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TWO HEIFERS WITH GONADAL DYSGENESIS AND THE SEX CHROMOSOMAL CONSTITUTION XY

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Chromosome defects in the mammalian complement most often involve the sex chromosomes. The consequence of sex chromosome defects varies very much and presents a wide spectrum of morphological and physiological defects. Sometimes changes with the exception of the genital organs are very mild, in spite of the fact that the genetical sex has been reversed.

In man *Harnden & Stewart* (1959) described a syndrom under the name of "pure gonadal dysgenesis". The main characteristic was a female eunuchoid type with the chromosome constitution 46/XY. A similar condition but under different nomenclature had been described earlier by *Swyer* (1955) and *Hoffenberg & Jackson* (1957). The condition has also been described later (*de Grouchy et al.* 1965).

A case of contradictory phenotype — chromosomal sex in cattle under the name of testicular feminisation was described by *Nes* (1966). The phenotype was female with well developed udder, rudimentary female and male genital ways and abdominal testicles. The karyotype was 60/XY.

Two heifers with a male karyotype will be described here.

MATERIAL AND METHODS

Casuistics

Case I. Heifer of the Swedish red and white (SRB) breed born in 1964 and belonging to a group of 10 heifers which were kept together with a bull for breeding. The heifer did not conceive

and was investigated by personnel from the Department of Obstetrics and Gynaecology, Royal Veterinary College[1]), and later moved to the department for closer investigation.

The heifer (Fig. 1), 25 months old, had a female appearance with comparatively long legs, a long narrow head and a relatively long and thin neck. Udder and teats were underdeveloped. She

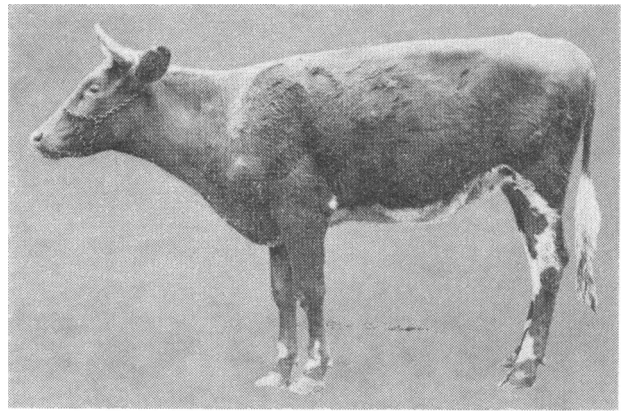

Figure 1. Case I. SRB-heifer with a relatively ordinary body conformation.

was fairly poor of muscles. The external genitalia were normal with the exception of an enlarged clitoris. Heat symptoms were never noticed.

Case II. Heifer of the SRB breed from a small herd within the duty area of the veterinary college. The owner called for insemination after having noticed heat discharge. On investigation at the moment of insemination a hypoplastic uterus and small, inactive ovaries were diagnosed. The animal (Fig. 2) showed a rather distinct male body conformation. The head was broad with short, strong horns, broad neck and short legs. Udder and teats were underdeveloped. The external genitalia were normal.

The heifer was kept at the veterinary college for about two months. Heat symptoms were never seen and it is probable that the owner had been mistaken about heat.

For karyotype studies blood leucocytes were cultured according to a modification of the method of *Moorhead et al.* (1960).

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[1]) We are much indepted to this department for cooperation with the clinical investigation of both cases.

Skin and lung tissue was cultured according to *Basrur et al.* (1963).

At slaughter the sexual organs were removed. The ovaries were fixed in acetic-acid-alcohol 1 + 3. Different parts of the ovaries were embedded and sectioned at 10 μ and stained in Gomori's hematoxyline.

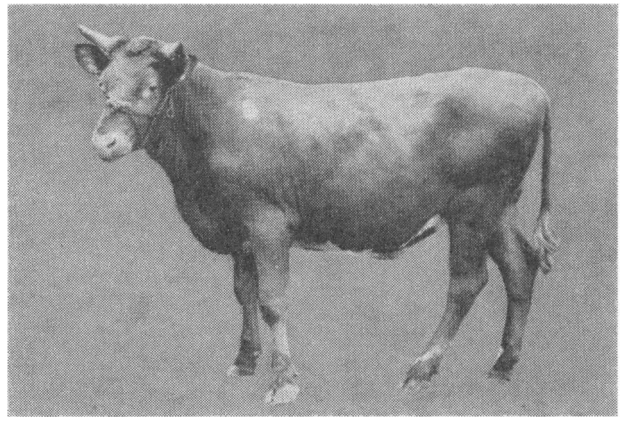

Figure 2. Case II. SRB-heifer with a bullish body conformation.

