STUDIES ON SWINE TESTICULAR FEMINIZATION SYNDROME

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SUMMARY

Further investigations were carried out for a family of TFS pigs, which consisted of 560 individuals from at least 8 generations in sucession, in terms of family analysis, production performance, karyotype and high resolution idiogram of G—banded chromosomes. Approaches were also made on genetic and pathogenic mechanisms of this disease.

(Key Words: swine, testicular feminization syndrome, family analysis, karyotype, high resolution G—banding, pathogenic mechanism.)

INTRODUCTION

Testicular feminization syndrome (TFS), also referred to as Androgen Insusceptibility Syndrome, is the most common form of male pseudohermaphroditism in human. For animals, TFS was first reported in mice (Lyon et al. , 1970), and was considered to be caused by a single sex— linked mutant gene. From then on, TFS was detected respectively in horses, cattle, sheep and rats, all exhibiting similar clinical symptoms, such as female phenotype, male testes, no estrus, no fertility, uterine hypoplasia, vigina atresia, and XY type of sex chromosomes.

We conducted relatively detailed genetic analyses on a family of TFS pigs in 1984. The results indicated that this disease belonged to male pseudohermaphroditism, which is genetically due to a X— linked testicular feminization mutant gene, i. e. tf. When tf—carrier sows were mated to a normal boar, the offspring varied from normal males and females to carrier females or sexually abnormal pigs. From then onwards reserches on pigs of this family were carried on , and till now 560 pigs from 8 generations have been observed. Some of the results are reviewed and interpreted thereinafter.

FAMILY ANALYSIS

Data were analyzed for 50 litters from 10 carrier sows which were sexually normal themselves but delivered pigs exhibiting sexual deviation, as shown in Table 1. The 1 : 1. 89 sexual ratio of males to females in Table 1 apparently contradicted the natural sexual ratio that should be 1 : 1. When sex deviation pigs had been grouped into males, the ratio became 1 : 1. 03, in agreenment with natural sexual ratio. Moreover, these abnormal pigs made up 22. 03% of the population, which was tested to be not significantly different from the expect ratio 1/4. ($P > 0.05$)

PERFORMANCE TEST

Reproduction performance The average litter size (ALS) for a tf—carrier sow was 11. 30 offspring among which 3. 08 were male, 5. 74 were female and 2. 52 were abnormal, whereas that for a non—carrier littermates sow was 9. 38±3. 78 offspring with 5. 0±1. 77 males and 4. 38±2. 56

Research supported by the National Funds For Natural Science (3880616)

females. To eliminate litter size effect on reproductivity, statistics for the carrier sows was rearranged only representing those that had as large litter size as noncarrier sows did. The results so calculated for these carrier sows came out to be 10.10±3.11 with 2.80 ± 1.69 males, 5.00±1.49 females and 2.30±1.34 sex deviation pigs. The difference in ALS between carriers and noncarriers is not significantly different (P>0.05).

Table 1. Distribution of offspring from tf—carrier sows

Number of sows	Number of litters	Number of offspring			
		Total	Males	Females	TFS pigs
2	6	66	17	34	15
30	4	56	15	30	11
14	6	70	20	35	15
5	1	12	4	6	2
6	7	65	18	34	13
1	5	58	16	28	14
4	5	52	13	25	14
3	6	67	15	38	14
13	5	63	21	27	15
21	5	56	13	30	13
Sum	50	565	152	287	126

Table 2. Results of fattening comparison between TFS pigs and their normal littermates

Year	Sex	Samples no.	Body weight(kg)		ADG[1](g)	FE[2]
			Initial	Final		
1991	TFS pigs	4	19.00±3.97	92.75±4.37	554.5±41.6[a]	3.26
	female	4	20.63±5.42	88.88±11.09	509.3±53.1[a]	3.38
	male	4	21.25±3.23	91.94±8.36	570.1±54.1[a]	3.45
1992	TFS—pigs	6	31.38±8.59	94.50±11.11	579.0±66.6[b]	3.29
	female	6	30.47±9.28	90.88±11.98	554.2±73.0[b]	3.54
	male	6	33.63±8.61	106.75±14.21	670.9±75.5[a]	3.13

[a,b]—Means within a column with different subscripts were significantly different(P>0.05)

[1]— ADG=average daily gain

[2]— FE=feed efficiency

Growth rate Comparision experiments were conducted in 1991 and 1992 respectively with paired sampling of boars, normal gilts and sex deviation pigs within litters, while they were weighing from 20 to 90 kilograms or so. The corresponding diets were identical in nutrition in both experiments. DE and CP for starter diets were 13.40 MJ/kg and 16.0% respectively while those for the finisher were 13.40 MJ/kg and 13.7%.

The ADG in the two experiments collapsed with each other, indicating the greatest ADG for barrows, followed by that of sex deviation pigs. ADG for normal sows was the lowest. Analysis of variances demenstrated that the differenies of ADG in 1991 trial were not significant (P>0.05), but those in 1992 trial were significantly different from zero as a result of the signicantly greater ADG of barrows than that of sex deviation pigs and normal sows. FE (feed efficienly) showed similar tendency as ADG.

