There are obvious practical difficulties in monitoring transitory changes to the blood-brain barrier that may occur during electroconvulsive therapy, and little study has been made of such changes. Bolwig *et al* found an enhanced passage of horse radish peroxidase across the rat blood-brain barrier lasting for from 30 to 60 seconds during an epileptic seizure induced by electric shock.² They proposed that the increased permeability was due not to epileptic neuronal activity but rather to acute hypertension. In earlier work they had reported a considerable temporary increase in cerebral blood flow and an increase in the permeability of the blood-brain barrier to small molecules in patients receiving electroconvulsive therapy.⁶

Though it is unlikely that a single blood sample taken 15 minutes after treatment would show altered serum myelin basic protein immunoreactivity, any change in immunoreactivity during a course of treatments over several months would presumably be detected. In this study electroconvulsive therapy, either as a single episode or as a course of treatments, did not affect serum myelin basic protein immunoreactivity. This suggests that, at least in so far as serum myelin basic protein immunoreactivity can be assumed to be a marker of cerebral damage and vascular permeability, no changes occurred; if they

did they were so transient or small that they were undetectable by this method.

References

- ¹ Kendall RE. The present status of electroconvulsive therapy. *Br J Psychiatry* 1981;139:265-83.
- ² Bolwig TG, Hertz MM, Westergaard E. Acute hypertension causing blood-brain barrier breakdown during epileptic seizures. *Acta neurol Scand* 1977;56:335-42.
- ³ Eng LF. Brain related antigens. In: Thomas DGT, Graham DI, eds. *Brain tumours: scientific basis, clinical investigation and current therapy*. London: Butterworths, 1979:109-20.
- ⁴ Biber A, Englert D, Dommasch D, Hempel K. Myelin basic protein in cerebrospinal fluid of patients with multiple sclerosis and other neurological diseases. *J Neurol* 1981;225:231-6.
- ⁵ Palfreyman JW, Thomas DGT, Ratcliffe JG. Radioimmunoassay of human myelin basic protein in tissue extract, cerebrospinal fluid and serum and its clinical application to patients with head injury. *Clin Chim Acta* 1978;82:259-70.
- ⁶ Bolwig TG, Hertz MM, Paulson OB, Spotoft H, Rafelson OJ. The permeability of the blood-brain barrier during electrically induced seizures in man. *Eur J Clin Invest* 1977;7:87-93.

(Accepted 13 January 1984)

Carcinoid tumour secreting dopa

B K SHARMA, B J SMITS, R ROBINSON, SYLVIA BURNS, E N TROUNSON

Abstract

A middle aged woman referred for an abdominal mass was found to have large amounts of dopa (3-4-dihydroxyphenylalanine) metabolites in her urine. At operation a tumour affecting almost the entire left lobe of the liver was removed. Histologically the tumour was a metastatic carcinoid. After operation the excretion of dopa metabolites fell substantially, confirming that the tumour was the source. Apparently owing to an enzyme defect the tumour had been unable to decarboxylate dopa.

These findings are further evidence of a neural origin for the endocrine system of the gut.

Introduction

Both carcinoid tumours and phaeochromocytomas cause distinctive clinical features by the production of highly reactive amines from aromatic amino acids. Their origin has been ascribed to cells of the APUD (amine precursor uptake and decarboxylation) series.¹

Carcinoid tumours typically convert tryptophan to 5-hydroxytryptophan and 5-hydroxytryptamine. Phaeochromo-

cytomas and neuroblastomas decarboxylate dopa (3-4-dihydroxyphenylalanine) to form dopamine, noradrenaline, and related catecholamines; malignant variants may lack decarboxylase and secrete the amine precursor, dopa. We describe a patient suffering from a histologically proved carcinoid tumour who was found to be excreting large quantities of dopa metabolites.

Case history

A 56 year old woman had complained of epigastric pain for eight to 10 years with intermittent attacks of fever and jaundice. An abdominal mass had been present for a similar period, which was thought to be a pancreatic cyst. She was referred to the gastroenterology clinic, and a hard, irregular mass descending 8 cm from the costal margin was noted. She appeared otherwise well and was neither anaemic nor jaundiced. A grade 3/6 systolic murmur was heard maximally at the lower left sternal edge. Blood pressure was stable at 110/70 mm Hg. Isotope and computed tomographic scans indicated hepatic metastases. At laparotomy the left lobe of the liver was almost entirely replaced by tumour; it was excised. No primary growth was identified.

