Cerebral abscess in hereditary haemorrhagic telangiectasia: report of two cases in a family

N. H. DYER

From the London Hospital

The diagnosis of cerebral abscess can be difficult and requires a high index of suspicion; thus, any associated syndrome with characteristic and easily recognized features may be a help. Hereditary haemorrhagic telangiectasia is a familial disorder which is characterized by a hereditary tendency, the presence of typically distributed telangiectases, and episodic haemorrhage from those telangiectases (Osler, 1901). Cerebral abscess may occur as a complication of hereditary haemorrhagic telangiectasia (Lancet, 1960), and so its stigmata may suggest the possibility of this condition.

Two patients with hereditary haemorrhagic telangiectasia who developed cerebral abscess are described. Both recovered, and the diagnosis of the second case was facilitated by the knowledge of the first. The patients were second cousins, and were briefly mentioned in the family study of Penfold and Lipscomb (1943; cases IV 1 and III 5). This complication has not been reported previously in two members of the same family although in the large study of Hodgson, Burchell, Good, and Clagett (1959), one case of abscess was mentioned together with another case in which the brain contained an area of porencephaly, which probably resulted from infarction, but might have represented a healed abscess.

CASE REPORTS

CASE 1 M.R. suffered from occasional epistaxis at the age of 14, and small telangiectases were present on the lips and tongue. A shadow was noticed on chest radiography at the age of 20 (Fig. 1).

In 1955 (aged 27), he suddenly noticed loss of feeling around both sides of the mouth which lasted for a few minutes. Twelve hours later, he developed numbness of the tips of the fingers of the left hand and drooping of the left corner of the mouth. Thirty-six hours later, the entire left hand had become numb, and he complained of a right frontal headache which became more severe and he was admitted to hospital.

Examination revealed an alert man with typical telangiectases of the face and fauces, and clubbing of the finger and toe nails. He was not cyanosed. Tone was slightly increased in the left arm but there were brief episodes of marked hypertonia and tremor. Power was reduced in the left hand but normal elsewhere apart from a left lower facial weakness. The left hand was ataxic. Reflexes were increased in the left limbs with an extensor plantar response. Position sense was severely impaired in the left fingers but not in the toes, and there was a small area of hypalgesia on the left hand.

Haemoglobin was 16·3 g. per 100 ml. The red blood cell morphology was normal. The white cell count was 14,600 per c.mm. (78% neutrophils). Radiography of the skull was normal. A single blood culture was sterile.

He developed occasional spikes of fever to 99-5°F. (37·5°C), drowsiness, bilateral papilloedema, and progressive left hemiparesis. On the sixth day, exploration was decided on, as he had developed neck stiffness and signs of brainstem compression with bilateral ptosis.
defective conjugate deviation of the eyes, and absent convergence. Craniotomy was performed (Mr. D. W. C. Northfield), and a right fronto-parietal abscess was found. It contained 40 ml. of thick green pus, from which non-haemolytic streptococci were cultured. Six weeks later, the abscess capsule was excised. It was situated above the middle of the posterior limb of the Sylvian fissure at a depth of 2 cm. and measured $5 \times 2.5 \times 1.5$ cm.

Review of the pulmonary lesion at the age of 31 showed a bilobed opacity in the right lower lobe with feeder vessels, and further shadows in the left lower lobe (Fig. 2). Pulmonary angiography confirmed the presence of arteriovenous fistulae in both lungs. Surgery was not performed because of the bilateral nature of the disease. However, at the age of 33, he had his first haemoptysis, and an arteriovenous fistula 5 cm. in diameter was removed by a right basal segmentectomy (Mr. J. R. Belcher).

Apart from finger clubbing, this patient did not show the typical signs of a pulmonary arteriovenous fistula, as he was not cyanosed, was not significantly polycythaemic, and had never had a pulmonary brut. However, a pulmonary shadow in the presence of hereditary haemorrhagic telangiectasia suggested the diagnosis. In this case excision of the largest fistula was performed for haemoptysis and not because of the risk of abscess.