RESULTS

Karyotype

Table 1 presents the result of chromosome analysis. Both cases showed a normal male karyotype 60/XY. Fig. 3 is an

Table 1. Results of chromosome analysis.

	Tissue	Chromosome number					Sex	Cells counted
		58	59	60	61	62		
Case I	skin		2	26	1		XY	29
	lung	1	1	21			XY	23
	blood	1	2	23	1		XY	27
Total		2	5	70	2			79
Case II	skin	1	1	34	1		XY	37
	lung	1	2	18			XY	21
	blood	1	1	20			XY	22
Total		3	4	72	1			80

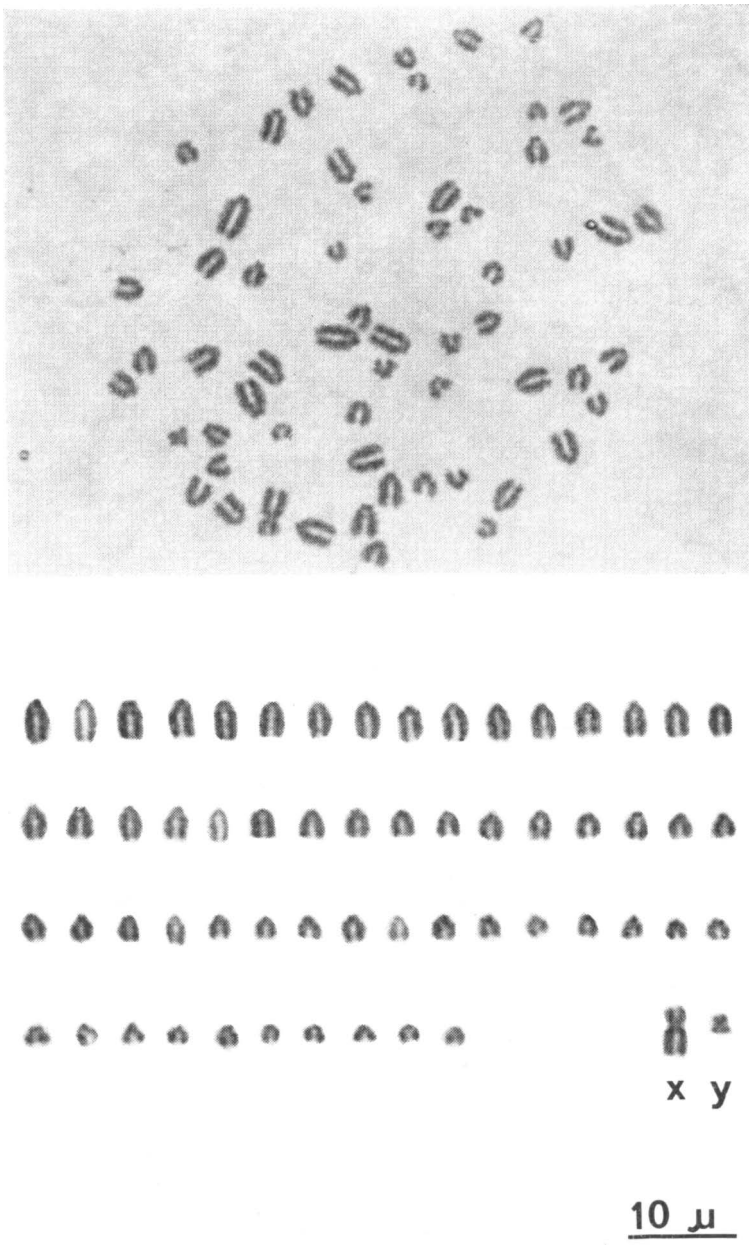

Figure 3. Normal 60/XY karyotype from skin culture of Case I.

example of a metaphase from Case I, skin tissue and with the corresponding karyogram.

Sex chromatin

Sex chromatin studies were made on cells from buccal and vaginal epithelium, but they were not conclusive. This is in accordance with statements made by *Struck* (1961) and others for cattle.

