Metastatic ovarian carcinoid tumour

R. T. J. HOLL-ALLEN
B.Sc., M.B., F.R.C.S., D.L.O.
Senior Surgical Registrar, Queen Elizabeth Hospital,
Birmingham 15


Case report

The patient was a multiparous, unmarried female, age 66 years. She presented with a history of sudden onset of varicose veins some months previously, followed by oedema of the ankles for 6 weeks. Eight years previously she was investigated extensively for post-menopausal vaginal bleeding, no cause being found at that time. At the same time a duodenal ulcer was discovered, and treated successfully with a medical regimen. Five years later, a severe attack of diarrhoea was diagnosed clinically and radiologically as due to diverticulitis, and controlled with adequate doses of 'Lomotil'.

On examination the patient was fit, and abdominal examination was essentially negative. Rectal examination revealed a large, firm mass in the pouch of Douglas. This was confirmed vaginally, but the mass appeared separate from the uterus, right-sided, and fixed to the lateral pelvic wall. Both legs showed varicosity of the long saphenous systems, together with minimal oedema of the ankle to mid-calf regions.

Operation. A laparotomy was performed through a lower, right paramedian incision. The terminal ileum was obstructed due to an extensive tumour. There was a large mass of glands along the right ovarian vein, particularly at the junction of the vein with the vena cava. Both lobes of the liver contained numerous metastatic tumour deposits. The pelvis contained a large, incarcerated, solid tumour of the right ovary, with involvement of the uterus medially, and the pelvic wall laterally. A total hysterectomy, bilateral salpingo-oophorectomy and radical excision of the right ovarian vessels, and lymph nodes as far as the vena cava, were performed. An ileo-transverse colostomy was also necessary to bypass the obstruction in the small bowel. Following operation she made a complete clinical recovery, the ankle oedema subsiding and the varicose veins completely resolving.

The diarrhoea temporarily cleared, only to return after 4 months. At the same time, she began to develop more symptoms and signs of the malignant carcinoid syndrome, namely flushing attacks, facial cyanosis and attacks of breathlessness. The diarrhoea became uncontrolled. One year after operation, the liver has enlarged to fill approximately the upper half of the abdomen, and contains palpable secondary deposits of tumour. Despite all these problems she manages to lead a reasonably active life.

Post-operatively, the 24-hr urinary excretion of 5-hydroxyindole acetic acid was 45 mg (upper limit

FIG. 1. Argentaffinoma. (a) Haematoxylin and Eosin. (b) Diazo reaction.
of normal—10 mg/24 hr). This result would have been considerably higher had it been estimated prior to the removal of the bulky, secreting tumour.

Histology. Sections taken from the tumour show the typical features of an argentaffinoma, with no underlying malformation (Fig. 1).

Discussion

Enterochromaffin or argentaffin cells (Nicolas, 1891; Kultschitzky, 1897; Schmidt, 1905; Masson, 1914) are granular cells normally present in epithelial tissues derived from endoderm comprising the mucosa of the alimentary tract from stomach to colon, biliary tract and pancreatic ducts (Vialli & Ersparmer, 1933). Argentaffin carcinoma (carcinoid tumour) is a relatively low-grade malignant tumour originating from such cells. The distribution of this tumour, in decreasing order of frequency is appendix, colon, duodenum, ileum, jejunum, stomach, biliary tree and pancreas. Carcinoid tumours of the genital tract are rare, the metastatic variety being the least common (Karsh, 1951; Wolfe, 1955; Novak & Novak, 1958; Lincoln, 1966). Primary tumours usually develop in pre-existing benign cystic teratomas of the ovary (Stewart, Willis & de Saram, 1939; Sauer et al., 1958; Evans, Harris & McDougall, 1959; Willis, 1960) and metastatic tumours originate from the gastro-intestinal tract (Karsh, 1951; Wolfe, 1955; Roberts & Sjördems, 1964; Quinn, 1965). Suggested methods of spread are direct extension, lymphatic permeation, transperitoneal and vascular spread. In this case, a combination of direct extension and transperitoneal spread is suggested.

