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Melamine Toxicity in Pigs

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ABSTRACT

Three farms in Penang, Malaysia, reported illness in grower-finisher pigs with discarded kidneys from abattoir. Affected animals were inappetant, anorexic, thin, dull, and depressed. The episode was closely related with the feed formulation changes, where soybean and fishmeal were replaced with yeast. No significant mycotoxin levels were detected in both the feed and yeasts. However, high levels of melamine were detected in yeast (30,064 ppm) and finished feed (750 to 1500 ppm), which exceeded the acceptance level set by WHO (<2.5 ppm). Nonetheless, prominent gross abnormalities were detected, except for the lesions in the kidneys during necropsy. The affected kidneys were enlarged and yellowish in colour, firm in consistency and the cortical surface was wrinkled and dimpled. Dilated cortical and medullary lesions with yellow gritty crystalline materials were also observed. A microscopic examination revealed the lesions of acute tubular nephrosis, interstitial nephritis with multiple cysts in the kidney cortex. After the removal of the yeast source in the feed, the illness and kidney lesions were in remission.

Keywords: Acute renal failure, kidney, melamine toxicity, pigs, yeast

INTRODUCTION

Melamine (1,3,5-triazine-2,4,6-triamine) is an industrial chemical which is used to produce melamine resins (polymers of melamine) such as plastic kitchen items, urea, and fire retardant. It contains high nitrogen content which when added to animal feed or milk, gives the false impression of higher protein content. Although melamine is not approved for usage in animal food, there were multiple cases of renal failures fatalities reported in dogs and cats in 2007 (Bhalla *et al.*, 2009). The cause was related with contaminated feed with high level of melamine that led to a massive recall of pet food in North America. The contamination was traced back to the wheat gluten imported from China which contained a high level of melamine. In addition, recent cases of nephrolithiasis and acute kidney injury among children in China have been linked to ingestion the milk-based infant formula contaminated with melamine (Bhalla *et al.*, 2009). The melamine contamination was not limited to pet food, adulteration also were detected in livestock which included chicken, fish, and swine feed (Reimschuessel *et al.*, 2008). A syndrome characterized by progressive weight loss, wasting, and jaundice, with high mortality has been reported in swine herds in Malaysia. This is the first melamine toxicity case in the country.

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BACKGROUND OF THE STUDY

This case study involved three individual farms that are located in Penang, Malaysia. The farms were Farm X- Kampung Valdor, Farm Y- Kampung Selamat and Farm Z- Tasek. During the first quarter of 2008, meat inspector at the local abattoir condemned kidneys from pigs that originated from Farm X, and the rejected kidneys were from apparently healthy animals. Due to the complaint, an in-depth histopathologic and clinical investigation was initiated. At about the same time, abnormal illnesses were detected in grower-finishers in Farms Y and Z. During the investigation, feed samples and raw materials were dispatched for toxin analysis in the Vet Food Agro Diagnostics, Selangor and Pacific Laboratory, Singapore, respectively, whilst affected kidneys were delivered to Universiti Putra Malaysia for histopathological studies.

RESULTS

The clinical investigation in Farm X showed that grower-finisher pigs were inappetant, anorexic, thin, dull, and depressed. Meanwhile, the herd performance was poor and pigs were about 3-4 weeks behind their compatriots expected i.e. 80-95 kg instead of 100-120kg bodyweight. The episode started three weeks following the change in the feed formulation diet for grower-finisher pigs, where the protein source in soybean and fish meal was substituted with yeast at an inclusion rate of 5%. However, no increase in mortality was detected. The morbidity rate of the affected pigs gradually rose from 20% to 50% over a period of 2 weeks. Feed intake was decreased between 30% up to 50%. The farmers became concerned and reported the case to the investigating veterinarian when the state abattoir reported to the producer that a number of kidneys were condemned from clinically healthy pigs. Farm Y and Farm Z also reported similar clinical signs and abattoir findings.

