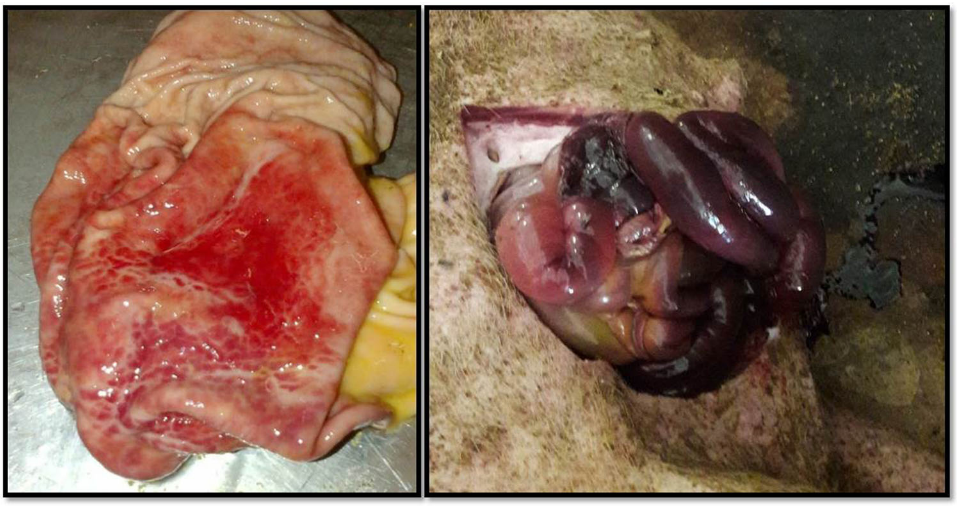

FIGURE 3 On postmortem examination performed on eight pigs, the animals showed serious gastritis and haemorrhagic intestinal content

TABLE 1 Laboratory investigations performed on samples collected in the herd during three different visits

Samples	Methods	Aetiologic agent/aim
First visit:		
Brain, spleen, kidney and intestines	Bacteriology (brain was cultured on blood agar supplemented with NAD and Gassner agar, as well as spleen and kidney were cultured on blood agar and Gassner agar)	*Streptococcus suis, Haemophilus parasuis*, *Salmonella*, *Escherichia coli* and other possible bacterial agents
Brain	PCR	Pseudorabies virus (PRV)
Second visit:		
Brain, meninges, heart, spleen, liver, lymph nodes and intestines	Histology and immunohistochemistry	- Microscopic evaluation of tissues-Confirmation of the results obtained with the other diagnostic methods
Water	Chemical analysis established for potable water[29]	Quantification of chemical and microbiological hazards
Third visit:		
Water, muscle, kidney and liver	Arsenic speciation with spectrometric method[30]	Quantification of inorganic and organic arsenic

TREATMENT

Although there are many methods for water treatment and arsenic removal,[1] the high cost implications and prolonged time of removal technologies' installation led to the decision to minimise the use of groundwater to prepare the liquid meal. The farmer was recommended to replace 50% of the water content in the liquid meal with dairy whey (accordingly with a balance of nutrients in the diet), with a consequent 50% reduction of arsenic. The reason for this choice lies in the widespread availability of dairy whey in Northern Italy, as a result of the presence of cheese-making industries (e.g., Parmigiano Reggiano and Grana Padano).[16] The water dilution adopted led to a reduction in the daily intake of inorganic arsenic estimated from 2669 to 1334 μg per pig, assuming approximately 15 L of water is ingested daily. Considering total arsenic, the daily intake was reduced from 5115 to 2557 μg per pig; it is not possible to exclude the eventual role of organic arsenic in the clinical case, as Rice et al.[17] considered the pig a relatively sensitive species.

OUTCOME AND FOLLOW-UP

During the weeks after water dilution with dairy whey, the clinical signs and mortality decreased until their complete disappearance 4 weeks later. Since the manifestation of this clinical case, the farm has started to regularly use dairy whey with no recurrence of clinical signs. Other investigations on meat (speciation by liquid chromatography system and mass spectrometry) were performed at slaughter (slaughter live-weight of 170 kg, around 4 months later) excluding human hazard related to food safety (mean level: 10 μg/kg; mid-level between results reported by López-Alonso et al.[18] and Jorhem et al.[19] in pigs routinely inspected at slaughter). In the following months, the farmer started to consider other arsenic-removal techniques to durably guarantee water quality.

DISCUSSION

The present clinical case provides early suggestion of chronic arsenic poisoning in pigs, a species in which only a few acute cases have been described. Due to clinical evidence of chronic arsenic toxicity in humans and the frequent cases of intoxication at very low dosages over years leading to tumours and skin changes,[5] the maximum concentration of this element that can be present in drinking water is set at a level of 10 μg/L across Europe. This legal level has decreased over years with increasing knowledge of the toxicity in humans attributed to small quantities of arsenic. The same growing knowledge led the CCME to decrease the maximum level of 500 μg/L suggested in 1987 for drinking water used for livestock to 25 μg/L. Publications in the 1980s reported animal studies showing haemorrhagic gastrointestinal lesions in animals,[20] although publications relating to pigs are uncommon.