BIOCHEMICAL FINDINGS

In view of the duration and nature of the enlarged liver a diagnosis of metastatic carcinoid seemed likely; however, urinary excretion of 5-hydroxyindole acetate was normal. By chance, a urine specimen was examined chromatographically for phenolic acids. Large amounts of dopa metabolites were found, particularly 4-hydroxy-3-methoxyphenyllactic acid and homovanillic acid. After operation the urinary output of both these metabolites fell substantially; 4-hydroxy-3-methoxyphenyllactic acid was no longer detectable and excretion of homovanillic acid was only marginally raised.

The tumour tissue was examined by high performance chromatography. There were no detectable amounts of 5-hydroxytryptamine, 5-hydroxytryptophan, dopamine, or noradrenaline, but a substance with the chromatographic mobility of dopa was present. Neither dopa decarboxylase nor dopamine β -hydroxylase was detected.

George Eliot Hospital, Nuneaton, Warwickshire CV10 7BL

B K SHARMA, MB, MRCP, medical registrar

B J SMITS, MB, FRCP, consultant physician

E N TROUNSON, FRCPATH, consultant pathologist

Warwick General Hospital, Warwick CV34 5BW

R ROBINSON, PHD, FRSC, chief biochemist

SYLVIA BURNS, BSC, biochemist

Correspondence to: Dr B J Smits, Department of Gastroenterology, Walsgrave Hospital, Coventry CV2 2DX.

HISTOLOGICAL FINDINGS

Microscopically the moderately large tumour cells with rounded nuclei were devoid of mitoses. They were often in solid clusters separated by strands of vascular tissue. The outermost cells in each cluster were sometimes columnar, however, and such cells lining empty channels produced the structure of a tubular adenoma. Diazo and argentaffin reactions were negative but argyrophil granules were plentiful in some of the cells. The appearances were characteristic of metastatic carcinoid.

Discussion

Carcinoid tumours include not only the classical midgut varieties but histologically similar tumours arising from endocrine cells in the hindgut or in bronchus, biliary tract, stomach, or pancreas. Argyrophil granules, indicative of polypeptide hormones, are usually present but the tumours in the foregut do not usually give the argentaffin reaction for 5-hydroxytryptamine.²

Carcinoid tumours secreting the catecholamines dopamine and noradrenaline have been described.³ Our patient's tumour appeared unique in that it was unable to decarboxylate dopa, apparently owing to an enzyme defect. The resulting dopa metabolites have previously been observed only in association with neuroblastoma or malignant pheochromocytoma.^{4,5}

The presence of such neurotransmitters in a carcinoid tumour is further evidence of the close relation between gut endocrine cells and the nervous system. This was first indicated by the APUD concept and attested by subsequent observations,

notably the detection of neurone specific enolase in carcinoid and other endocrine tumours.^{6,7}

The detection of dopa metabolites in urine by chromatography is a relatively simple procedure which should be employed more frequently in the investigation of obscure abdominal neoplasms.

We thank Mr G A Court for his help with this case and for permission to publish.

References

- Pearse AGE, Welbourn RB. The apudomas. *Br J Hosp Med* 1973;10: 617-24.
- Grahame-Smith DG. The carcinoid syndrome. In: Bondy PK, Rosenberg LE, eds. *Metabolic control and disease*. 8th ed. Philadelphia: Saunders, 1980:1695-1707.
- Goedert M, Otten U, Suda K, et al. Dopamine, norepinephrine and serotonin production by an intestinal carcinoid tumor. *Cancer* 1980;45: 104-7.
- Robinson R. The clinical chemistry of pheochromocytomas. In: Varley H, Gowenlock AH, eds. *Symposium on clinical chemistry of monoamines*. Amsterdam: Elsevier, 1963:63-70.
- Bell M. Observations on the biochemical diagnosis of neuroblastoma. In: Bohron C, ed. *Neuroblastoma: biochemical studies*. Berlin: Springer-Verlag, 1966:42-51.
- Tapia FJ, Barbosa AJA, Marangos PJ, et al. Neuron-specific enolase is produced by neuroendocrine tumours. *Lancet* 1981;i:808-11.
- Roth J, LeRoith D, Shiloach J, Rosenzweig JL, Lesniak MA, Havrankova J. The evolutionary origins of hormone neurotransmitters and other extracellular chemical messengers: implications for mammalian biology. *N Engl J Med* 1982;306:523-7.

