

MANAGEMENT OF SEVERE ANAEROBIC INFECTIONS IN OBSTETRICAL AND GYNAECOLOGICAL CASES WITH METRONIDAZOLE

(Four Case Reports)

by

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Summary

Management of four cases, two obstetrical and two gynaecological, with severe anaerobic infections, have been presented.

The role of metronidazole in the management of these severely ill patients with anaerobic infections has been discussed.

It is concluded that but for the availability of metronidazole in our armamentarium of treatment, it would not have been possible for us to achieve an uneventful recovery for these patients.

Over the past few years, the importance of the non-sporing anaerobes has been increasingly recognised in infections of the female genital tract (Hite *et al*, 1947; Thadepalli *et al*, 1973; Swenson *et al*, 1973; Bartlett *et al*, 1977). Most of the infections are associated with a mixed flora of aerobes and anaerobes and Gorbach and Bartlett (1974) rightly pointed out that "the role of any single species in this complicated menage is difficult to ascertain."

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The anaerobicidal activity of metronidazole has been reported by Ingham *et al* (1975). Sprott and Ingham (1979) have reviewed the current trends in the treatment of infections due to the non-sporing anaerobes.

We were inspired to undertake this study by the pioneering work of Willis *et al* (1974, 1975 and 1978) who have demonstrated the successful use of metronidazole (which acts only in obligate anaerobes), for the treatment and prevention of these infections. They not only showed that metronidazole helps the patients but also identified the obligate anaerobes as primary pathogens.

Material and Methods

In this communication, we present our experience with metronidazole in 4 seriously ill patients with severe anaerobic infections.

Case 1

I. P., 30 year old was admitted with a history of eight months' amenorrhoea and prolonged leaking of the membranes for 4 days. She presented with a foul smelling vaginal discharge and intra-uterine foetal death. The pregnancy was terminated by vaginal craniotomy. The next day, she showed signs of a generalised peritonitis for which she was explored and 500 ml

of pus were drained. All the organs showed signs of inflammation and the tubes were pouring pus into the peritoneal cavity. A total abdominal hysterectomy with a bilateral salpingectomy was then performed.

On admission, she was given metronidazole 400 mg 8 hourly, orally and gentamicin 80 mg 8 hourly, intramuscularly. Post-operatively, metronidazole was administered 500 mg 8 hourly, in the form of a rectal enema and gentamicin was given intramuscularly.

On the 10th post-operative day, the patient went into a prehepatic coma and renal failure which was confirmed by investigations, to be due to septicaemia. This necessitated a change of the route of administration of metronidazole to the intravenous route and gentamicin was reduced to 20 mg 8 hourly. On the 14th post-operative day, she developed a superficial gaping of the abdominal wound and a bone deep pressure sore 15 x 15 cms at the sacral region which healed with the administration of oral metronidazole and ampicillin without any surgical intervention. The patient was discharged in a perfectly healthy condition. The histopathology report showed chorioamnionitis and pyometra (Fig. 1).

Case 2

Following a caesarean section at Karjat for prolonged labour, N. A., a 33 year old patient presented in a febrile, toxic condition shown by the TPR, and a complete muscle-deep gaping of the abdominal wound pouring out pus. A profuse foul smelling vaginal discharge was also present and specimen for culture were taken.

On the first day, the patient was administered 500 mg ampicillin 12 hourly, and 80 mg gentamicin 8 hourly. This therapy was continued for 3 days. The same condition, however, persisted, hence 500 mg metronidazole 8 hourly, was added to the regimen in the form of a retention enema. Within 24 hours, the TPR settled and the patient showed signs of improvement. As the patient could tolerate oral feeds well, metronidazole 400 mg 8 hourly and ampicillin 250 mg 6 hourly were administered by mouth and gentamicin 80 mg was continued intramuscularly.

