

Suspected gossypol toxicosis in a sow herd

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Summary

A 550-sow farrow-to-finish herd reported an increased incidence of sudden death in sows. Results of gross necropsy indicated severe ascites, hepatomegaly, cardiomegaly, and pulmonary edema, suggesting heart failure. This diagnosis was supported by a finding of hyperkalemia in nine of 14 sows blood sampled. Cottonseeds observed in the feed contained gossypol, a compound known to be cardiotoxic, at concentrations of 62 to 83 mg per kg. The diet was replaced and evidence of toxicosis abated over the subsequent 3 months.

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Sow mortality has been attributed to a myriad of causes, including infectious disease and intestinal accident. However, in the absence of a more evident etiology, toxic insult should also be considered, particularly when there is a sudden increase in mortalities. An investigation should include a complete history of recent events, including change of feed companies, change of feed ingredients, and change from old crop to new. A minimum database should include post mortem results for sows and samples of blood and feed obtained for laboratory analysis. This case report describes a toxic insult and its likely cause.

Case description

In May of 1999, a producer reported a concern about six sows that had died suddenly during the previous 3-week period. The affected herd was a 550-sow farrow-to-finish operation with the sow barn and nurseries on the home site, and two sepa-

rate finishing sites. The herd was multiplying its gilts internally and receiving semen from a commercial boar stud. The herd was serologically positive for porcine respiratory and reproductive syndrome (PRRS) virus (HerdChek ELISA; Idexx Laboratories, Westbrook, Maine) and for *Mycoplasma hyopneumoniae* (ELISA; DakoCytomation Inc, Mississauga, Ontario, Canada). There had been sporadic PRRS virus-associated problems in the nursery, but no clinical signs had been seen in the sow herd. The sows were vaccinated against PRRS, leptospirosis, parvovirus, erysipelas, and *Escherichia coli*.

One sow had died the morning of the initial visit and was available for necropsy. The sow appeared bloated on gross examination, and the abdomen contained 12 to 16 liters of straw-colored fluid containing pieces of grayish fibrin. The urinary bladder was intact and the uterus and intestines appeared normal. The liver was greatly enlarged and was a grayish tan color. It appeared autolyzed, and samples for histopathology were not obtained. The heart was enlarged, and the lungs were wet and heavy. Swabs were obtained of abdominal fluid, liver, lungs, and pericardial fluid and were submitted to the Animal Health Laboratory, Guelph, Ontario, for bacterial culture to rule out acute bacterial infection. Blood samples were obtained from 14 sows and submitted for serum chemistry.

Unusual material had been noticed in the sow ration pellets delivered weekly over the previous 3 weeks. Small black flecks with short hairs attached to them were again seen in the pellets in the most recent delivery of feed. The producer had contacted the feed mill when these flecks were initially seen and was told that just before the manufacture of the sow feed, a dairy ration containing cottonseed was being made.

The mill manager suggested that there might have been some carryover of cottonseed into the sow ration, but felt that this would be of little concern. Deliveries continued to be made weekly for the next 4 weeks, with the farm staff noting that cottonseed was evident in each load of feed.

Samples were collected from the sow and gilt rations and submitted to the Animal Health Laboratory, Guelph, Ontario, and to the Animal Health Diagnostic Laboratory, Michigan State University, East Lansing, Michigan, for gossypol analysis. It was recommended that all sow diets be replaced immediately. In the 3-month period subsequent to this visit, there were four more sudden deaths and three abortions.

Diagnostic test results

Cardiomegaly and hepatomegaly, in association with pulmonary edema and excessive abdominal fluid, were consistent with congestive heart failure. The swabs submitted for bacterial culture revealed no significant growth. Gossypol concentrations in the three feed samples submitted were 62 and 83 mg per kg in sow feed and 18 mg per kg in gilt feed. Serum chemistries of nine of the 14 animals tested had elevated serum potassium levels, ranging between 7.3 and 10.0 mmol per L (normal range, 4.7 to 7.1 mmol per L).