The principal route of exposure to arsenic in human is by ingestion; therefore, food safety relating to meat from food-producing animals exposed to arsenic might represent a human health hazard[13] and needs to be considered. The water dilution adopted in this clinical case led to a reduction in the daily intake of inorganic arsenic from 2669 to 1334 μg per pig. Although the dosage achieved is still very high, being well above the threshold of acute toxicity for humans (200 μg/L; 10 ppm in liver and kidney), the pig is considered quite resistant to arsenic poisoning, with 100–200 mg/kg being considered the lethal dose. It is likely that the levels contained in the water on the farm involved in the present clinical case were not sufficient to trigger acute symptomatology, but arsenic was able to accumulate in the pig during the first weeks of the growing cycle (from 30 to 60 kg), resulting in a later onset chronic and persistent symptomatology until the cause was eliminated. Arsenic concentrations found in the organs of the dead animals excluded acute toxicity (for diagnosis in pigs, kidney and liver tissues concentrations of 10 ppm are considered significant[21]), but were greater than concentrations reported in bibliography for healthy animals; in kidney, our finding was 31 μg/kg, compared to 19[19] and 11 μg/kg[18]; in muscle and liver, arsenic concentrations were 20 and 18 μg/kg, respectively, versus 3 and 13 μg/kg.[18] Jorhem et al.[19] reported higher reference levels in seemingly healthy pigs in muscle and liver (24 and 23 μg/kg, respectively). However, the concentration of arsenic decreases rapidly in various tissues of the body after ingestion ends,[22] and that might explain the difficulties encountered in reporting a reference parameter for arsenic concentrations in each tissue. This rapid decrease of arsenic concentration in tissues, supported by final investigations we performed at slaughter, significantly reduced the possible risk to human health related to the food safety. However, other food safety investigations at slaughter on arsenic residuals in meat should be encouraged in the Italian geographical area of the present case. Compared to certain regions in the world that are severely affected by arsenic groundwater contamination (Bangladesh, China, Mexico, United States and India[7]), most concentrations in Europe are relatively low, with a few exceptions associated with particular geological formation. For example, arsenic contamination of drinking water is a public health problem in several Italian areas due to the volcanic origin of the territory. Arsenic values in drinking water are typically between 20 and 50 μg/L in large areas of Italy (e.g., Tuscany, Lombardy, Lazio, Campania[23]) and since 2010, an official 'state of emergency' for the water supply was declared in 128 Italian municipalities. Despite that, in our knowledge, no wide national or regional epidemiological investigation on food-producing animals has been carried out at slaughter in Italy.

It is imperative to highlight that farmers are legally required to keep the risk of biological, chemical and physical contamination of feed as low as reasonably achievable (EC Regulation 183/2005, art. 4), and the provision of a high-quality feed to food-producing animals is mandatory from an animal welfare point of view (EU Directive 98/58/EC). For these reasons, arsenic removal techniques are strongly recommended in similar cases of exposure (e.g., coagulation and flocculation, adsorption and ion exchangers' use, membrane filtration, etc.; see Choong et al.[1]). Dilution and dispersion methods, used in this case, allowed a very rapid solution, should be considered only temporary.

Literature describes several gross and histopathological changes in animals exposed to chronic level of arsenic.[24] However, as with our findings, most pathology and histopathology reported are non-specific and a diagnosis of chronic exposure to arsenic requires other specific investigations. In this investigation, it was decided to not perform blood analysis due to its low efficiency as an indicator of long-term exposure of individuals to arsenic, as it is metabolised from blood within a period of several hours,[25] and no correlation was found between the level of arsenic in the blood and the level of arsenic in the drinking water.[26] In this investigation, we performed kidney analysis on dead animals. Urine analysis would also have been useful and could aid the understanding of excretion of both organic and inorganic forms of arsenic.[27]

A limitation of this clinical case was the lack of investigation on astrovirus type 3, which has been recently reported in Italy in sows with similar clinical signs.[28]

In conclusion, it can be suggested that the daily ingestion of about 2700 μg of inorganic arsenic (>5000 μg of total arsenic) in pigs weighing 60 kg for a period of 6 weeks might cause chronic intoxication. This investigation underlines that water quality analysis is an important consideration in on-farm disease investigations, both for infectious and toxicological agents. It is not possible to exclude that many clinical cases in geographical areas with high concentrations of inorganic arsenic in the groundwater are often unexplored because of their unspecific and slow onset. For this reason, more investigations on meat from food-producing animals at slaughter in the specific area of Italy should be encouraged to guarantee food safety.

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CONFLICT OF INTEREST

The author declares that she has no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

ETHICS STATEMENT

The present study was conducted under field conditions during routine animal management and procedures; for such reason, the application of the provisions of EU Directive 2010/63 on the protection of animals used for scientific purposes was not necessary and no formal authorisation was required by law. All the animals were reared in agreement with

EU Directive 120/2008 laying down minimum standards for the protection of pigs.

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