The vaginal and abdominal wound discharge reduced gradually. On the 10th day of metronidazole, the abdominal wound was free from

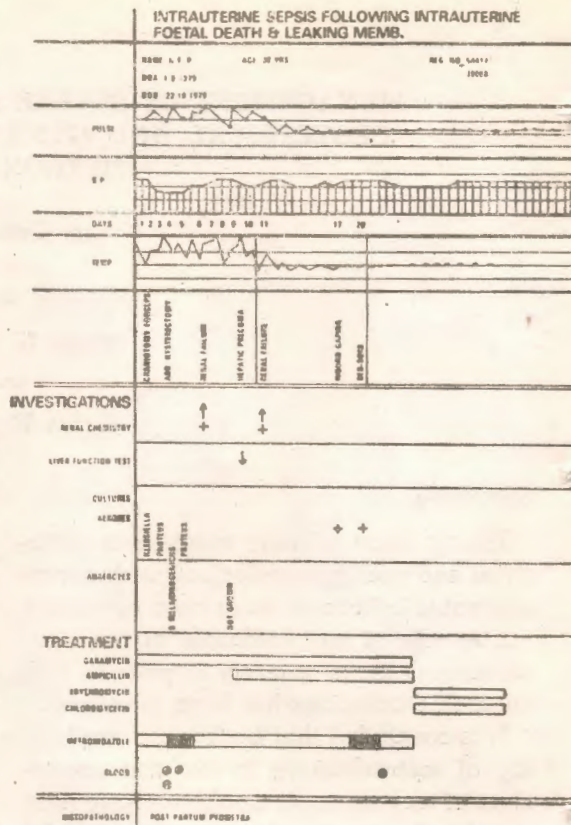


Fig. 1

discharge and organisms. The patient was taken for resuturing. Chloramphenicol was then added to the metronidazole therapy and the stitches were removed on the 10th day. The union was good and the patient was discharged (Fig. 2).

Case 3

B. P., 60 year old was diagnosed as having peritonitis following appendicitis. On exploration, the appendix and the colon were found to be normal. Perforations on the fundus and the posterior aspect of the uterus were however found discharging a greenish necrotic material into the peritoneal cavity. The tubes and the ovaries were normal. A panhysterectomy was therefore performed. The post-operative therapy consisted of parenteral penicillin and gentamicin and on the second day, oral metronidazole was added. The patient

PUERPERAL SEPSIS
(FOLLOWING CAESAREAN SECTION)

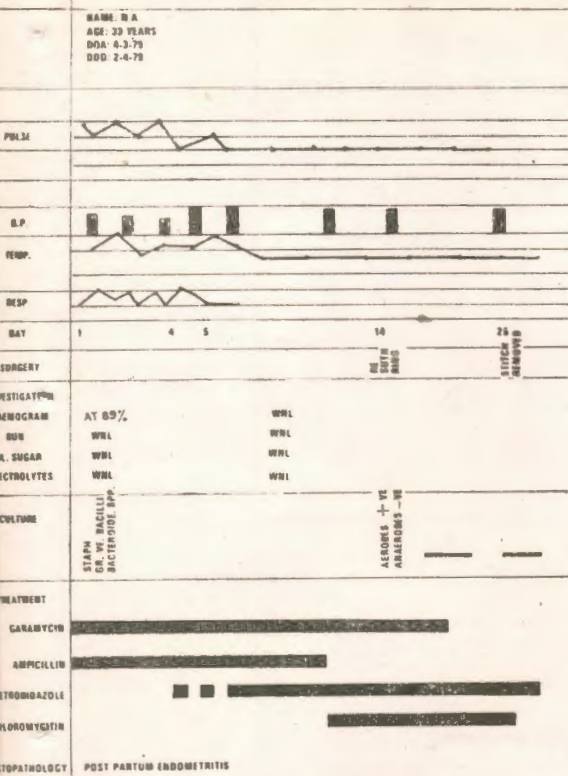


Fig. 2

developed gaping of the abdominal wound on the 10th day. The same was sutured after 5 days and the patient was discharged two weeks later. The histopathology report showed a suppurative endometritis with myometrial necrosis and perforation (Fig. 3).