**FIG. 2. Case 1. Chest radiograph at the age of 31. The arteriovenous fistula in the right lower lobe has increased in size. Early lesions can just be seen in the left lung.**

**CASE 2** L.H. as a boy suffered from epistaxes which were initially severe but have become progressively less profuse. He also developed winter bronchitis which has become more disabling.

At the age of 21 he had several haemoptyses, and chest radiography revealed a shadow in the right middle zone, which was diagnosed as a pulmonary arteriovenous fistula after extensive investigation. Small telangiectases were now present on the nasal septum. There was clubbing of the finger nails. He appeared polycythaemic and was moderately polycythaemic with haemoglobin values varying from 17.8 to 19.8 g. per 100 ml. (120-135%) and red cell counts ranging from 5.76 to 6.13 million per c.mm.

At this time, a blood film was found to contain abundant oval and elliptical red cells, and elliptocytosis was diagnosed. This was associated with splenomegaly and evidence of increased haemolysis.

Over the years, further arteriovenous fistulae have appeared in both lungs and increased in size (Figs. 3 and 4), but he has had no more haemoptyses. Moreover, the polycythaemia has disappeared owing to haemorrhage from the telangiectases and haemolysis of the elliptocytes, so that the packed cell volume has varied from 41 to 45%.

At the age of 24, he had a sudden, severe episode of retrosternal pain but an E.C.G. excluded cardiac infarction. Between the ages of 23 and 25, he developed six or seven episodes of unconsciousness. Some were syncopal but others were epileptiform. On one occasion, there were left-sided clonic movements, right-sided headache, and vomiting which was followed by transient left-sided weakness. The cerebrospinal fluid contained 60 mg. protein per 100 ml. but was otherwise normal. None of these episodes followed haemoptysis.

At the age of 45, he developed a left upper quadrantic visual field defect which was preceded by a right temporal headache. E.E.G. showed a focal right-sided abnormality. Pulmonary function studies indicated a right-to-left shunt and mild airways obstruction.

When aged 50, there was sudden onset of severe frontal headache, 'muddled thinking', dim vision, malaise, and fever. He was admitted to hospital the next day after an epileptic convulsion.

Examination revealed a flushed man with a low-grade fever up to 100°F. (37.8°C.). He had typically distributed cutaneous and mucosal telangiectases. His finger nails were clubbed. There was no cyanosis. Pulse rate was 100 per minute. Blood pressure was 120/70 mm. Hg. His chest was emphysematous and contained scattered ronchi and crepitations, and a systolic murmur was heard at the right base. Although he was alert and orientated, he showed evidence of a left-sided post-central lesion with global dysphasia, dysgraphia, dyslexia, finger agnosia, inversion of objects on copying, right-sided sensory and visual inattention, astereognosis, and slight right hemiparesis. There was no neck stiffness and the optic fundi were normal.

Haemoglobin was 14.9 g. per 100 ml. The white cell count was 11,000 per c.mm. Two blood cultures were sterile. The E.S.R. (Westergren) was 5 mm. in one hour. Skull radiography was normal. The chest radiograph...
showed arteriovenous fistulae in both lower zones and in the right upper lobe. An E.E.G. revealed a focal disturbance in the left temporal region. Lumbar puncture produced cerebrospinal fluid under normal pressure, which contained 55 mg. protein per 100 ml. but was otherwise normal.

The headache and fever persisted, and his right hand became numb and clumsy. On the sixth day, he had another epileptic convolution, developed a higher temperature, and became confused. There was neck stiffness and increase in the hemiparesis. Lumbar puncture revealed turbid cerebrospinal fluid which contained 10,000 white cells per c.mm., most of which were neutrophils, 1,000 mg. protein, 15 mg. glucose and 582 mg. chloride per 100 ml. No organisms were seen or cultured. Bilateral carotid arteriography and echo-encephalography showed no shift of midline structures. He was treated with antibiotics but remained febrile, although the hemiparesis improved.

Ventriculography was attempted, and during exploration through a parietal burr hole, the abscess was located in the left temporoparietal region, and 20 ml. of thick green pus was aspirated. A few organisms were seen on the smear but proved difficult to culture and were thought to be attenuated streptococci. The abscess cavity communicated with the lateral ventricle. He made a slow recovery. Further aspirations yielded no pus and no other abscesses were located. The abscess cavity was not excised.