A high concentration of 5-hydroxytryptamine (5-HT) has been demonstrated in carcinoid tumours (Lembeck, 1953, 1956; Page et al., 1955; Snow et al., 1955; Thorson, 1958), and further support for the argentaffin cell origin of 5-HT has been put forward by Ersparmer (1954) and Benditt (1958). 5-HT produced in the body is taken up by the platelets (Rand & Reid, 1951; Humphrey & Jaques, 1954; Humphrey & Toh, 1954), and inactivated by amine oxidase, notably in the liver (Blaschko, 1952), resulting in 5-hydroxyindole acetic acid (5-HIAA) which is excreted in the urine. Urinary 5-HIAA is greatly increased in the malignant carcinoid syndrome (Page et al., 1955). All the available evidence suggests that 5-HT, or its metabolites, or both, are responsible for the malignant carcinoid syndrome of right-sided cardiac lesions, bronchospasm, peripheral vasomotor disturbances and diarrhoea (Cassidy, 1930; Thorson et al., 1954).

In retrospect, in this patient the initial symptom was diarrhoea, the unusual features being varicose veins, ankle oedema and an ovarian mass. The varicose veins could well be explained by mechanical pressure of the ovarian tumour on the femoral veins, or, alternatively, by pressure of the metastases on the inferior vena cava. Direct humoral influence on the blood vessels is improbable, in view of the known vasoconstrictor effect of 5-HT (Lewis, 1958) and complete recovery following surgery. A similar explanation is put forward for the ankle oedema, as it likewise completely resolved following surgery. The early features of the carcinoid syndrome in this case can be explained by direct liberation of 5-HT into the systemic circulation via the ovarian veins, bypassing the liver amine oxidase (Sauer et al., 1958; Quinn, 1965), as removal of the tumour produced complete remission of symptoms. The subsequent gradual appearance of the malignant carcinoid syndrome is almost certainly due to the hepatic metastases liberating 5-HT directly into the hepatic veins, again bypassing the liver amine oxidase.

The action of 'Lomotil' in controlling adequately the diarrhoea for 3 years remains unexplained.

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**Case reports**


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**Defibrination syndrome in phlegmasia cerulea dolens**

G. L. Saha
M.R.C.P.
Registrar in Chest Diseases, High Wycombe and Aylesbury Area at Tindal General Hospital, Aylesbury

Phlegmasia cerulea dolens is an uncommon but well established clinical entity (Stallworth et al., 1965). It is characterized by massive venous occlusion in a limb with intense violaceous cyanosis, woody oedema, loss of arterial pulsations and sometimes gangrene (Annotation, Brit. med. J., 1967). Incoagulability of the blood with hypofibrinogenenaemia and thrombocytopenia has occasionally been described in this condition in those cases which are associated with an obvious primary pathology (Rosenberg & Zullo, 1958; Meek & Maurer, 1959; Fogarty et al., 1963; Annotation, Brit. med. J., 1967). A case is described of recurrent phlegmasia cerulea dolens with defibrination syndrome in an otherwise healthy 14-year-old mongol boy.

**Case report**

The patient was admitted on 17 July 1967 with a history of pleuritic pain in the right side of his chest for a few days, pain in the left groin and swelling of the whole of the left lower limb for 2 days. A diagnosis of deep vein thrombosis with pulmonary infarction had been made by the attending doctor and he had been put on phenindione prior to admission.

On examination the whole left lower limb was swollen, violaceous and showed woody oedema. Arterial pulsations were absent in this limb apart from the femoral. Examination of the heart and abdomen showed no abnormality and rectal examination was negative. The chest showed signs of a small right-sided effusion. Treatment with phenindione was continued. Blood was sent for prothrombin estimation 36 hr after starting phenindione. Surprisingly, the prothrombin time was found to be greatly prolonged with no clot formation for over 2 min. A Schneider titre showed a plasma fibrinogen level of less than 50 mg/100 ml. After addition of fibrinogen to the plasma the prothrombin and kaolin–cephalin times were still greatly prolonged, with a prothrombin time of 50 sec, suggesting that there were deficiencies of other clotting factors (Annotation, Brit. med. J., 1965). These may, however, have been due to the phenindione. Whole
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R. T. Holl-Allen

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