

Unusual Presentation of Choriocarcinoma

A Case Report

W. T. VILLET, D. F. DU TOIT, C. CONROY

SUMMARY

We report the management of a case of malignant trophoblastic disease which presented initially as a haematemesis and melaena from a gastric metastasis. The patient had had a tubal sterilization 4 years previously. The management of trophoblastic disease in general is also discussed, and the importance of chemotherapy is stressed.

S. Afr. med. J., 55, 96 (1979).

Gestational trophoblastic neoplasms are characterized by abnormal proliferation of the trophoblast. They fall into the three categories of benign hydatidiform mole, invasive mole, and highly malignant choriocarcinoma. Trophoblastic hyperplasia without hydrops is a related benign lesion. Like normal gestational trophoblast, the tumours tend to invade adjacent tissues. Tumour erosion of blood vessels with resultant blood spread, and even spontaneous regression after termination of pregnancy, are curious features of these neoplasms. Chorionic gonadotrophin is produced by proliferating trophoblast, and thus the titre of the secreted hormone may be serially measured. Prognosis is influenced by duration of disease, tumour type, presence and location of metastases, hormonal monitoring, and response to, and complications of, therapy. Complete and sustained remissions are being reported in more than 90% of cases despite evidence of spread. Genetically the tumour tissue is dissimilar from that of the host, since the fetus may be regarded as an allograft. Trophoblastic neoplasms are potentially foreign to the host. Thus it has been theorized that immunological rejection of the metastatic choriocarcinoma during chemotherapy may be an associated factor in the responsiveness of such a tumour to this therapy.¹ A unitary view of trophoblastic overgrowth as a continuum of hyperplastic and neoplastic phenomena has been suggested.² The degree of trophoblastic proliferation occurring in hydatidiform mole is now graded.¹ Therapeutic categories based on prognosis determine the management of patients.²

Departments of Anatomical Pathology and Surgery, Tygerberg Hospital and University of Stellenbosch, Parowvallei, CP

W. T. VILLET, F.F. PATH. (S.A.), Senior Specialist
D. F. DU TOIT, F.C.S. (S.A.), F.R.C.S., Registrar
C. CONROY, M.B. CH.B., Clinical Assistant

Date received: 14 July 1978.

CASE REPORT

A 30-year-old Coloured woman was admitted to our surgical unit with a history of 5 uncomplicated pregnancies. She had had bilateral tubal ligation 4 years before admission. For 4 months she had experienced progressively more severe headaches, with weakness and weight loss, menorrhagia and dyspepsia.

Severe haematemesis followed ingestion of large quantities of analgesics taken for the headaches and dyspeptic complaints. On examination the patient was shocked and had a haemoglobin level of 7 g/100 ml. Signs of recent weight loss were also apparent. The respiratory and cardiovascular systems were clinically normal.

Abdominal examination revealed previous nephrectomy, appendectomy and sterilization scars. The nephrectomy had been performed for renal stones. Melaena was evident on rectal examination.

A barium meal study elicited an irregular gastric lesser curvature, but was otherwise normal. The gastroscopy findings were those of haemorrhagic gastritis, possibly precipitated by the analgesics. A routine chest radiograph revealed a 3-cm round shadow in the left upper lobe of lung. The appearance of this shadow was suggestive of a metastatic lesion.

A second episode of haematemesis occurred 14 days later, which necessitated a repeat gastroscopy examination. This revealed a small ulcerated nodule on the greater curvature of the stomach. The ulcer crater contained blood.

At laparotomy a small raised lesion was found in the stomach wall. The macroscopical appearance was that of a benign leiomyoma and warranted local excision. Apart from a slightly enlarged uterus, the abdominal organs were normal. No metastases could be found in the abdominal cavity.

The histological examination of the tumour was that of a choriocarcinoma which had metastasized to the stomach. Necrotic tumour thrombus partially occluded blood vessels in the submucosa. No chorionic villi were present. A probable uterine origin was proposed. Subsequent investigation revealed a positive pregnancy test and markedly raised human chorionic gonadotrophin levels in the serum and urine (β -subunit; Biodata HCG-BETA Kit). Serum levels in excess of 200 000 IU were monitored every 24 hours. In view of this, as well as the 4-month history and possible clinical involvement of the brain, the patient was considered to be in a high-risk group.^{2,3} Thus post-operative combination chemotherapy consisting of methotrexate, actinomycin D and chlorambucil was begun, as for group III patients.² On the 4th day of treatment the patient developed signs of acute respiratory failure, and on the next day she died. Permission for post-

mortem examination could not be obtained. It was thought that haemorrhage into a cerebral metastasis was the likely cause of death.

