CARCINOID SYNDROME — REPORT OF A CASE IN A CHINESE

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Carcinoid tumours have occasionally been identified by pathologists doing routine histological studies on appendices or appendicular tumours removed by surgeons in Singapore. The present case, however, appears to be the first reported locally to show the characteristic physiological effects that may be associated with the presence of this tumour, and which form the diagnostic features of the carcinoid syndrome. Carcinoid tumours are usually small submucosal tumours, hard and with a yellowish cut surface which fluoresces. They occur slightly more in men than women, at all ages, most commonly in the appendix where they are usually single, or in the terminal ileum and small intestine where they are frequently multiple. But they also occur in many other sites. Local spread is limited, but some may occur to the regional lymphatics. Metastases occur primarily in the liver, but also widely in other sites. They usually have a very slow rate of growth and surgical removal of secondary deposits is well worth while. Carcinoid tumours of the rectum tend to be rather different in that very few of them metastasise and generalised physiological effects of rectal carcinoids are uncommon. The pathological features of carcinoid tumours have been reviewed by Morson (1958).

Under certain circumstances carcinoid tumours are of particular interest to the physician because they may present with diarrhoea and cardiovascular complications. These tumours are probably derived from the Kultchitzky cells of the gastrointestinal tract, which contain granules that stain red with haematoxylin and eosin, black with silver impregnation methods, and turn a rusty red with the Diazo method. The granules are apparently formed by formalin interaction during fixation with 5-hydroxytryptamine (also known as serotonin). Carcinoid tumour cells may be packed with these granules, and the tumours liberate 5-hydroxytryptamine into the circulating blood.

Under normal circumstances about 1% of the essential aminoacid tryptophane ingested is converted to 5-hydroxytryptamine. The latter has many pharmacological actions and is doubtless of physiological importance in the regulation of intestinal movement and peripheral vascular changes. In the presence of a carcinoid tumour as much as 60% of the dietary tryptophane may go to form 5-hydroxytryptamine, and the abnormally high blood levels of this tend to produce diarrhoea due to excessive intestinal mobility, and vasomotor disturbances. The clinical aspects of the carcinoid syndrome have been authoritatively reviewed by Waldenström (1958).

CASE REPORT

A 44 year old Chinese housewife was admitted in October 1960 complaining of a rash on her face, recurrent flushing, persistent diarrhoea and central chest pain.

The patient was well until shortly after the delivery of her fourth child in 1954. She then noticed a recurrent light red rash on her nose and cheeks. The flush gradually darkened in colour and deepened in intensity, and became a permanent dusky red. Meanwhile she began to have recurrent generalised flushing over her whole body. In late 1955 she had some discomfort in her lower right abdomen. This persisted, and in 1956 she noticed a small lump in the right iliac region. This gradually increased in size until in early 1957 it was as big as a small football. From 1955 onwards she also had increasing diarrhoea, until she was having four or five watery bowel motions every day. The stools were yellow in colour, had a normal odour and did not appear to contain blood, excessive mucous or obvious undigested food. She began to lose weight although her appetite remained unimpaired.

In April 1957 she had a laparotomy at another hospital, and the mass in her right iliac fossa was found to be a tumour involving the appendix and right ovary. The tumour was removed together with a right salpingo-oophorectomy and appendicectomy. The histological report on the tumour stated: "This is granulosa cell tumour with the "cylindrical" type of structure, being not clearly differentiated into either the theca or luteal arrangement. Cystic spaces are present and mitoses are almost totally absent. The degree of malignancy is probably low".

The patient made an uneventful recovery from the operation, but the diarrhoea and flushing continued. Following the operation there was a change in her menstrual periods, which previously had been regular once a month and now occurred every two weeks. Her voice also changed and became squeaky, weaker

and higher pitched. The generalised flushing gradually increased in severity and frequency, and she noticed associated palpitations and eventually a tight sensation in the praecordium sometimes amounting to pain. The flushing and associated symptoms tended to occur after food and whenever she was emotionally disturbed, but following a flush she found that food and emotion could not produce another attack for at least half an hour. By 1960 she was having an average of five attacks a day.

