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A CASE OF TRUE HERMAPHRODITISM

A FURTHER REPORT

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[WITH SPECIAL PLATE]

The clinical and pathological findings in this case have already been reported (Armstrong, 1955; Case 1). The right gonad was predominantly a testis in which the seminiferous tubules were mostly represented by hyaline ghosts, only the outlines of the cells being recognizable; Sertoli cells were present in some tubules and there were numerous large masses of interstitial (Leydig) cells (Special Plate, Fig. 1). There was at least one atretic ovarian follicle in the right gonad (Plate, Fig. 2). The left gonad was an ovary and contained numerous atretic follicles, corpora albicantia, small atrophic cystic follicles (Plate, Figs. 3 and 4), and at the hilum a conspicuous number of interstitial cells.

The present report describes the sex chromatin of skin, oral mucosa, and internal genitalia, identified by the methods of Moore, Graham, and Barr (1953) and Moore and Barr (1954, 1955). The neutrophil morphology, following the criteria of Davidson and Smith (1954), is also described, and a full account is given of the very unusual blood-group findings because they may be related to the hermaphroditism and are interesting in themselves.

Examination for Sex Chromatin

Skin.—Over half the epidermal nuclei were chromatin-positive. Chromatin-positive nuclei were not found in an area about 1 mm. wide extending through the specimen.

Oral Mucosa.—Scrapings from both cheeks were chromatin-positive; 25% of suitable nuclei showed the typical planoconvex mass at the nuclear membrane.

Internal Genitalia.—Sex chromatin was identified in the interstitial cells of ovo-testis (Plate, Fig. 5), theca cells of ovo-testis (Fig. 6) and of ovary (Fig. 7), mucosa and muscle of uterus, uterine tube, and vas deferens. It was, however, present with less than the usual frequency, and often smaller in amount than in the normal female. Sex chromatin was not found in the Sertoli cells of the ovo-testis (Plate, Fig. 8), nor in the lining cells of the ovarian follicles, (Fig. 9); these cells did not display the clear chromatin pattern found in nuclei in which diagnosis is technically possible. Professor Barr (Barr, 1956) has examined these sections and the skin biopsy and agrees with the description above; he believes that the unusual appearances are due to technical causes and that the internal genitalia should be regarded as chromatin-positive.

Blood Films.—Neutrophils of typical female morphology were found in only two to three per 500 neutrophils examined. A further two to three neutrophils displayed a "drumstick" closely resembling the typical morphology, but were rejected because they were not quite solid, presenting a relative paleness at the centre or the periphery. It has not been our experience that these rejected neutrophils are found so frequently in the male. Fig. 10 on the Special Plate shows the five neutrophils most nearly fulfilling Davidson's criteria of female morphology in a count of 500; the first (a) is typical, the second (b) is very slightly pale in the centre, the third (c) and the fourth (d) show a more definite pale portion towards the periphery, and the fifth (e) is flattened on one side. Fig. 11 shows three neutrophils from the same count of 500; these were rejected as (a) a definite racket, (b) a minor lobe, and (c) a sessile knob. The exposure given during development of the prints has been varied so as to give the best reproduction of the microscopical appearances; all parts of the same print had identical exposures.

The Blood Groups

The ABO group of the patient is unusual. Her red cells are not agglutinated by anti-A or by anti-B sera, therefore they appear to be Group O; but her serum, though it contains the anti-A, lacks the anti-B expected of a Group-O person. She is a secretor and her saliva contains the H substance expected of a Group-O person, but it also contains B substance. The urine also contains B substance.

We can find nothing like this reported in the literature. The B₃ of Moullec *et al.* (1955) can clearly be distinguished, and so can the B_w of Levine *et al.* (1956). The peculiar B mentioned by Dunsford *et al.* (1956) was incompletely investigated and no comparison is possible.

Examples of an analogous condition in which the cells are apparently Group O though the serum lacks anti-A and the saliva contains A substance were described in 1942 by Gammelgaard and in 1956 by Wiener and Gordon. In 1957 Weiner *et al.* described two more examples; they were able to study the genetic basis of the phenotype and found it to be due to normal A genes and normal secretor genes acted upon by a rare and independent modifying gene, y, recessive in its effect. The genotype yy interferes with that function of A genes which normally would result in the presence of the antigen A on the red cells. The genotype yy has no effect on the B or H antigen. Had the patient been a normal subject we would have guessed that her blood and saliva adumbrated the existence of a complementary modifying gene, but as it is the blood-group abnormality seems more likely to be connected in some way with the hermaphroditism.

Serological Details.—It is only in the ABO system that the patient is outstanding; her groups in the other systems are normal.

Absence of B from Red Cells.—Agglutination tests on saline suspensions of the cells with many anti-B and anti-A+B sera were negative. Suspending the cells in albumin had no effect. The indirect antiglobulin test using anti-B serum was negative. The absence of B substance was, however, shown most convincingly by the sensitive tests of absorption and of elution: the red cells failed to absorb anti-B, and failed to give up anti-B on being heated after exposure to the antibody. The strength of the H-antigen of the patient's red cells appeared to be between that of an average Group O and an average Group B.