Case 4

S. J., 27 year old, case of stage II carcinoma cervix was admitted with a foul smelling, blood stained vaginal discharge and post-coital bleeding. Speculum examination revealed a fungating necrotic growth with a copious blood stained discharge. Cultures taken yielded both aerobes as well as anaerobes.

On the morning of surgery, 500 mg of metronidazole I.V. and 60 mg of gentamicin were administered. A Wertheim's hysterectomy was

performed and the same therapy was continued for 48 hours after which gentamycin I.M. and metronidazole 400 mg 8 hourly was given orally. The third day post-operation culture grew some anaerobic organisms but subsequent cultures were free of organisms and the patient was discharged after 3 weeks (Fig. 4).

Discussion

Gorbach and Bartlett (1974) reported endometritis following caesarean section in 10-20% of the cases; earlier, Pearson and Anderson (1970) had reported a 6% incidence. Phillips and Sussman (1974) observed that when a caesarean section is done after a prolonged rupture of the membranes, amnionitis is an hazard with an excessive contamination of the operation field with the endogenous bacteria, including anaerobes. Garsher and Ledger (1976) have made a prospective six months' survey of infection/morbidity after a caesarean section. The incidence of post-operative infections was found to be 40.4% in patients who had intensive foetal monitoring, 20.4% in those who had no foetal monitoring and 5% in patients who had elective repeat caesarean section.

Pyometra is a fairly frequent infection involving the anaerobic bacteria in older women with carcinoma of the cervix or of the endometrium, the predisposing factors being cervical stenosis arising spontaneously or after cauterization or radiation. Sugiyama *et al* (1972) showed that the exudates in carcinoma cervix almost always grow anaerobic bacteria. They found that 39 out of 46 cultures from patients with infections associated with carcinoma of the cervix contained anaerobic bacteria, out of which 23 yielded anaerobes exclusively. Thadepalli *et al* (1973) and Swenson *et al* (1973) reported the incidence of anaerobic infections in cases of endome-

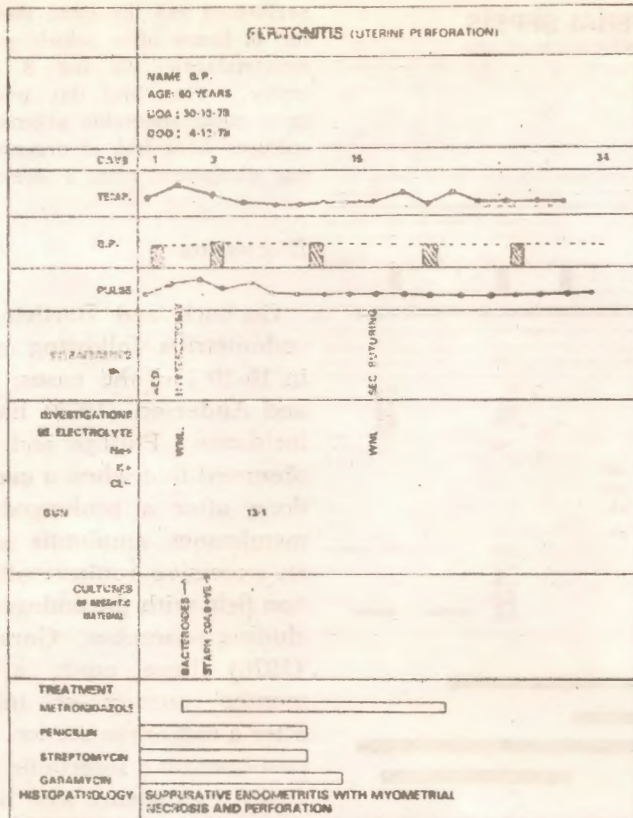


Fig. 3

tritis and pyometra to be 10% and 92.8% respectively.

It is now well established that a foul smelling suppurative inflammation is almost always due to the obligate anaerobes (Alteimier, 1938); Bodner *et al*, 1970; Gorbach and Bartlett, 1974). A copious foul smelling discharge is the hallmark of nonclostridial anaerobic infections (Willis, 1977).