As a young man he exhibited the classical signs of a pulmonary arteriovenous fistula together with transient cerebral disturbances and chest pain. He developed a permanent visual field defect later. The correct diagnosis was suspected because of experience with case 1. The diagnosis had to be pursued relentlessly and was not confirmed until the abscess was needled during ventriculography. Surgical removal of the multiple pulmonary lesions is not feasible.

**DISCUSSION**

The connexion between these two uncommon conditions is the presence of a pulmonary arteriovenous fistula, which is now a well-recognized associated lesion of hereditary haemorrhagic telangiectasia. There are no reported cases of cerebral abscess complicating it in which a pulmonary lesion is stated to be absent (Table I). Thus abscess is a complication of the fistula rather than the telangiectases. The first report of cerebral abscess complicating a pulmonary vascular shunt is usually accredited to Reading (1932), although Jaffé (1929) had previously described an infant who had multiple haemangiomata of many organs, including the lungs, and died of cerebral abscess and meningitis; neither case had hereditary haemorrhagic telangiectasia. Latour, Puech, Hertault, and Grolleau (1965) found
TABLE I

REPORTED CASES OF HEREDITARY HAEMORRHAGIC TELangiectasia WITH CEREBRAL ABSCESS

<table>
<thead>
<tr>
<th>Hereditary Haemorrhagic Telangiectasia</th>
<th>First Author</th>
<th>Age</th>
<th>Sex</th>
<th>Family History</th>
<th>Episodic Haemorrhage</th>
<th>Telangiectases</th>
<th>Pulmonary Arteriovenous Fistula</th>
<th>Polycythaemia</th>
<th>Associated Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Definite (classical triad)</td>
<td>Hedinger</td>
<td>46</td>
<td>M</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Haemangiomata of tongue</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Kushlan</td>
<td>55</td>
<td>F</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>Osteomyelitis</td>
</tr>
<tr>
<td></td>
<td>O'Neill</td>
<td>22</td>
<td>F</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>Not stated</td>
<td>Not stated</td>
</tr>
<tr>
<td></td>
<td>Taber</td>
<td>27</td>
<td>M</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Syrop</td>
<td>35</td>
<td>M</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Smith</td>
<td>43</td>
<td>F</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Present report(M.R.)</td>
<td>27</td>
<td>M</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Borderline</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Present report (L.H.)</td>
<td>50</td>
<td>M</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Borderline</td>
<td>Respiratory</td>
</tr>
<tr>
<td>Probable (condition likely although triad not stated)</td>
<td>Weiss</td>
<td>27</td>
<td>M</td>
<td>Not stated</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Steinberg</td>
<td>39</td>
<td>F</td>
<td>Not stated</td>
<td>+</td>
<td>Haemangiomata of tongue</td>
<td>+</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Meacham</td>
<td>11</td>
<td>M</td>
<td>Not stated</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>Not stated</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Hodgson</td>
<td>1959</td>
<td>Not stated</td>
<td>+</td>
<td>Not stated</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Latour</td>
<td>26</td>
<td>F</td>
<td>Not stated</td>
<td>+</td>
<td>Not stated</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Possible</td>
<td>Stern</td>
<td>43</td>
<td>M</td>
<td>-</td>
<td>Not stated</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>Glenn</td>
<td>39</td>
<td>F</td>
<td>Not stated</td>
<td>+</td>
<td>Not stated</td>
<td>Angioma of tongue</td>
<td>+</td>
<td>-</td>
</tr>
</tbody>
</table>

1Reports by Chambers (1955), Lindén (1953) or Lodin (1952) and Wood (1956) include no data by which hereditary haemorrhagic telangiectasia may be diagnosed or excluded.

*Present at about the time of abscess development.