An examination of PigCHAMP (Swine Data Management, Wheatland, Iowa) performance reports for May to October 1999 indicated that, compared to similar time frames in previous years, the average wean-to-first service interval had increased from 6 to 8 days, percent sows bred by 7 days post weaning had decreased from 93.0 to 87.8%, average non-productive sow days (NPD) had increased from 56.8 days to 68.1 days, and average NPD per parity record had increased from 22.0 days to 27.7 days.

Discussion

In this case, the presenting complaint was increased sow mortality, which a necropsy

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suggested was due to cardiac failure. The history included contamination of the feed with components of a dairy ration. Possible causes of toxicosis include the ionophores lasalocid, narasin, and salinomycin. Monensin was ruled out because it would not normally be fed to lactating cows, and there were no clinical signs to suggest that monensin had been added to the sow feed by accident. At the accepted inclusion rate for cattle of 22 mg per kg feed, it would not be possible for monensin to have reached toxic levels in limit-fed sows, as the LD₅₀ of monensin in swine is 16.7 mg per kg body weight.¹ Although not apparent at any time in this herd, severe dyspnea, which is reported in pigs with monensin toxicosis, has also been observed in pigs with acute gossypol toxicosis, accompanied by a good appetite almost until death.² Gross post mortem lesions of monensin toxicosis occur primarily in skeletal muscles and cardiac musculature.¹ Since the sow ration had contained cottonseeds for several weeks, and cottonseeds contain gossypol, a polyphenolic binaphthalene pigment and recognized toxin, suspicion centered on this ingredient as the cause of toxicosis, and gross post mortem findings were consistent with presumed gossypol toxicity.

Gossypol is present in the cottonseed pigment glands, which are retained after the hull is removed, and are responsible for 2 to 5% of the weight of the seed.³ Gossypol content varies considerably with the strain of cottonseed, the location in which it is grown, climatic conditions during the year it is grown, and the extraction procedure.² Much literature relating to gossypol infers that in swine, no deleterious effects are experienced at free gossypol concentrations in feed below 0.01% (100 mg per kg).^{4,5} Although the gossypol concentrations in the diets in this herd were not particularly high, it was not possible to determine the content in feed in earlier deliveries. A published case report of gossypol toxicosis in South Africa reported that dietary levels varying between 5 and 68 mg per kg of free gossypol were sufficient to cause clinical signs in swine, including acute death in sows, fertility problems, and poor growth.⁶ Furthermore, there is documented evidence of liver accumulation of gossypol, and pigs are amongst the most avid accumulators.² Therefore, toxic effects may not be manifest immediately after gossypol is fed, and may continue for a period after

withdrawal of the feed, suggesting that release of accumulated stores is involved in the etiology of toxicosis. Moreover, cottonseed also contains another pigment, gossyverdurin,² which is more toxic than gossypol and may be responsible for the finding that signs of cottonseed toxicosis may not always reflect the gossypol concentration in the feed.^{2,3} Gossyverdurin levels were not determined in this case.

Gossypol binds to amino acids, making them unavailable during the digestive process.² Binding of gossypol to the free epsilon amino groups of lysine makes lysine unavailable for protein synthesis, causing hypoproteinemia and severe edema.² Impairment of growth and hypoprothrombinemia may also be attributable to inhibition of protein synthesis. Anemia may result from chelation of iron to gossypol, which also inhibits release of oxygen from hemoglobin.⁶⁻⁸ Gossypol is highly lipid soluble and primarily eliminated via feces; a minor amount is eliminated as a conjugate in urine.^{2,3}

Gossypol inhibits testicular lactic dehydrogenase (LDH) by competitive inhibition of a cofactor required for LDH activation,^{3,7,9} and is an effective antifertility drug in males. It may also affect female reproduction in swine and rats, having potential direct effects on the embryos, as well as a luteolytic action that may disrupt pregnancy.^{2,7}