Genital organs

Case I (Fig. 4). The vagina was narrow and underdeveloped. The uterus was clearly hypoplastic. The ovaries were almond

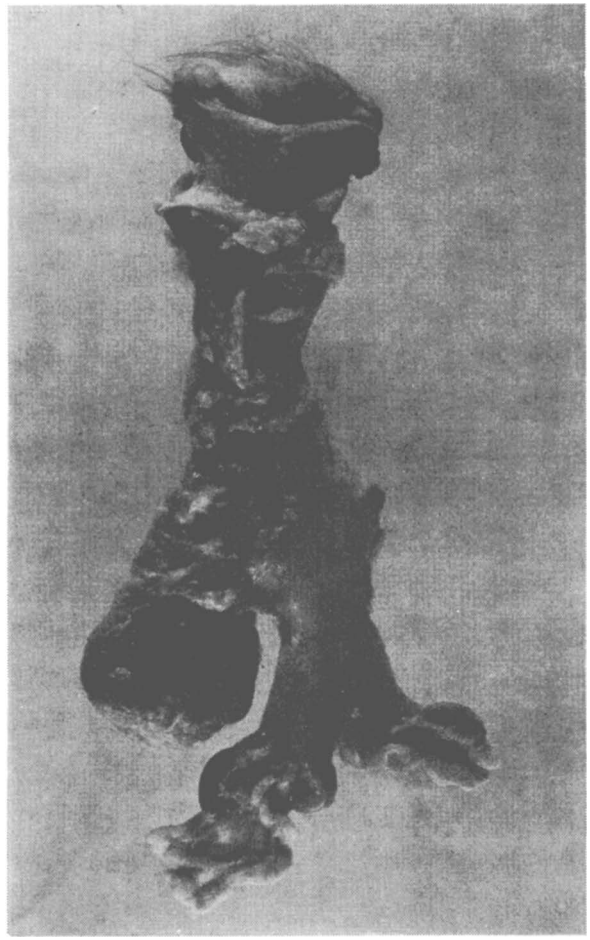

Figure 4. Sexual organs from Case I. Enlarged clitoris, hypoplastic uterus and ovaries.

shaped with a narrowing caudal pole. Longitudinal folds were seen at the surface. Measurements: Left ovary: 33 × 16 × 7 mm. Right ovary: 38 × 14 × 7 mm.

Case II (Fig. 5). The vagina was normal but the uterus hypoplastic. The ovaries resembled those of Case I with the characteristic longitudinal folding. Measurements: Left: 33 × 12 × 5 mm. Right: 40 × 12 × 6 mm.

The follicular system

As the picture was similar in the two cases, they will be described in common. Although no quantitative evaluation has

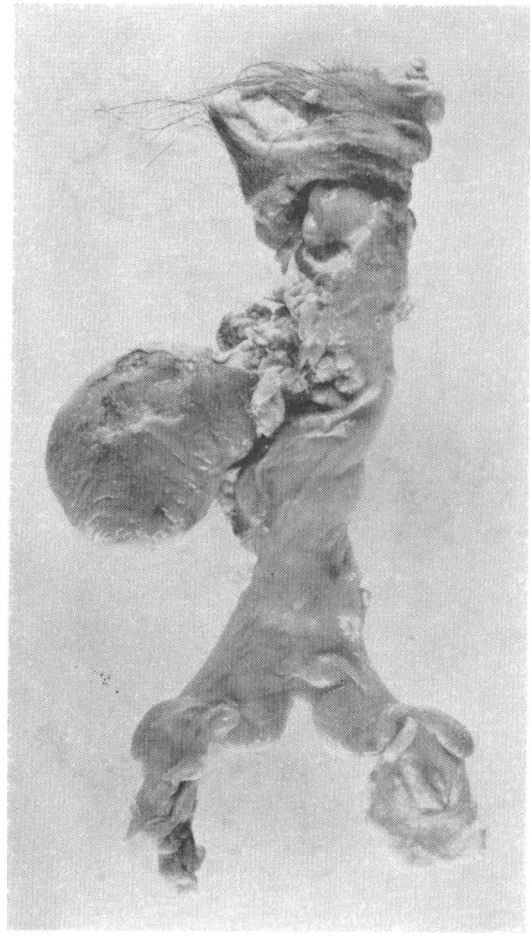

Figure 5. Sexual organs from Case II. Hypoplastic uterus and ovaries.

