concentration was 12.5 mg/l. Treatment was changed to metronidazole 400 mg three times daily and cultures rapidly ceased to grow *C difficile*. The organism was not isolated over the succeeding 18 months and radiological changes suggested a resolving infection. The patient had no gastrointestinal symptoms at any time during the illness.

Discussion

Osteomyelitis caused by anaerobic bacteria is rare, and we are not aware of any previous reports of *C difficile* causing this disease. *C difficile* was first isolated by Hall and O'Toole,³ who found it to be part of the normal gastrointestinal flora of infants. Smith and King⁴ reported the isolation of *C difficile* from several extraintestinal sites, and more recently it has been implicated as the causative agent of pseudomembranous colitis.⁵

The interesting features of this case are the unusual site of infection for this organism, the length of time over which the organism was isolated despite apparently appropriate treatment, and the development of penicillin resistance during treatment.

The source of the organism was probably the patient's own gastrointestinal tract, but the possibility of environmental infection cannot be excluded. Possibly the infection did not occur until after the initial drainage. The first abscess may have been sterile, as suggested by the first culture results, and merely a response to the foreign body present. It is unclear why the organism persisted for so long. On some occasions only very few

organisms were present and thus enrichment media were required for isolation. The production of spores in vivo could explain the organism's persistence. The development of resistance to antibiotics during treatment is certainly not uncommon, and its occurrence in the present case added interest to an already interesting case. It is worth noting that transferable drug resistance in *C difficile* has recently been reported.⁶

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Twin pregnancy with complete hydatidiform mole (46,XX) and fetus (46,XY): genetic origin proved by analysis of chromosome polymorphisms

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Abstract

In a case of complete hydatidiform mole with fetus the genetic origins were defined by the use of chromosomal polymorphisms. The fetus had a normal 46,XY karyotype with evidence of the presence of both maternal and paternal chromosomes. The mole was 46,XX and of androgenetic origin. There was no evidence of a maternal contribution, and duplication of paternal chromosomes was shown.

In such atypical molar pregnancies examining genetic polymorphisms yields much more information than do sex chromosome studies and karyotyping, particularly in confirming the diagnosis and defining the origin and aetiology of the condition.

Introduction

Hydatidiform mole may be separated into two entities on the basis of histopathology,^{1,2} cytogenetics,³⁻⁸ and biochemical

markers.^{5,7} Complete moles lack the presence of a fetus, are almost always female, and are androgenetic in origin.^{3-5,7} In contrast, partial moles have a range of villi from normal to hydatidiform, focal rather than conspicuous hyperplasia, and evidence for the presence of a fetus.² When karyotype analysis of the placenta and fetus has been carried out partial moles have generally been found to be triploid.^{1,6-10} Cases of mole with co-existent fetus must now be assessed in the light of these findings.

Patient and methods

The patient was a 27-year-old woman who had given birth to a normal girl in 1972 and a normal boy in 1976. She presented in her third pregnancy at eight and a half weeks of gestation with a uterus size of 14 weeks. Ultrasound examination showed the presence of a fetus. When she was seen again three weeks later with painless vaginal bleeding and an enlarged uterus no fetus was detected on scanning. The pregnancy was terminated by suction evacuation at 15½ weeks because of a suspected mole.

Macroscopic examination of the specimen showed a large mass of molar tissue comprising clusters of translucent thin-walled cysts ranging from 2 to 20 mm in size, encased in clotted blood. A small portion of apparently normal placenta associated with some membranous material was seen and appeared to be separate from the main bulk of the vesicular mass. Also present was a partially macerated male fetus with a crown-rump length of 4.5 cm and a foot length of 6 mm, and therefore estimated to be between 8 and 10 weeks of gestational age. Further examination showed no external abnormalities, all limbs being present and with the normal number of digits. On dissection no abnormalities were detected in the internal organs.

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Cultures were set up of molar tissue, amniotic membrane associated with the normal placenta, and fetal muscle, as described.⁸ Suitable metaphase spreads for detailed analysis were obtained from the molar tissue and the amniotic membranes. Chromosome preparations were also made from blood lymphocytes of the mother and father.

Karyotypes of the molar tissue, amniotic tissue, and the mother and father's lymphocytes were examined by a modification of the acetic-saline-Giemsa and trypsin techniques.¹¹ Polymorphisms of the C banding and Q banding were examined using previously described methods,^{12,13} while lateral asymmetry was studied in cells grown in 5-bromodeoxyuridine.¹⁴

Results

Pathology—Routine histopathological examination of the cystic area of the placenta confirmed a hydatidiform mole with a low level of cellular atypia of the trophoblast. Microscopical examination of the macroscopically normal placental tissue showed villi that had undergone a moderate degree of perivillous fibrin deposition, which was reported to be of doubtful clinical importance. There was no histological evidence of malignancy in any of the tissue.

Cytogenetic studies—G-banded karyotypes of both parents were normal. G banding of cells grown from the molar tissue showed them to be karyotypically 46,XX. The amniotic cells were, however, 46,XY. Figure 1 shows the result of C banding the number 1 chromosome of the maternal, paternal, molar, and amniotic cells. The C-banding

FIG 1—Inheritance of number 1 chromosomes as determined by C banding. Figure shows androgenetic origin of mole and presence of number 1 chromosomes from both parents in twin.

pattern of the molar tissue showed two identical number 1 chromosomes, both paternally inherited. The paternal inheritance of number 1 chromosomes was confirmed by lateral asymmetry (fig 2), which showed two identical number 1 chromosomes in the mole having a class I pattern of lateral asymmetry¹⁴ seen only in the father. The C-banding pattern of the number 1 chromosomes from the amniotic cells showed one to have come from the father and the other to be maternally derived. Lateral asymmetry patterns of these chromosomes confirmed that one number 1 was derived from the father—that is, that with the small class II pattern—while the number 1 with the larger heterochromatin region with the simple lateral asymmetry pattern was maternal in origin. Though Q banding was relatively uninformative, it confirmed a maternal contribution to the fetus in that one number 22 chromosome in the fetus had a satellite of medium intensity seen only in the mother.