As gossypol is a cardiotoxin, death from cardiac failure is expected. If enough gossypol is fed over a sufficient period of time, necrosis of cardiac musculature occurs, resulting in heart failure.^{2,6} Acute death occurs at an LD₅₀ of 550 mg gossypol per kg body weight.⁷ Animals that die with minimal or no heart lesions are believed to have impaired cardiac conduction, which results in acute heart failure and death.^{3,7} Hyperkalemia causes similar ECG changes in humans and swine.⁶ However, comparable ECG changes may also result from gossypol binding to the free epsilon group of lysine or to phospholipids in the cytoplasmic membranes.^{4,5}

No gross postmortem lesions occur in many animals that succumb to gossypol toxicosis. In animals that do manifest lesions, the predominant finding is excessive fluid, sometimes red-tinged and containing clumps of fibrin, in the abdominal, thoracic, and pericardial cavities.^{2,5} The tra-

chea is often filled with froth and the lungs are edematous with widened interlobular septa. The heart may be pale, mottled, or streaked, and flabby or enlarged or both. Liver lesions are also a consistent necropsy finding. The liver may be enlarged and friable, with rounded edges, and may be mottled with a lobular pattern. Histologically, heart lesions range from none to severe myocardial necrosis, with degeneration and vacuolated fibres.^{2,3} Fibres may also be separated by edema. There is centrilobular hepatic congestion and necrosis. Swollen cells, portal triad congestion, pyknosis, perivascular edema, bile retention, and severe fatty change are seen with varying degrees of necrosis.^{2,3}

Morgan² suggested eight criteria for a diagnosis of gossypol toxicosis (Table 1). The herd in this case exhibited signs of acute toxicosis (likely acute cardiotoxicosis) and more chronic reproductive signs. The clinical profile of hyperkalemia supported the observation of acute cardiotoxicity resulting in death of sows. Long-term effects were manifest primarily as reduced fertility, which is consistent with the release of accumulated gossypol. It has been reported that sows receiving cottonseed meal for approximately 94 days before farrowing had fewer pigs, fewer live pigs, and fewer pigs surviving for 21 days.⁷ It has also been postulated that feeding cottonseed to sows during attachment of embryos (25 to 26 days after ovulation) may reduce embryonic viability.⁷ Occurrences of toxicosis often occur only after the animals have consumed affected feed for several weeks to several months, which suggests that gossypol has accumulated to a toxic level with resulting clinical signs, which may include death.²

Treatment options for gossypol toxicosis are limited. Cottonseed must be removed from the diet immediately, and dietary supplementation with vitamin A, iron, and lysine is recommended to limit gossypol damage. Ferrous sulfate added to the diet at a rate of 1 part iron to 1 part gossypol will almost completely neutralize the toxicity of gossypol.^{3,8} Generally, it is recommended that the concentration of gossypol in the diet of swine must be less than 0.01% (100 mg per kg) to be safe.^{3,8} The producer in this case elected only to remove the affected diets.

It is quite possible, in this case, that summer infertility of swine was a confounding

Table 1: Eight criteria¹ for diagnosis of gossypol toxicity in a swine herd

History of cottonseed meal, whole cottonseed, or cottonseed hulls in the diet.

Feed analysis by an official gossypol testing laboratory determines the presence and level of free gossypol.

History of sudden death or chronic dyspnea, depression, anorexia, and possibly red urine, or overall herd problem of animals that are not doing well or repeat breeders.

History of no response to antibiotics or other treatments.

Necropsy performed by a veterinarian familiar with the signs and lesions of gossypol toxicosis.

Histopathology interpreted by a pathologist familiar with gossypol toxicosis.

Other disease processes ruled out, eg, monensin and vitamin E-selenium toxicity.

More than one animal affected.

¹ Adapted from Morgan SE (1989).²

factor with respect to the increase in non-productive sow days. In northern latitudes, reproductive parameters of swine may change due to alterations in daylight hours and changes in pineal gland function with varying photoperiod.¹⁰ Longer wean-to-service intervals are reported in the summer months, as well as increase in normal recycles; farrowing rates are reduced and delayed puberty is reported in gilts.¹⁰ However, the increased sow death loss in May and June was not explainable by heat stress, as temperatures were moderate. By October 1999, PigCHAMP records and clinical observations indicated that the herd had returned to relatively normal reproductive function compared to previous records in similar seasonal time frames.

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