Table 2. Distribution of follicular types among 100 randomly chosen follicles per ovary.

	Anovular		Growing foll. with degener. oocyte	Degener. growing foll. cf. text
	Follicles	Cords		
Case I				
right ovary	35	15	12	38
left ovary	32	25	12	31
Case II				
right ovary	17	33	11	39
left ovary	23	39	17	21

been made, one can state that the number of follicles was reduced. The follicles present have been classified into three different classes. The classification has been based on 400 follicles randomly chosen from the four ovaries, 100 from each ovary. The distribution of the different types is presented in Table 2. In addition to the three types there was found one normal-looking

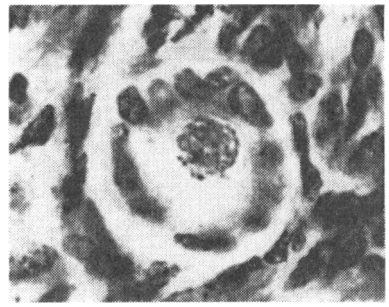

Figure 6. Normal-looking primary follicle. Only one of this type was found out of 400 counted follicles (× 650).

primary follicle with a normal oocyte (Fig. 6) and nucleus and one Graafian follicle. The oocyte nucleus of this was degenerated. The following classification was made.

Anovular cords and follicles. These were found in the cortex and resembled those described by *Settergren* (1964) under the name mentioned. They were either solid or had a central cavity (Fig. 7) (types 1 and 2 in Settergren's classification). There were also medular anovular cords (Fig. 7) which also fits Settergren's description.

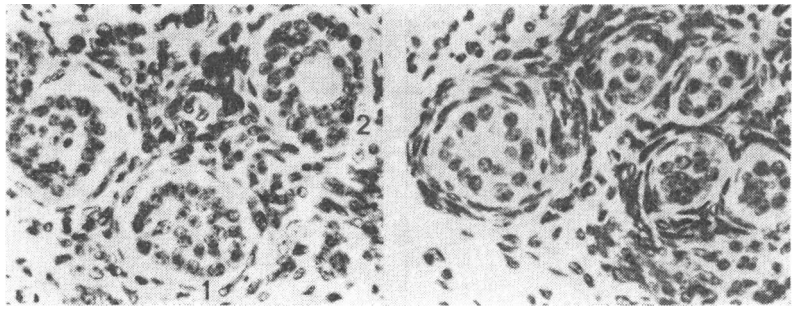

Figure 7. Left: Anovular cortical cord type one (1) and two (2) according to *Settergren*'s (1964) classification. Right: Anovular medular cords (× 275).

Growing follicles with degenerating oocyte nucleus. (Fig. 8). The normal very characteristic oocyte nucleus (with chromosomes at dictyotene) of growing follicles was never seen. On the contrary the nuclear chromatine showed evident signs of degeneration and was stained very weakly. It could hardly be detected without phase contrast.

Degenerated growing follicles. This type (Fig. 9) is a "follicle" consisting of an assembly of follicular cells, some of which could show signs of degeneration. We have interpreted this as a result of oocyte death and disappearance, and consequently these "follicles" did not start as anovular ones.

Investigation of relatives

The karyotypes of the mother and two maternal half-sisters of Case II were investigated in leucocyte cultures. They were all

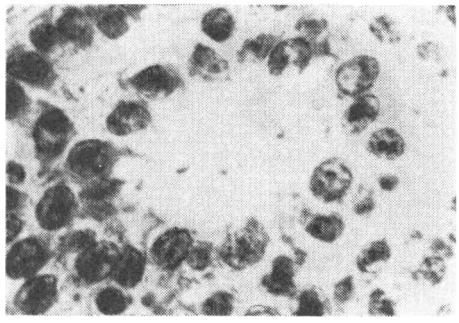

Figure 8. Growing follicle with degenerating oocyte. Note chromatine rests in the oocyte (phase contrast × 650).

