CONGENITAL DOPAMINE-SECRETING NEUROBLASTOMA
WITH CLINICAL AND BIOCHEMICAL REMISSION

BY
E. M. BRETT*, T. E. OPPÉ, C. R. J. RUTHVEN, and M. SANDLER
From the Paediatric Unit, St. Mary’s Hospital, London, and the Bernhard Baron Memorial Research
Laboratories and Institute of Obstetrics and Gynaecology, Queen Charlotte’s Maternity Hospital, London

(RECEIVED FOR PUBLICATION DECEMBER 3, 1963)

Neuroblastoma, a disease of early childhood, may
be present at birth (Wells, 1940; Potter and Parrish,
1942; Bodian, 1959; Gross, Farber and Martin, 1959;
King, Storaasli and Bolande, 1961; Dargeon, 1962;
Voorhess and Gardner 1962a). Such cases are more
likely to undergo remission than those occurring
later in life (Bodian, 1959).

Since Isaacs, Medalie and Politzer (1959) first
noted an increased catecholamine production by
patients with neuroblastoma, there has been a
growing number of subsequent reports indicating
that tumours belonging to the neuroblastoma-
ganglioneuroma group are predominantly secretors
of dopamine, the precursor of noradrenaline

We report the following case of congenital
neuroblastoma, as the first to our knowledge in which
biochemical remission has been noted to accompany
’spontaneous’ tumour regression.

Case Report
L.C. was born at St. Mary’s Hospital on June 14, 1962,
the second child of a healthy 23-year-old woman who had
been well during pregnancy. Delivery was normal, the
birth weight was 7 lb. 10 oz. (3.5 kg.), and the baby
breathed and cried at once but appeared rather pale.

Next day, pallor had increased and there was abdominal
distension caused by firm enlargement of the liver. The
spleen was not palpable. There was slight oedema of the
legs and lower abdomen. During the next few days
his liver enlarged progressively to the right lower quadrant.
His weight and pallor increased, the haemoglobin
concentration falling from 14.5 g., 100 ml. on the second
day of life to 7.5 g. on the thirteenth. An intravenous
pyelogram on the ninth day showed normal renal pelvis
and calyces on both sides with possible slight downward
displacement of the right kidney. A radiological
skeletal survey showed no abnormality.

On the thirteenth day of life laparotomy was performed
by Mr. L. Bromley who found an enlarged liver with many
small nodules, white and stony hard, chiefly on the under
surface of the right lobe, but also present in the left lobe.
Kidneys, spleen, and intestine appeared normal. A small
biopsy taken from the right lobe of the liver consisted
mainly of highly vascular neoplastic tissue made up of
small darkly-staining cells with rudimentary rosette
formation (Fig.). A fibrillar background was present
but no differentiated larger ganglionic cells were seen.
The tumour was thought to be best classified as a neuro-
blastoma (Dr. E. Foot). Its site of origin remains
unknown.

Irradiation was not considered advisable, and it was
decided to give large doses of vitamin B12 intramuscularly.
Treatment was started at 15 days of age with 1 mg. on
alternate days, increasing four days later to 1 mg. daily.

For a time his condition remained poor, and increasing
abdominal distension, due partly to increase in size of the
liver and partly to ascites, caused moderate respiratory
embarrassment. Oedema of the legs, abdomen, arms,
and face became marked. It was noticed that the
circumference of the right upper arm was slightly larger
than the left. A bone-marrow biopsy from the right
tibia at 24 days of age showed no abnormal cells. His
haemoglobin tended to fall, and he required three small
blood transfusions, the first at the time of laparotomy.

At the age of 6 days a 24-hour collection of urine was
assayed for catecholamine metabolites: the output of
4-hydroxy-3-methoxymandelic acid (VMA) was 17·4 mg.
and that of 4-hydroxy-3-methoxyphenylacetic acid (HVA)
9·4 mg., using the methods, respectively, of Pisano, Crout
and Abraham (1962) and of Ruthven and Sandler (1962).

Abdominal distension and oedema gradually diminished,
and his haemoglobin remained at a satisfactory
level, until at the age of 8½ weeks, he was considered well
enough to be discharged home, treatment being continued
with 1 mg. daily of vitamin B 12 i.m. At the time of
discharge his liver margin reached the right lower
abdominal quadrant. Two weeks afterwards, he was

* Present address: Hospital for Sick Children, Great Ormond Street,
London.
well and thriving with no anaemia, and the liver was found to be smaller for the first time, its edge reaching 7·5 cm. below the right costal margin. The slight asymmetry between the upper arms persisted, the circumference on the left measuring 10 cm. and on the right 11·4 cm. The right side of the face appeared, as before, slightly larger than the left. The legs were equal in size. Apart from the differences noted, no other abnormality was found in the arms or face.