16 cases of cerebral abscess in 350 cases of pulmonary arteriovenous fistula collected from the literature. This is an incidence of 5%, which is the same as that in the earlier review of Purriel and Muras (1957). Latour et al. (1965) consider that the incidence of cerebral abscess complicating congenital heart disease with a right-to-left shunt bypassing the lungs is of the same order, although Boczo (1964) thinks that the incidence in pulmonary fistulae is considerably higher. The incidence of cerebral abscess in hereditary haemorrhagic telangiectasia has never been stated, but it can be estimated as about 1% if pulmonary arteriovenous fistulae occur in 15 to 23% of overt cases (Hodgson et al., 1959; Bergqvist, Hessén, and Hey, 1962). Hodgson et al. (1959) found that 40% of their 231 family members fully investigated had overt hereditary haemorrhagic telangiectasia and that there was one abscess.

The presence of classical hereditary haemorrhagic telangiectasia can act as a pointer to the diagnosis of cerebral abscess. However, in children the telangiectases may not have developed and more attention should be paid to the family history. Unfortunately this history may be lacking or uncertain in 14 to 20% of cases. Occasionally an abscess may develop in an adult before the classical triad appears (Smith, Bartholomew, and Cain, 1963). The presence of cyanosis, clubbing of fingers, and polycythaemia, indicating a pulmonary arteriovenous fistula, is often masked by anaemia in this condition (Table I), and was of little help in the two cases reported. The pulmonary murmur was often missed or misinterpreted in the cases described in the literature. Cutaneous telangiectases or epistaxis may occur in association with pulmonary arteriovenous fistulae in the absence of hereditary haemorrhagic telangiectasia.

Neurological disturbances occur in 25 to 30% of patients with proven pulmonary arteriovenous fistulae (Le Roux, 1959). They include headache, faintness, diplopia, vertigo, visual and auditory symptoms, speech defects, syncope, epilepsy, parasthesiae, numbness, and pareses. The signs may be transient or permanent and symptoms are often recurrent. Neurological disturbances in hereditary haemorrhagic telangiectasia are much less common and almost always indicate the presence of a pulmonary arteriovenous fistula. Symptoms should never be attributed to cerebral telangiectases. Most authors cite anoxia, polycythaemia, or both as the cause of neurological dysfunction. However, air embolism has been demonstrated in the presence of pulmonary lesions (Crafoord, 1950) but it only occurs after haemoptysis. Sterile embolism from thrombi in the sac of a pulmonary arteriovenous fistula could occur (Hunter, 1965). Cerebral angioma may occasionally be present (Chandler, 1965) but some symptoms remain completely unexplained.
Cerebral abscess is thus only responsible for a small proportion of the neurological disturbances in hereditary haemorrhagic telangiectasia, but as it carries a high mortality without treatment, early diagnosis is essential, and it should always be excluded by appropriate investigations. In the two cases reported here, the abscesses probably resulted from bacteria or septic emboli bypassing the pulmonary filter and lodging in the brain. Neither case was significantly polycythemic at the time of the disaster. Therefore secondary bacterial invasion of an area of encephalomalacia resulting from cerebral thrombosis is unlikely (Stern and Naffziger, 1953). However, anoxia causing focal cerebral necrosis without vascular occlusion (Berthrong and Sabiston, 1951) or sterile emboli from the peripheral vessels or sac of the fistula may have played a part. Maier, Himmelstein, Riley, and Bunin (1948) and Stevenson (1953) have suggested that infection could arise in the pulmonary arteriovenous fistula itself, which then discharges septic emboli, but such ‘endocarditis’ has not been demonstrated histologically. Often a primary source of infection cannot be found (Table I), but a number of cases have suffered from bronchitis, as in case 2, or chronic osteomyelitis (Muri, 1953). The absence of antecedent infection and the preferential localization in the brain with no abscesses at other sites has also been commented on in congenital heart disease (Sancetta and Zimmerman, 1950).

SUMMARY

Two cases of cerebral abscess complicating hereditary haemorrhagic telangiectasia are described. The patients were members of the same family. Reported cases of cerebral abscess associated with hereditary haemorrhagic telangiectasia have been examined and the pathogenesis discussed. Other causes of neurological disturbance in this condition are briefly reviewed, and it is emphasized that cerebral abscess should always be considered.

I would like to thank Professor C. Wilson, Dr. K. M. A. Perry, Mr. J. R. Belcher, and Mr. D. W. C. Northfield for permission to publish these cases, and Dr. R. A. Henson for helpful criticism of the paper.

REFERENCES