In this study, we have presented two obstetrical cases, one of chronic amnionitis and the second of endometritis with wound infection following caesarean sections for prolonged rupture of the membrane and two gynaecological cases, of which one is

a case of carcinoma stage II and the second pyometra resulting in uterine perforation following post-cervical stenosis.

The cases reviewed in this report clearly show that all of them had mixed infections, aerobic as well as anaerobic. All of them recovered uneventfully with metronidazole therapy. Although the first case went into a prehepatic coma and kidney shut down, she too recovered without any residual effect.

Cerat *et al* (1977) studied the rate of excretion following the administration of a single oral dose of 500 mg of metronidazole to volunteers with both normal or impaired renal function and found no sig-

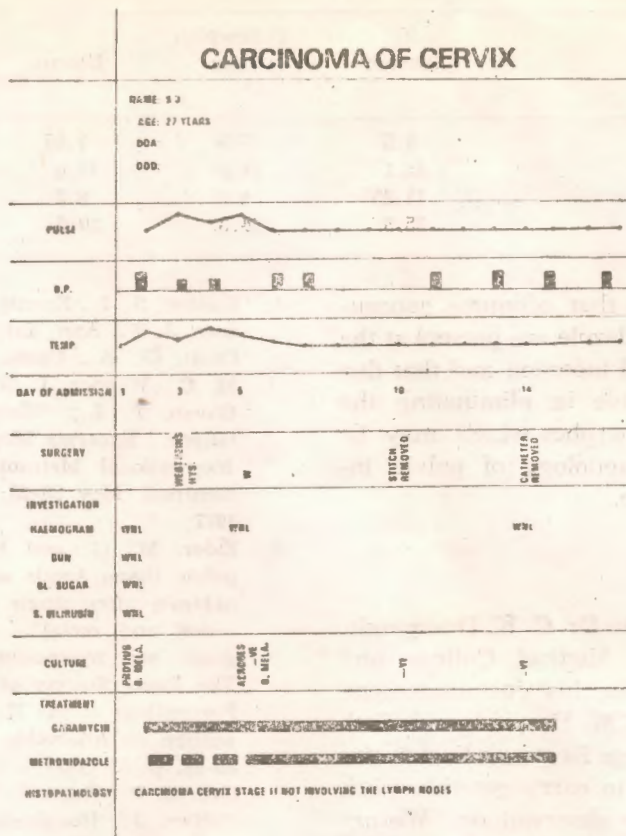


Fig. 4

nificant change, indicating that a single oral dose was metabolised similarly by both normal subjects and those with absent or severely impaired renal function.

Gabriel *et al* (1979) studied that pharmacokinetics of metronidazole in patients with chronic renal failure and recommended that the dose of intravenous metronidazole should not be specifically reduced in anuric patients and accumulation of metabolites would not occur because they are rapidly removed by dialysis.

Metronidazole has proved to be a very effective antimicrobial agent when used for the treatment of infections caused by

the anaerobic bacteria. Metronidazole has bactericidal activity against most of the anaerobes and this phenomenon is probably responsible for the rapid and dramatic response to the drug in all our seriously ill patients.

Fleder and Kane (1979) studied the pelvic tissue levels achieved by metronidazole after a single or multiple dosing following oral or rectal administration and found that the levels in the myometrium and fallopian tube were similar and that these are equal to the serum levels. The mean levels of metronidazole (ug/ml) in the serum and the pelvic tissues with four dosage regimens are shown below:

Dosage	Serum	Fellowpian tube	Uterus	Time after dose (in minutes)
400 mg orally x 1	8.5	7.5	7.05	212.9
400 mg orally x 4	15.1	14.0	13.6	212.2
1 gm rectally x 1	11.25	9.3	9.2	213.75
1 gm rectally x 4	25.3	24.3	20.5	—

The data shows that adequate concentrations of metronidazole are present at the site of the potential infection and that this dose will be effective in eliminating the Gram-negative anaerobes which may be implicated in the aetiology of pelvic inflammatory disease.

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