Absence of Anti-B from Serum.—No trace of anti-B could be found. Tests were carried out at various temperatures against cells suspended in saline solution and in albumin and with cells treated with papain. Anti-A and anti-A₁ were present and in normal amount.

Presence of B in Saliva.—The patient's saliva contains a large amount of B substance, but not quite so much as that found in the saliva of most B secretors. It also contains H substance in amount as great as that in Group-O-secretor saliva (which is greater than that found in Group-B-secretor saliva). Her saliva, as would be expected, also contains some Le^a substance.

Other Groups.—These were: MsMs, P₁, CDe/CDe, LubLub, Kk, Le(a-b+), FyaFya, and JkbJkb. The antisera used were: anti-M, -N, -S, -s, -U, -Mia, -Vw; anti-P₁, -P+P₁; anti-D, -C, -c, -C^w, -E, -e, -V; anti-Lu^a, -Lu^b; anti-K, -k; anti-Le^a, -Le^b; anti-Fya, -Fyb; anti-Jk^a, -Jk^b.

It is difficult to believe that such an extraordinary ABO group finds itself merely by chance in a body so extraordinary in other ways. It seems reasonable to expect that in time the two conditions will be seen to be connected.

Discussion

The mechanism by which the XX chromosome pair causes the female gonad to be developed in preference to the male is unknown; therefore it is not possible to do more than speculate as to the causes leading to the development of testicular and ovarian tissue in the same individual. Freemartins in cattle and swine may develop testicular and ovarian tissue in the presence of a normal set of chromosomes. Domm (1939) has reported that female chicks produce a testis if the ovary is removed soon after hatching. Evidently it is not necessary in every case to postulate a genetic cause for hermaphroditism. In the present case, however, the association between the excessively rare ABO blood group findings, which must be genetic, and the hermaphroditism leads one to search for a genetic mechanism capable of producing both findings at one stroke.

Plunkett and Barr (1956) discussed the possible causes leading to sex-chromatin findings in skin and neutrophils similar to ours in two cases of Klinefelter's syndrome. They suggested that an X chromosome may have been involved in a reciprocal interchange or translocation. The ABO blood group findings suggest that the patient may be homozygous for a gene interfering with the function of the B genes in a way analogous to the action of the genotype yy described above. Perhaps our patient is in reality heterozygous for the interfering gene, but the action of the normal dominant allele is lost because it is on the other chromosome involved with X in a reciprocal translocation.

Summary

A further report is made on a case of true hermaphroditism of which a clinical account has already been given.

The skin and oral mucosa are chromatin-positive. The internal genitalia are chromatin-positive, but the typical chromatin mass is smaller and less frequent than usual. Two to three neutrophils per 500 counted displayed the typical female "drumstick."

The blood group is O, but there is no anti-B substance in the serum. The patient is a secretor, and B substance is found in the saliva and urine.

It is suggested that reciprocal interchange between an X chromosome and an autosome carrying a gene necessary for the placement of B on the red blood corpuscles is responsible.

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FULMINATING STAPHYLOCOCCAL PNEUMONIA ASSOCIATED WITH INFLUENZA VIRUS C

REPORT OF A FATAL CASE

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Taylor (1949) first isolated influenza virus C in 1947 from a patient suffering from a mild influenzal illness. The occurrence of this virus in human illness which has been recorded since then (Francis *et al.*, 1950; Fukumi *et al.*, 1951; Styk, 1954; Minuse *et al.*, 1954; De Meio *et al.*, 1955; Andrews and McDonald, 1955) has shown that it is usually associated with mild or trivial infections of the respiratory tract. A few authors have, however, described more severe illness. Gerber *et al.* (1952) isolated the virus from U.S. naval recruits in whom "pneumonia of unknown aetiology" was diagnosed; Grist (1955) found serological evidence of infection in four adults admitted to hospital with a diagnosis of pneumococcal pneumonia; and Librach (1956) described the cases of two patients with "severe bronchopneumonia" in whom infection by influenza virus C was diagnosed on serological grounds. None of these infections, however, proved fatal.

The occurrence of fulminating staphylococcal pneumonia complicating infections by the influenza viruses A and B is well recognized (Stuart-Harris, 1953). This paper describes a fatal case of *Staphylococcus aureus* invasion of the lungs in association with influenza virus C, which was isolated 18 hours before death.

Case Report

A housewife aged 46 was admitted to hospital at 7 a.m. on July 6, 1956, because of severe dyspnoea from an extensive pneumonia. Her previous health had been good until the preceding week, when she had developed a mild infection of the upper respiratory tract. She did not take