At the age of 3½ months bilateral inguinal swellings were detected and a few days later he was found to have incarcerated indirect inguinal herniae. These reduced spontaneously, but bilateral inguinal herniotomy was performed by Mr. Bromley; he noted, on palpating the liver through the right inguinal ring, that it was smaller than previously with smooth edge and surface, apart from a few small nodules on the inferior surface of the right lobe. The right kidney felt normal, but the right suprarenal gland was not palpated.

Post-operative progress was normal, and the child continued to thrive. At 6 months of age his liver was no longer enlarged.

Further urinary assays of VMA and HVA have been made at regular intervals and have shown a progressive fall (Table). The specimens at 3 months of age and subsequently have shown normal levels for a child in this age-group.

The child has continued to thrive with normal motor and mental development, and now, at the age of 17 months, appears a healthy happy boy.

Since the age of 3 months his B 12 injections have been reduced to alternate days, and since 7 months have been given successfully by his mother, whose intelligent co-operation has made possible his management at home.

**Discussion**

The treatment of neuroblastoma with vitamin B 12 is controversial. Although a dramatic response to such treatment was claimed by Bodian (1959), his findings have not been confirmed by King et al. (1961) or by Dargeon (1960). Bachmann (1962) has recently collected 1,030 cases of neuroblastoma from the literature and has shown that clinical cure, ascribed to a variety of therapeutic regimens, was claimed for 25%. It appears that many of these cures were due to spontaneous regression of tumour tissue. The younger the age of onset, the more

<table>
<thead>
<tr>
<th>Age (mth.)</th>
<th>VMA (mg./24 hr.)</th>
<th>HVA (mg./24 hr.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 days</td>
<td>17-4</td>
<td>9-4</td>
</tr>
<tr>
<td>14</td>
<td>6-5</td>
<td>7-5</td>
</tr>
<tr>
<td>3</td>
<td>1-9</td>
<td>1-0</td>
</tr>
<tr>
<td>9</td>
<td>1-0</td>
<td>1-0</td>
</tr>
<tr>
<td>13</td>
<td>0-8</td>
<td>0-6</td>
</tr>
<tr>
<td>15</td>
<td>1-9</td>
<td>2-5</td>
</tr>
<tr>
<td>17</td>
<td>1-8</td>
<td>2-4</td>
</tr>
</tbody>
</table>
likely is such regression to occur. It is therefore not possible in the present case to claim more than a fortuitous association between vitamin B12 treatment and the clinical outcome.

Several workers have used the biochemical activity of the tumour, as reflected by the urinary excretion of catecholamines and their metabolites, to chart the clinical progress of the patient (Greenberg and Gardner, 1960; von Studnitz, 1960; 1962; von Studnitz et al., 1963; Smellie and Sandler, 1961; Voorhess and Gardner, 1961, 1962a, b; Betteu and Käser, 1962; Kontras, 1962; Young, Steiker, Bongiovanni, Koop and Eberlein, 1963; Sourkes et al., 1963; Rosensteiu and Engelman, 1963; Williams and Greer, 1963). Williams and Greer (1962, 1963) have pointed out from their own experiences and from a study of the literature that the measurement of HVA, the major metabolite of dopamine, and of VMA, the major metabolite of noradrenaline, provide sufficient information to make a diagnosis in most cases of this secreting tumour.

In the patient described here, comparatively vast concentrations of these metabolites were excreted in the urine initially. Coinciding with an improvement in the patient’s clinical state and with tumour regression, levels gradually fell to normal, providing valuable biochemical confirmation of apparent clinical cure.

Summary

A case of congenital neuroblastoma of unknown origin with multiple hepatic metastases is reported. Regression of the tumour was associated with a return to normal of the initially very high levels of 4-hydroxy-3-methoxymandelic acid (VMA) and 4-hydroxy-3-methoxyphenylacetic acid (HVA) in the urine. These values have remained within normal limits up to the age of 17 months.

REFERENCES

Congenital Dopamine-secreting Neuroblastoma with Clinical and Biochemical Remission
E. M. Brett, T. E. Oppé, C. R. J. Ruthven and M. Sandler

Arch Dis Child 1964 39: 403-405
doi: 10.1136/adc.39.206.403

Updated information and services can be found at:
http://adc.bmj.com/content/39/206/403.citation

These include:

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/