DISCUSSION

Choriocarcinoma is a relatively rare tumour, usually found in women of child-bearing age.

A rare cause of haematemesis and melaena is metastatic gastric choriocarcinoma. The onset of the massive bleed may have been precipitated by tumour erosion of the vessel wall as well as by the large amount of aspirin ingested to relieve the headaches. Besides the haemorrhage as evidence of spread, the headaches and the radiological lung lesion are suggestive of cerebral and pulmonary involvement. Metastatic spread to the stomach can occur from any widely-disseminated malignancy.

Ober *et al.*⁴ reported the lungs to be universally involved, followed in frequency by brain, liver, kidneys, small intestine, spleen, and vagina. The metastatic tumour may be small, haemorrhagic and necrotic, and may give rise to severe haemorrhage, as in our case.

The primary tumour was most likely situated in the enlarged uterus in this case. In view of a rather non-specific history apart from sterilization 4 years previously, the possibilities of origin of the tumour can be pointed out. Choriocarcinoma is preceded by hydatidiform mole in one-third to one-half of cases.⁵ The remaining cases are about equally divided between preceding spontaneous abortions, preceding normal pregnancies, and about 2-3% follow ectopic pregnancies. Rarely, the tumour is of a non-gestational type, when it appears as a component of a germ cell neoplasm of the ovary, but, very rarely, it may be in a pure form. An unusual feature of this case is the manifestation of this malignancy more than 4 years after an apparently effective tubal sterilization. This disease usually becomes manifest within 2 years of a preceding molar or non-molar pregnancy. However, this interval may be up to 9 or 10 years.⁵ Curiously, the tumour may manifest years after hysterectomy, or after the menopause. Also, lack of a demonstrable primary lesion is well documented; and the primary lesion may have regressed, leaving a cyst, a scar, or iron pigment from old haemorrhage in the case of a testicular tumour. This case thus partly demonstrates the very variable nature of this tumour.

Brewer and Gerbie⁶ described 2 cases of focal choriocarcinoma in an otherwise normal placenta. The placenta was described as being non-molar and normal except for a focal area of marked trophoblastic proliferation. It was suggested that this could represent the very early development of choriocarcinoma, and that it may have explained some cases of metastatic disease following non-molar pregnancies or abortions. 'It provides a challenge to pathologists to examine small, focal lesions of the placenta that look like haemorrhage, infarction or chorangioma.'⁶

In the management of trophoblastic disease, a therapeutic classification based on prognosis is ideally utilized by Jones.² The categories are as follows: group I — non-metastatic. Titre and duration of disease less important.

All histopathological diagnoses. Group II — metastatic (low risk). Apparent metastases in sites other than liver or brain. Titre less than 100 000 IU/24 hours, duration of disease less than 4 months. All histopathological diagnoses. Group III — metastatic (high risk). Apparent metastases in sites other than liver or brain. Titre greater than 100 000 IU/24 hours, duration of disease greater than 4 months. All histopathological diagnoses. Group IV — metastatic (high risk) — brain and liver. Titre and duration of disease less important. All histopathological diagnoses.

Group I includes cases of undelivered hydatidiform mole, recently evacuated molar pregnancy, persistence of human chorionic gonadotrophin titre after evacuation of a mole, and choriocarcinoma after abortion or full-term delivery. Prognosis is generally best for this group, and worst for group IV. Most patients are cured by evacuation of the uterus alone, but close follow-up is essential.

Group II patients present with pulmonary, pelvic or vaginal lesions. Single-agent chemotherapy using actinomycin D and methotrexate sequentially results in cure rates approaching 100%. When resistance to the first drug occurs, the second drug is then given.

Group III patients with apparent metastases in sites other than the liver or brain most successfully respond to early combination chemotherapy, and response rates range from 70% to 80%. Treatment consists of actinomycin D, methotrexate, and chlorambucil given simultaneously for 5 days. The combination of actinomycin D and methotrexate with cytoxan is also effective. When abnormal liver function studies or evident toxicity to methotrexate occurs, actinomycin D and 6-mercaptopurine are used in combination. Combination chemotherapy consisting of vincalublastine, actinomycin D, and bleomycin is effective in metastatic testicular choriocarcinoma.

Group IV patients present with metastatic choriocarcinoma in the brain and liver, but are still curable if diagnosed early. There may be no gynaecological symptoms. An antecedent hydatidiform mole or pregnancy may have occurred several years before the onset of symptoms. Thus these patients are often admitted to services other than gynaecological. They are predisposed to life-threatening haemorrhage. In a patient with a cerebral metastasis, haemorrhage into this area is the commonest cause of death. This fatal haemorrhage may occur during the course of therapy when the tumour is being reduced in size. This was most likely the final course of events in our patient.