History indicated that in all the three farms, where the disease was observed, feed formulation changes occurred within 4-5 weeks after introducing yeast source originated from China, and supplied by the same importer. Yeast was included in the diets at between 2.5 to 5%. In the investigation, no clinical or pathological disease was observed in grower-finisher pigs with yeast replacement at 1.6% in the diet (Table 1) at the fourth farm (Farm A). A tentative diagnosis of toxicity of an unknown origin was attributed with differential diagnosis of mycotoxicosis and heavy metals at that time.

During necropsy, a gross examination revealed no other prominent abnormalities, with the exception of kidney pathology and a general loss in body condition. The affected

TABLE 1
Clinical description of melamine toxicity in 4 farms

	Farm X Kg. Valdor	Farm Y Kg. Selamat	Farm Z Tasek	Farm A Kg. Selamat
Clinical signs	Thin, inappetence, dull, depressed	Minor episodes of sick pigs, kidney lesion in abattoir	None. kidney lesion detected in abattoir	No syndrome and no complaint from slaughter house
Affected age group	Grower to finisher	Grower to finisher	Grower to finisher	None observed
Morbidity (%)	20-50	2	2-3	0
Severity of kidney lesions	Severe	Moderate	Moderate	Not observed
Inclusion rate of contaminated yeast (%)	5	2.5	2.5	1.6
Feeding period	2-3 wks	4 wks	4-5 wks	4-5 wks

kidneys were yellowish, discoloured, enlarged, hard in consistency with wrinkling and dimpled cortical surface (*Fig. 1A*). In addition, dilated cortical and medullary lesions, with yellow gritty crystalline materials extending into the ureter, were also detected (*Fig. 1B*). In more severe cases, the kidneys were reduced in size, with clear pitting and dimpling, were dark red brown in colour and with the cortex and medulla atrophied resembling hydronephrosis (*Fig. 1C* and *1D*).

The microscopic examination revealed lesions of acute tubular nephrosis, and interstitial nephritis with multiple cysts in the kidney cortex (*Fig. 2A*). Interstitial nephritis may have been attributed to other infections, i.e. leptospirosis. Multiple stages of tubular neprhosis were also detected indicating involvement of acute toxicity. The collecting tubules remain intact and no casts were detected inside the tubules (*Fig. 2B*).

However, no significant mycotoxin levels were detected in both the feed and yeast samples. The chemical analysis of the yeast showed that the melamine levels were at as high as 30,064 ppm and crude protein of 60-75%. A typical yeast product contained about 45-55% of crude protein. The level of melamine contamination in the feed was between 750 and 1500 ppm, exceeding the acceptance level of <2.5 ppm, as

Fig. 1A: The affected kidney showing yellowish discolouration with dimpled cortical surface

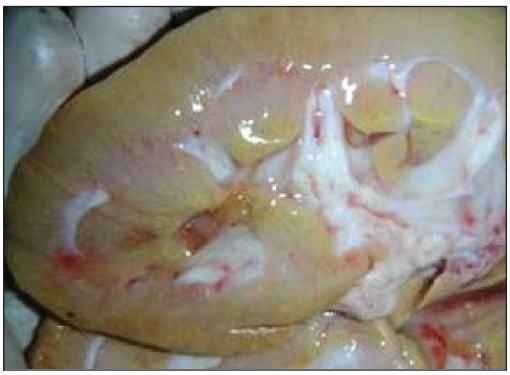

Fig. 1B: Yellowish crystalline material was detected at the medullar upon longitudinal dissection

Fig. 1C and 1D: Dark red brown with medulla atrophied resemble grossly hydronephrosis was detected in suspected chronic cases