Discussion

During a study of the genetic origin of hydatidiform moles we have examined 66 moles. Fifty of these were complete, having

no evidence for the presence of a fetus, while the other 16 were partial with evidence for the presence of a fetus, seen as fetal vasculature in the pathological sections of the tissue. In three cases there was macroscopic evidence of a fetus. When genetic analysis of the partial moles was carried out they were found to be triploid with one maternal and two paternal contributions.⁸

FIG 2—Inheritance of pattern of lateral asymmetry in chromosome 1.

The case described here was the first in which we have found a diploid mole associated with a fetus. G banding of chromosomes from the fetal amnion and molar tissue showed that while the amniotic cells were 46,XY the molar cells were 46,XX, suggesting that this was a dizygotic twin pregnancy in which one of the pair of twins had developed into a mole. Dizygotic twin pregnancies normally occur in about one in 110 pregnancies.¹⁵ Dizygotic twin pregnancies in which there was a normal placenta associated with a fetus and a separate molar mass were reported by Beischer,¹⁶ who found 30 such cases in a review of 92 cases of molar pregnancies associated with a fetus. In 18 of these cases the twin fetus was, in fact, live born. Since 1966 about 15 further cases of mole with coexistent fetus which could represent a twin pregnancy, and one case of a triplet pregnancy where there was a separate molar mass and two normal placentas,¹⁷ have been reported.

In Beischer's series the sex of the fetus associated with the mole in the dizygotic twin pregnancies was reported in 13 of the cases and found to be male in seven and female in six. In later reports, where the sex of the coexisting fetus was identified, there were six male to three female fetuses.¹⁷⁻²⁵ In the triplet pregnancy associated with the mole¹⁷ both fetuses were male. Our report adds another case of a male fetus coexisting with a molar pregnancy, the sex having been confirmed by cytogenetic analysis.

In most cases the molar tissue and the normal placenta with fetus were delivered separately and were obviously two separate entities. In some cases, however, as in ours, the diagnosis of a dizygotic pregnancy was made possible by the results of genetic studies. Beischer and Fortune²⁶ described two cases in which sex chromatin studies gave positive (female) results in the molar tissue and negative (male) results in the normal placenta, so

providing a diagnosis of dizygotic twins. Sex chromatin studies are, however, of limited value in studying molar pregnancies associated with a fetus where triploidy, indicative of a partial mole, could be missed.

Karyotyping of the fetus was carried out in some cases,^{17 20 24-26} though attempts to culture the molar tissue were not always successful.^{20 24} Two other cases have been described^{25 26} in which the karyotype of the molar tissue associated with the twin fetus was found to be 46,XX. Karyotyping is again of limited value in examining the relation between the mole and the fetus, particularly when they are of like sex.

Much more information, in terms of confirming the diagnosis and in studying the origin and aetiology of these atypical molar pregnancies, may be obtained from examining genetic polymorphisms. We have described the first case of twin pregnancy with mole in which genetic polymorphisms were examined. Studies of the molar, fetal, and parental chromosomes showed that the mole was both androgenetic and homozygous for the polymorphic markers studied, thus confirming the pathological diagnosis of complete mole. These studies also confirmed the normal origin of the fetus by showing that the chromosomes had been derived from both parents.

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IT has already been observed, that colds are the effect of an obstructed perspiration; the common causes of which we have likewise endeavoured to point out, and shall not here repeat them. Neither shall we spend time in enumerating all the various symptoms of colds, as they are pretty generally known. It may not however be amiss to observe, that almost every cold is a kind of fever, which only differs in degree from some of those that have already been treated of.

No age, sex, or constitution is exempted from this disease: neither is it in the power of any medicine or regimen to prevent it. The inhabitants of every climate are liable to catch cold, nor can even the greatest circumspection defend them at all times from its attacks. Indeed, if the human body could be kept constantly in an uniform degree of warmth, such a thing as catching cold would be impossible: But as that cannot be effected by any means, the perspiration must be liable to many changes. Such changes, however, when small, do not affect the health; but, when great, they must prove hurtful.

DID mothers reflect on their own importance, and lay it to heart, they would embrace every opportunity of informing themselves of

the duties which they owe to their infant offspring. It is their province, not only to form the body, but also to give the mind its most early bias. They have it very much in their power to make men healthy or valetudinary, useful in life, or the pests of society.

BUT the mother is not the only person concerned in the management of children. The father has an equal interest in their welfare, and ought to assist in every thing that respects either the improvement of the body or mind.

It is pity that the men should be so inattentive to this matter. Their negligence is one reason why females know so little of it. Women will ever be desirous to excel in such accomplishments as recommend them to the other sex. But men generally keep at such a distance from even the smallest acquaintance with the affairs of the nursery, that many would esteem it an affront, were they supposed to know any thing of them. Not so, however, with the kennel or the stables: A gentleman of the first rank is not ashamed to give directions concerning the management of his dogs or horses, yet would blush were he surprised in performing the same office for that being who derived its existence from himself, who is the heir of his fortunes, and the future hope of his country.

(Buchan's *Domestic Medicine*, 1786.)