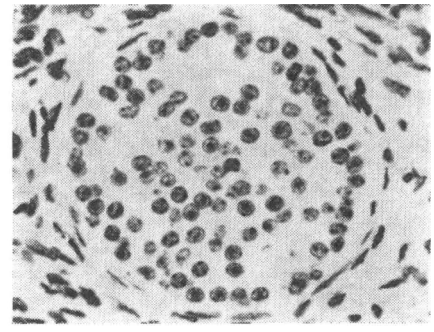

Figure 9. Growing follicle. The oocyte has degenerated and disappeared. Cf. text (× 275).

normal. No close relatives of Case I were available for investigation. The father of Case I is an AI-bull with normal fertility. The father of Case II was a private owned bull whose fertility is unknown. No relationship existed between the two heifers.

DISCUSSION

In man there are two syndroms, testicular feminisation and pure gonadal dysgenesis, where an abnormal sex differentiation has resulted in a female phenotype in spite of a male chromosomal sex. Testicular feminisation has also been described in cattle (*Nes* 1966).

Pure gonadal dysgenesis was defined by *Harnden & Stewart* (1959) having a female or eunuchoid body conformation with bad developed bust and infantile female gonads. The ovaries are aplastic or remain as fibrous streaks (agenesia). *Boczkowski & Teter* (1966) emphasize that the diagnose should not be used unless follicles are completely absent. If the pure clinical definition is applied, several types of sex chromosome constitutions will be included: in addition to XY also XX and mosaics XO/XX/XXX, XO/XY and others. Such a definition has been disputed by *Sohval* (1963).

The two cases described in this article have some characteristics in common with pure gonadal dysgenesis in man: the XY-karyotype and the body conformation to some extent. However, the conformation varied between the two cases, one showing a rather normal heifer type, the other diverging towards a male type. In addition the ovaries were characterized by hypoplasia and dysgenesis and not by aplasia. Follicles were present although reduced in number and showing a clearly abnormal appearance. Consequently we prefer to characterize the two cases under the name of gonadal dysgenesis.

The histological appearance of the ovarian follicles are interpreted in the following way. The number of oocytes has been considerably reduced from the beginning. This has resulted in the formation of anovular follicles and cords. A certain number of primary follicles has contained oocytes. We have found one normal-looking primary follicle (Fig. 6). When the follicles have started to grow, the oocyte has degenerated, possibly as a consequence of the presence of the Y-chromosome. Most of the growing follicles have stopped at that stage but some have continued to the stage of anthrum formation. When the oocyte has

degenerated and disappeared, the resulting "follicle" resembles the anovular cords. However, they contain several layers of follicular cells and become much bigger (compare Figs. 7 and 9).

The clinical appearance of pure gonadal dysgenesis in man has been thought to be a consequence of disturbed androgen-estrogen balance in the fetus. Support for this theory is given by *Jost* (1947, 1961) who showed that rabbit fetuses being gonadectomized developed into phenotypical females. The cause of a "fetal castration" arising in spontaneous cases is unclear. One can speculate upon the effect of a gene mutation or the position effects of genes following translocation or inversion.

If the theory of "fetal castration" is applied upon the present cases in cattle, even a partial "fetal castration" must have been sufficient to change the development into a female direction. What kind of a defect gene action having caused this partial sex reversal is impossible to say. As far as we have been able to judge, the two cases have no relationship which could make a common origin probable.

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SUMMARY

Two heifers of the Swedish red and white (SRB) breed showed hypoplasia of the genital organs and the sex chromosomal constitution XY. The hypoplastic-dysplastic ovarian follicular system is given a more detailed description. No relationship was found between the two cases.

ZUSAMMENFASSUNG

Zwei Färsen mit Hypoplasie der Gonaden und der Geschlechtschromosomenstatus XY.

Zwei Färsen, die der Schwedischen roten und weissen (SRB) Rasse gehörten, zeigten Hypoplasie der Genitalorgane und die Geschlechtschromosomenkonstitution XY. Das hypoplastische-dysplastische follikuläre System der Eierstöcke wird näher beschrieben. Keine Verwandschaft wurde zwischen den beiden Fällen gefunden.

SAMMANFATTNING

Två kvigor med könskörtelhypoplasi och könskromosomstatus XY.

Två SRB-kvigor visade hypoplasi av könsorganen och könskromosomkonstitutionen XY. Det hypoplastiska-dysplastiska follikelsystemet i ovarierna beskrives mera i detalj. Ingen släktskap kunde påvisas mellan de båda fallen.

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