KARYOTYPE AND HIGH RESOLUTION IDIOGRAM OF G—BANDED CHROMOSOMES

High resolution G—banding techniques for chromosomes with cultured pheripheral blood were employed to investigate whether or not any chromosomal aberration had occurred in these sex deviation pigs. The karyotype for TFS pigs exhibited 38,XY. The idiogram was analysed to be $2n=38=12m+10sm+4st+12t$, demonstrating that the sexually abnormal pigs were genetically males with normal male chromosomal constitution.

We applyed thymidine,5—bromouracil and actinomycin D in culture of pheripheral blood to make chromosomes lengthened and exhibit more bands when microphotographed. With a view to obtaining clearer bands, chromatographic scaning was utilized in idiogram analysis, and idiograms with 577 bands were available from prophase and metaphase cells, Accordingly, high resolution idiograms of G—banded chromosomes were drawn. The idiograms did not show any structural difference between sexually normal and abnormal pigs, suggesting that mutation of tf gene might only be that at molecular level.

GENESIS MECHANISM

The sex deviation pigs were phenotypically females, with vaginal lips and orifices that were of normal sizes. However two elliptical buds with clear boundary were found on the very part equivalent to scrotum of a male pig, The buds were hard, elastic and movable when touched, and were verified to be testes by means of dissection examination. The sex deviation pigs had larger groins than the normal boars,and was always complicated by hernia. When dissected at 4 months of age, they could be found with vaginas that is almost as large as normal ones, and underdevoloped uterine bodies and uterine horns. Some exhibited vagina atresia while some had end—closed uterine horns. They had no oviducts or ovaries. The testes were attached to blander ligaments by deteriorated testicular cords and testicular muscles. There were no epididymis, no spermatic duct, no penis, or glans penis. There were also no accessory sexual glands. When slanghtered at 8 months of age,the sex deviation pig could be found with two small and elliptical testes weighing 60 to 80 grams in either subcutaneous fat of the groin or abdominal cavity. The mammary glands, which had already started developing,were approximately of the same size as a normal sow. Histological inspection discovered these pigs with hypoplasia of seminiferous tubules,average diameter of which was 68μ while in contrast that of their normal male littermates was 255 μ. Their seminiferous tubules were filled with connective tissues. In some parts of these tubular walls there could be found spermatogonia, which did not carry on with their cell division into following stages. There were distributed a small number of interstitial cells in between seminiferous tubules, which were smaller and fewer, and more lightly stained than those of normal males. These evidences suggested that testitular tissues of these sex deviation pigs were denatured and deteriorated.

Expected to make certain the pathogenic mechanism of this disease,researchers in Tianjin Agricultural College,in cooporation with their colleagues in the National Animal Research Institute, Chinese Academy of Science, imported our sex deviation pigs and investigate testosterone concentration and estrogens to androgens receptor ratio. Their results showed that testosterone concentration increased with ages. Sixty minutes after they had been injected with luteinizing hormone(LH), their serum testosterone concentration reached the highest peak,namely 1.2 times as much as that before injection,and then decreased to the initial level in another sixty minutes afterwards. That the peak lev-

el of the sex deviation pigs was just 48% as much as that of normal boars indicated less efficiency of TFS pigs' testicular interstitial cells to synthetize, store and release testosterone. Level of testosterone receptors(TR)and esrtradiol receptors(ER) for skin cells was 12. 1±6. 2 fmol/mg. pr. and 8. 2±4. 4 fmol/mg. pr for sex deviation pigs and 12. 2 fmol/mg. pr and 2. 97 fmol/mg. pr for contrl boars. TR to ER ratios of sex deviation pigs to control boars were 1. 47 and 4. 10 respectively. Relative content of TR in sex deviation pigs was only 35. 9% as much as that in control boars.

DISCUSSION

A variety of sex deviations have so far been reported. The intersexes described herein were featured by testes with detriorated seminiferous tubules, reproductive cells at the stage of spermatogonia, retrograded Wolffian duct derivants, no epididymis, no spermatic duct, no penis or glans penis. However They had Mullerian duct derivants, vagina lips and orifices of normal sizes, retrograted uteruses, as well as female secondary sexual characters. The Karyotypes and high resolution G—banding idiograms indicated that chromosomes of these sex deviation pigs were normal in both number and structure, with heterogametically XY sexual chromosomes. Family analysis suggested that ,among the offspring of a tf—carrier sow or the whole family, sexually normal to abnormal pig ratio agreed with 3 : 1 as was theoritically expected. These results provided further evidences that this family of sexually abnormal pigs were genetically males, or more precisely male pseudohermaphroditism, whose genetic cause was a sex—linked testicular feminization mutant gene, namely tf. This disease was concluded to be testicular feminization syndrome.

Though TFS pigs were found to have interstitial cells in the testes of TFS pigs, which were able to release testosterone that increased with ages. However TFS pigs were demonstrated to be less efficient in synthetizing, storing and releasing testosterone than normal boars. That TR value of TFS pigs was approximately as much as that of normal males but ER value for the former was significantly greater suggested that TFS might not necessarily be a result of lacking testosterone receptor proteins, but might be attributed to qulitative abnormality of these receptors. This result was in agreement with human researches(Amrhein,1976;Pinsk ;,1981). The fact that over—increased ER value led to decreased TR/ER ratio might as well be another consideration for genethesis of this disease.

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