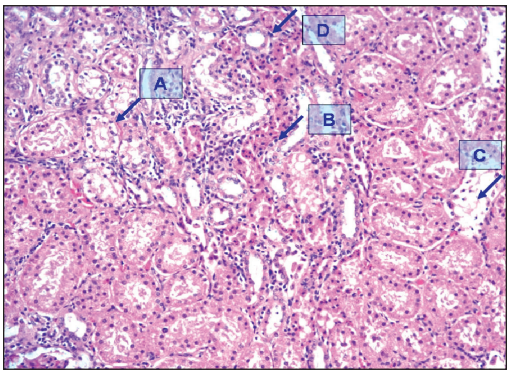

Fig. 2A: Kidney; cortex; pig. Acute tubular nephrosis, characterized by various stages of nephrosis; (A) cellular swelling, (B) esinophilic and pyknosis of the tubular epithelium, (C) karyorrhexia and karyolysis with sloughing of necrotic epithelium into the tubular lamina. (D) A healthy and normal tubular (H &E stain, X20)

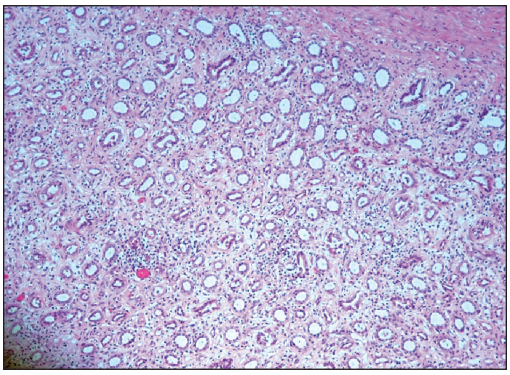

Fig. 2B: Kidney; medulla; pig. The collecting tubules remain intact, clean and no cast was observed, indicating there might be an obstruction in the upper pathway and at the early stage of lesion (H &E stain, X10)

set by the World Health Organization (WHO) during the WHO Expert Meeting to discuss on the Toxicological and Health Aspects of Melamine and Cyanuric Acid in Canada (Anonymous, 2008). On the suspicion of toxicity, the yeast was withdrawn from the diet. The disease syndrome was in remission clinically and a reduction of condemned kidneys in two weeks time at the affected farms.

DISCUSSION

Melamine is rapidly excreted in the urine (99% of the administrated dose would be excreted in 28 hour); however, it is precipitated in the distal renal tubules (Bhalla *et al.*, 2009). Meanwhile, degeneration of the proximal and distal tubules with crystalline material are common findings in melamine affected pigs (Nilubol *et al.*, 2009). In this study, the collecting tubules remained intact and no casts were detected (*Fig. 2B*). The lesion is primarily a consequence of the physical obstruction of the tubules causing reduced blood flow and glomerular filtration rate. Together with renal vasocondtriction and inflammatory mediators, acute renal failure is a consequence (Reimschuessel *et al.*, 2008). In chronic melamine toxicity, interstitial inflammation with large crystals and fibrous tissues would be detected (Bhalla *et al.*, 2009).

In this study, no crystals were detected via histology examination of kidney, as the uric/melamine crystals were dissolved in formalin and during tissue processing (Vernon, 2006). The urine of the affected animals was collected for further analysis, where higher level of blood urine nitrogen (BUN) and serum creatinine, together with crystalline material, were reported in the urine from the melamine affected pigs herd (Nilubol *et al.*, 2009).

In 2007, livestock feed was found to be supplemented with pet food scraps that were contaminated with melamine and melamine-related compounds such as cyanuric acid, ammelide and ameline (Anon., 2007) at 30-120 ppm. The risk of ingestion of meat products from animals with melamine residues has not been comprehensively assessed (Baynes *et al.*, 2008) and there was no meat withdrawal interval set for melamine in any food producing animal species (Buur *et al.*, 2008). The public is concerned about consuming meat from hogs and poultry exposed to melamine and/or its analogues. In this case study, the level of melamine toxicity

(750 to 1500 ppm) detected extremely surpasses the recommended level (<2.5 ppm) set by WHO. Thus, more comprehensive feed analysis and examination should be carried out to identify potent toxins before it is released into the livestock industry so as to help safeguard the public health. Meat withdrawal period in pigs exposed to contaminated melamine should be determined before it is safe for human consumption.

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