Before chemotherapy is instituted, a detailed history should be taken, and thorough clinical examination and laboratory tests should be performed.

Immunotherapy⁷ with cells or tissues from the husband, such as inoculation of peripheral lymphocytes or skin grafting procedures, or nonspecific BCG vaccination, among others, may result in rejection of the malignant trophoblastic tumour, or may even potentiate growth of the tumour. Thus, this field requires greater exploration.

The use of chemotherapy is strongly stressed, in view of the high cure rates which are now being achieved by this means.

We wish to thank Dr C. Vivier, Chief Medical Superintendent of Tygerberg Hospital, for permission to publish.

REFERENCES

1. Driscoll, S. G. (1977): *Hum. Path.*, **8**, 529.
2. Jones, W. B. (1975): *Clin. Obstet. Gynec.*, **18**, 247.
3. Hilgers, R. D. and Lewis, J. L. (1974): *Gynec. Oncol.*, **2**, 460.
4. Ober, W. B., Edgcomb, J. H. and Price, E. B. (1971): *Ann. N.Y. Acad. Sci.*, **172**, 299.
5. Ancel Blaustein (1977): *Pathology of the Female Genital Tract*, pp. 704 - 709. New York: Springer-Verlag.
6. Brewer, J. I. and Gerbie, A. B. (1966): *Amer. J. Obstet. Gynec.*, **94**, 692.

Lesser Curve Necrosis Following Proximal Cell Vagotomy for Gastric Ulcer

A Case Report

D. F. DU TOIT, C. B. KEMP

SUMMARY

A case of avascular necrosis of the lesser curve of the stomach following a highly selective vagotomy (HSV) for a gastric ulcer is reported. It is fortunately rare, but is a frightening complication. The necrosis, which is presumably ischaemic in origin, is caused by total devascularization of the lesser curvature of the stomach. The complication is usually diagnosed late and has a considerable mortality.

S. Afr. med. J., **55**, 98 (1979).

With highly selective vagotomy (HSV) the integrity of the alimentary tract is not breached and there is no anastomosis, thus minimizing the complication of leakage and bleeding. Other case reports describing necrosis of the lesser curvature following HSV for duodenal ulceration have been reported in recent literature.¹⁻⁷ No cases of lesser curvature necrosis following HSV for gastric ulcer have been recorded.

An HSV can be recommended for combined gastric and duodenal ulceration, or for gastric ulceration alone.⁸ HSV for gastric ulcers was found to be effective, but the final place of this procedure in the treatment of patients with both duodenal and gastric ulceration has still to be defined. Only long-term follow-up will clarify this.

The operative mortality rate was approximately 0,3%

for 5 539 cases reviewed when HSV was performed for duodenal ulceration.⁵ Necrosis of the lesser curvature occurred in 0,2% of the abovementioned series.

CASE REPORT

A 72-year-old Coloured woman was admitted to the surgical unit with severe haematemesis and melaena. No history of salicylate ingestion could be obtained, and she had had no previous episodes of gastro-intestinal haemorrhage.

On examination the blood pressure was 140/90 mmHg, pulse rate 110/min and the haematocrit 29%. She was of small stature with a mass of 46 kg. Cardiovascular, respiratory and abdominal examinations were within normal limits. Melaena was present on rectal examination. The urine analysis was normal and a chest radiograph was within normal limits.

A gastric ulcer measuring 1 cm in diameter on the lesser curvature of the stomach was demonstrated on gastroscopy and on a barium study. The appearance was that of a benign ulcer.

A laparotomy was warranted after a second major haemorrhage had occurred. At operation the stomach appeared normal. No ulcer could be seen or felt in the duodenum or along the lesser curvature. No perigastric fibrosis was present in the lesser omentum. The small and large bowels contained blood but because the haemorrhage had ceased, the proximal jejunum was empty.

In view of the patient's age and stature, an HSV was performed using the technique described by Amstrup.⁹ The dissection commenced at the pyloric region after the nerves of Latarjet had been identified, and was performed from below upwards. The left index finger was passed

Department of Surgery, University of Stellenbosch and Tygerberg Hospital, Parowvallei, CP

D. F. DU TOIT, M.B. CH.B., F.C.S. (S.A.), F.R.C.S.

C. B. KEMP, M.B. CH.B., M.MED. (SURG.)

Date received: 14 July 1978.