On examination the patient was in good general health. She had a marked dusky red rash over her cheeks and nose which did not fade on pressure, and a peripheral cyanosis of her fingers and toes. Whenever she was examined she developed a pronounced flush over her whole body, lasting about 20 to 30 minutes. She was not anaemic or jaundiced and had no palpable glands. Her liver was palpable one inch below the right costal margin, and was smooth and of normal consistency. Her spleen was palpable one inch below the left costal margin. She had a right lower para-median post-operative scar. No other abdominal masses were palpable. During her flushing attacks her heart rate was as high as 105 per minute and blood pressure rose to 140/85. But following an attack, in her normal basal state, her pulse rate was usually between 70 and 80 per minute and her blood pressure was 110/70. No other abnormalities were found in the examination of her respiratory, cardiovascular and nervous systems.

Clinical investigation showed: Haemoglobin 12.2 g.% (84%); W.B.C. 7,300/c.mm.; neutrophils 68%; lymphocytes 28% and monocytes 4%; E.S.R. (Westergren) 5 mm.; negative blood tests for the L.E. phenomenon. Serum proteins, 4.7 g.%, albumin 3.0 g.%, globulin total 7.7 g.%. Her urine contained no albumin and the deposit was microscopically normal. Her stools contained no cysts, ova or occult blood, and stool culture grew no bacteria of the Shigella or Salmonella groups. A chest X-ray was normal, and barium meal X-ray screening studies showed: "Normal appearance of the oesophagus, stomach and duodenum. In the follow through there was definite intestinal hurry so that 3 hours after ingestion of barium the radiopaque substance had reached the rectum. There was no evidence of a filling defect or obstruction in the coils of small gut outlined. The mucosal pattern of a few of the jejunal coils looked slightly coarsened but this did not appear to be constant. The large intestinal pattern appeared normal".

Blood taken during one of the flushing attacks showed a serum 5-hydroxytryptamine level of 0.063 ug/ml. (normal range 0.05-0.2 ug/ml., and range in carcinoid syndrome 0.25-6.5ug/ml. Pernow, 1958). Two 24 hour collections of urine were assayed for 5-hydroxy-indoleacetic acid and showed 120 mg. in 1,600 ml., and 94 mg. in 800 ml. respectively. (Normal range 2-10 mg/24 hours, and range in carcinoid syndrome 15-1,680 mg/24 hours. Pernow, 1958).

DISCUSSION

This patient showed the typical diarrhoea and flushing attacks of the carcinoid syndrome, with the permanent rash on her face and cyanosed extremities. She did not however show any signs of pulmonary or tricuspid stenosis which sometimes occur in this condition. The tumour removed from this patient's right iliac fossa, and which was reported to be a granulosa cell tumour, may in fact have actually been a carcinoid. Both are granular celled tumours, and the section was reported to show a cylindrical structure. A tubular arrangement occurs characteristically in carcinoid tumours.

The serum 5-hydroxytryptamine level in this case was reported to be within the normal range, but this involves a difficult assay technique and the normal result may have resulted from an experimental error. The diagnosis of a carcinoid tumour is proven in this patient by the two high figures for 5-hydroxy-indoleactic acid (5-HIAA) excretion in the urine. This substance is formed by the action of an amine oxidase on 5-hydroxytryptamine (5-HT) and is physiologically inactive, but is simple to estimate quantitatively.

The treatment of the carcinoid syndrome is primarily surgical if the causative tumour can be located in an operable site. Unfortunately the tumour is often difficult to find, and if careful radiological studies fail to reveal a tumour in the lungs it is probably justifiable to do an exploratory laparotomy. A number of anti 5-HT substances have been synthesised, but so far there have not been any reports that their administration is of definite value in this syndrome. A therapeutic possibility that does not seem to have been tried is isoniazid, which is known to inhibit a decarboxylase essential for the conversion of tryptophane into 5-HT. Presumably, even if isoniazid is effective in this condition, it would not have any immediate effect on the symptomatology because the tumour cells contain considerable amounts of preformed 5-HT available for liberation.

SUMMARY

A case of carcinoid syndrome is described in a Chinese woman. Brief reference is made to the pathology of carcinoid tumours and the management of this condition.

REFERENCES

Morson, B.C. (1958) in "Modern Trends in Gastro-enterology", Second Series, edited by F. Avery Jones. Butterworth & Co., London, p. 107-117.

Pernow, B. (1958) Ibid. p. 101-106.

Waldenström, J. (1958) Ibid. p. 92-100.