Carcinoid tumors arise from specialized epithelial cells (Kuschitsky cells) of the gastrointestinal tract. These cells can secrete 5-hydroxytryptamine (5-HT) and an excessive quantity of this substance produces a remarkable syndrome in patients suffering from metastasizing carcinoids with atypical cyanosis, flushing, diarrhea, asthma-like attacks and, in the late stages, valvar diseases of the right side of the heart (Böörck, Axen and Thornsen, 1952 and Thornsen, Böörck, Bjorkman and Waldenstrom, 1954).

The bizarre and inconstant nature of the symptoms can lead to diagnostic error as happened in the following case, the diagnosis of which was not established during life.

Case Report

A 67-year-old taxi-driver, previously in good health, had a 'heart attack' in 1958 and 'chest trouble' in April, 1959. In August, 1959, while driving, he fainted, hit a car ahead and received head injuries for which he was treated in the hospital. On examination his abdomen was found to be tense and rigid. All other clinical and relevant laboratory findings were within normal limits.

In 1960, from May to July, he was investigated for loss of weight, intermittent back and abdominal pain, episodic diarrhea and poor urinary stream. Examination revealed periodic increase of muscle tone. At no time was the urinary excretion of 5-hydroxy-indole acetic acid in the urine determined.

On October 4, 1960, he was admitted with retention of urine due to the enlarged prostate. His prostate was removed and he had no complications from the operation. During the post-operative period some curious symptoms appeared. He had a brief attack of wheezing and respiratory distress similar to asthma. His face, which was permanently red with telangiectases on the cheek and nose, showed unusual changes of colour, i.e. flushing with vivid redness, patches of cyanosis on a red background and blanching. A peculiar mental change was observed. He was slow to speak and answered questions, his face dull and expressionless. He showed limited movements and activity. Occasionally he lay in bed motionless, completely withdrawn from his surroundings. He would stand with body slightly flexed and his gait was slow with short steps not unlike that of Parkinsonism. There were no tremors. Sensation and
reflexes were unaltered. The other striking feature was the periodic increase of muscle tone. At times the abdominal muscles would become so tense and rigid as to make abdominal examination impossible. On November 10, 1960, while visiting the toilet he collapsed, became extremely dyspnœic and died quickly.

**Autopsy (Dr. Shackle)**

A firm, yellow, invasive carcinoid tumour was found in the ileum (Fig. 1). The mesenteric glands (Fig. 2) and the liver contained numerous metastatic deposits. The heart, the brain and their vessels were normal.

**Histology.** The tumour and the metastases (Fig. 3) showed the typical histology of carcinoid tumour with fine dusting and open appearance of the nuclear chromatin, and argentaffin granules (Fig. 4) on silver staining. Fluorescence was also observed in ultraviolet light.

**Discussion**

Malignant carcinoids are slowly growing tumours. Even with widespread metastases long periods of survival have been recorded (Cope, 1930; Mallory 1940).

The extensive metastases in this patient suggest that he had had this tumour for a long time. Had all his symptoms since 1958 been correlated and due attention paid to his permanently red face,
telangiectases and colour changes, a correct diagnosis could have been established.

The co-existence of peculiar mental change and periodic increase of muscle tone with abdominal rigidity are the most interesting and unusual features in this case. I have not been able to find a comparable case in the literature. There were no major arteriosclerotic changes nor was there any deficiency of nicotinic acid, which sometimes arises in this syndrome, to account for the mental change in this patient. As for the abdominal rigidity and increased muscle tone, there was no pain, tenderness or peritoneal irritation or any other peripheral factor to be held responsible for it. It appears that 5-HT was in some way responsible for the production of these symptoms.

Large quantities of 5-HT have been found in the brain and nerve ganglia (Page and Twarog, 1953; Amin, Crawford and Gaddum, 1954), and the enzymes decarboxylase and monoamine-oxidase that form and destroy it have also been discovered (Undenfriend, Weissbach and Bogdanski, 1957). Various investigators have shown (Page and Twarog, 1953; Woolley and Shaw, 1954; Marrazzi and Harts, 1955) that 5-HT plays a part in the functioning of nervous systems and normal mental processes. Injection of 5-HT into the ventricle of a cat produces lassitude and unwillingness to change position like the catatonia seen in mental disorders (Feldberg and Sherwood, 1954). Similarly administration of 5-hydroxytryptophan (5-HTP; serotonin-precursor) in animals produces changes in behaviour (Smith, 1960). Marrazzi suggested that accumulation of 5-HT could produce abnormal behaviour by inhibition of synaptic function. Serotonin is believed to be a chemical transmitter of nerve impulse (Brodie and Shore, 1957) and an intravenous injection can produce repetitive nerve impulses (Schneider and Yonkman, 1953). These experimental observations show that an excess of 5-HT in the brain can produce mental change and also excite nerve tissues to set up repetitive nerve impulses.

Woolley and Shaw (1954) on the other hand have produced evidence by using several anti-metabolites that cerebral deficiency of 5-HT is probably responsible for the mental change. The latter view has been strengthened by the observation of Gaddum (1953).

Although our knowledge of the cerebral metabolism of serotonin and the enzymes that form and destroy it, the substance that activates and blocks the enzymes to produce excess or deficiency of 5-HT, is insufficient, it is generally recognized that many substances such as LSD, harmala alkaloids (Woolley and Shaw, 1954) and 5-HTP (Smith, 1960) cause mental disturbance by upsetting the
5-HT contents of the brain. The possibility exists that some other indole products of the tumour or unidentified intermediary metabolites of 5-HT, having structural similarity, may behave in the same way and are capable of producing mental change. Whatever mechanism may be involved for the cerebral metabolism of serotonin, in the light of the above experimental evidences, and in the absence of any other known cause, the neurological and mental symptoms presented by this patient, along with attacks of flushing, strongly suggests that a disturbance of cerebral metabolism of serotonin was responsible for the symptoms.

I am most grateful to Mr. Stephen Power, Consultant Surgeon, for his generous guidance and helpful criticisms, and Dr. Shackle for the post-mortem examination and histology slides, Mr. Nicholson and Dr. Shackle for the photographs, and Miss Johns for her secretarial help.

REFERENCES


CHRONIC OSTEOMYELITIS OF THE ULNA OCCcurring IN SYRINGOMYELIA

R. S. PHILLIPS, F.R.C.S.

The Royal Infirmary, Edinburgh 3

Although, in this day and age, acute and chronic osteomyelitis are seen much less than formerly, the conditions are by no means rare. However, chronic osteomyelitis of the ulna in the absence of a compound fracture is uncommon.

Trueba and Morgan (1954) reporting a series of cases of acute osteomyelitis, found the ulna to be the site of infection in four of one hundred patients. Blanche (1952) in his series, found two in 50 patients. Green, Nyhan and Fousek (1956) found the ulna involved in nine, in their series of 99 patients. However, in these authors’ series, the lesion was acute and occurred in infancy or childhood.

Acute and chronic pyogenic osteomyelitis, in adults, are even less common conditions. Reviewing the literature of the past 35 years, a direct reference to the conditions could be found on three occasions only. Variava (1935) described the acute condition in a patient with a compound fracture of both forearm bones. The radius, however, was involved maximally. Dufour (1933) demonstrated the radiological history of one patient with chronic