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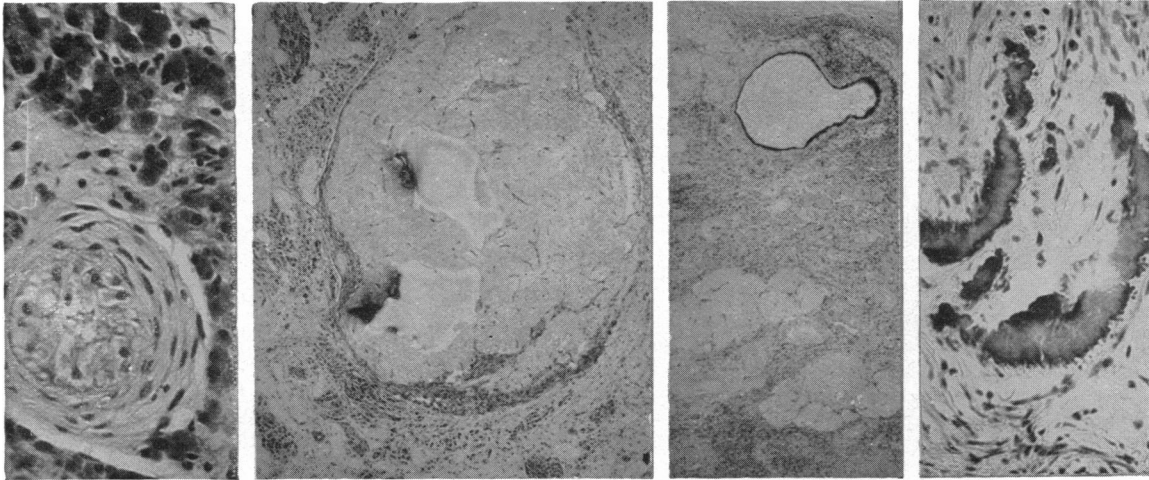


FIG. 1.—Right gonad: seminiferous tubule interstitial cells. (Haematoxylin and eosin. $\times 250$.) FIG. 2.—Right gonad: atretic ovarian follicle. (Haematoxylin and eosin. $\times 30$.) FIG. 3.—Left gonad: cystic ovarian follicle. (Haematoxylin and eosin. $\times 30$.) FIG. 4.—Left gonad: glassy membrane. (Haematoxylin and eosin. $\times 170$.)

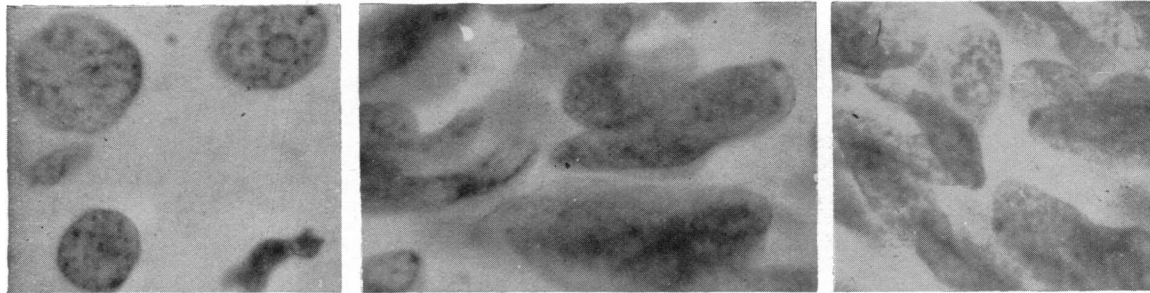


FIG. 5.—Right gonad: interstitial cells. Sex chromatin visible. (Feulgen. $\times 1,500$.) FIG. 6.—Right gonad: theca cells. Sex chromatin visible. (Feulgen. $\times 1,500$.) FIG. 7.—Left gonad: theca cells. Sex chromatin visible. (Feulgen. $\times 1,500$.)



FIG. 8.—Right gonad: Sertoli cells. Nuclei have a cloudy appearance. Sex chromatin not visible. (Feulgen. $\times 1,500$.) FIG. 9.—Left gonad: granulosa cells. Nuclei have a cloudy appearance. Sex chromatin not visible. (Feulgen. $\times 1,500$.)

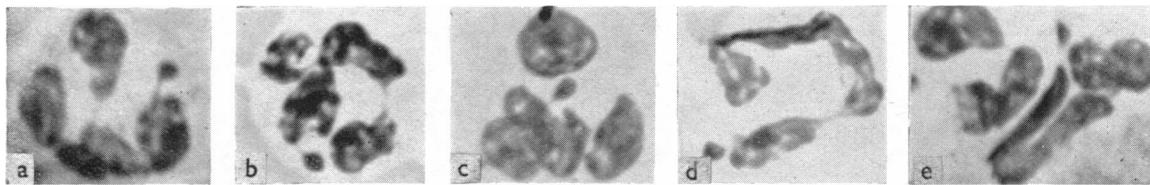


FIG. 10

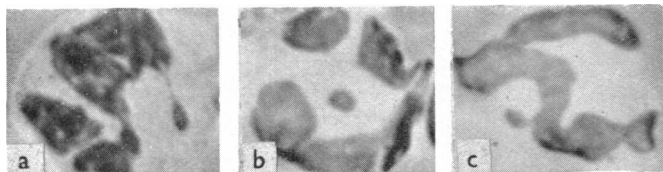


FIG. 11

FIG. 10.—“Drumsticks” from a count of 500 neutrophils. (For description see text.) ($\times 1,800$.)

FIG. 11.—Two rackets and one sessile knob from the same count of 500 neutrophils. ($\times 1,800$.)