(Accepted 1 December 1983)

ONE HUNDRED YEARS AGO The more callous amongst us become accustomed to the notices which appear in the *Gazette*, from time to time, of the imposition of quarantine on this or that frontier, so soon as the most distant whisper of cholera or plague comes to the ears of nations of easy sanitary virtue. The axiom may safely be laid down, that the less cleanly the people, the firmer believers are they in the efficacy of quarantine. That so barbarous a relic of the middle ages should still be regarded by rational people in the light of a precaution, is amazing to the ordinary mind. Far from checking disease, or keeping it out, quarantine has approved itself to be the best possible agent for its propagation. Sanitarians of the study justly condemn quarantine as paradoxical and useless; those who have had personal experience of its tender mercies find difficulty in putting their tongues to parliamentary adjectives expressive of its cruelty and inhumanity. We have before us an extract from a letter just written to friends in England by an English lady travelling with her two daughters to the Mediterranean coast of Spain, which gives a picture more graphic than columns of fine writing about the miseries (and perfectly needless) of the lazarettos. She writes:—"We had been informed by the Spanish consul that the quarantines on the Pyrenean frontier had been taken off; so that we had sent all our heavy luggage by sea, taking with us only a few necessities that we thought would be required in a journey of two or three days. When, however, we reached the French frontier, we learnt, to our amazement and disgust, that there was a nine days' quarantine to be undergone before we could proceed to Valencia. The lazaretto at Port Bore, on the Spanish frontier, was too full to accommodate us for two days; and these we managed to spend, without serious discomfort, at the French railway-station, where we speedily bespoke a room. At last, the time seemed endless. We were allowed to cross the frontier. A special train took our 'infected party,' consisting of more than thirty persons; and, almost before it stopped at Port Bore, soldiers surrounded it. We were made to alight like so many prisoners, and, headed by the doctor, made to enter a few at a time, with our hand-parcels, into a sort of closed shed, to be fumigated. A most villainous smell the place had, though we ladies were not kept in long. Then we passed before an officer, who took down our names, where we came from, etc. This process lasted about half an hour, when the whole party, headed by the doctor and the sanitary servants, with the red cross on their arms, carrying our parcels, wended its way to the lazaretto. We could not help laughing, the whole thing seemed so ridiculous; but our laughter was soon turned into horror, when we came to a standstill before a large broken-down *contadino's* house. We could hardly believe our eyes,

that ladies should have to enter such a place. However, there was no help for it, so we followed the doctor, who was to distribute the rooms. He had heard there were some English ladies coming, and so had reserved the best room for us. I will describe it. A small square room, with a low slanting roof, and the wooden floor perfectly black with dirt and saturated with carbolic acid and chloride of lime. There were three beds—if such they could be called; one chair, and two tin basins hung against the wall; no looking-glass or table of any sort. We begged the doctor to put in another bed, as a lady travelling companion did not care to leave us, which filled the room so completely that we could only dress one at a time. To ventilate the room, we had a window deep in the wall, about a yard high and half a yard wide (of course, we slept with it open); and, to crown all, the doctor had to pass through our room to get to his. There was a German lady who wanted to stay with us, but there was no room, so she had to go with the other female part of the community. The men had a kind of shutting-up bed, like tray-stands, upon which was a sort of mattress filled with leaves. The beds were arranged as in a hospital; I do not know how many in each room, or rather hay-loft. All these opened on to the passage-room, which served for dining, etc., and was fitted with a table composed of planks of wood on tressels. This was the first-class accommodation. The others lived in tents, and were fed by the Government. Before taking possession of our rooms, we all had to give our names, ages, what we were, and where we came from, which was all written down. By this time, it was late in the afternoon, so we made inquiries about dinner. There was a fixed tariff, 5½ francs each person, for lunch and dinner, coffee in the morning extra. This was not so bad; in fact, we were agreeably surprised, as we had been told we should have to pay 8 francs each. The food was very bad: garlic and potatoes for first dish; then baccala, a rough kind of smoked codfish, cooked with tomatoes and oil; then some sort of nondescript mess of meat, and some fruit. As we had no change of linen, we washed our own things one at a time, then took them up on the mountain to dry while we sat about. This sort of life lasted four days, when the order came to shorten the quarantine, so we had four days instead of seven. The doctor was exceedingly kind, and helped us with our luggage, which, besides being fumigated with sulphur when we arrived in the van, had, when we left, to be all opened and fumigated again." It is, perhaps, lucky that nothing worse than discomfort and dirt befell these adventurous voyagers; but what is to be said of a system of sanitary police that pins its faith to precautionary measures such as are above described? (*British Medical Journal* 1884;iii:921.)