The 'Happy Puppet' Syndrome

B. D. BOWER* and P. M. JEAVONS

From the Department of Paediatrics and Child Health, University of Birmingham, and the Children's Hospital, Birmingham

In 1965 Angelman described three children whose clinical features were sufficiently similar to warrant the constitution of a new syndrome—so-called 'Puppet Children'. It was immediately apparent to us that two patients whom we had studied for several years conformed to his description. Moreover, they show certain unusual EEG features which, we suggest, constitute another aspect of the syndrome.

Angelman's 'Puppet' children were grossly subnormal, had major fits, and frequent infantile spasms or minor fits. The more specific features were: easily provoked and prolonged paroxysms of laughter, ataxic jerky movements like the movements of puppets, and the ability to protrude the tongue to an unusual degree. Physical examination showed brachycephaly, a horizontal occipital depression, certain ocular features, and apparent prognathism with a common facial appearance, difficult to describe but illustrated in his paper. Skull x-ray films showed a vertical inclination of the base, and all cases showed spikes and slow waves in their EEGs at some time.

The histories of our two cases are as follows.

Case Reports

Case 1. This girl was born at full term of a normal delivery and had an uneventful neonatal period. The birthweight was 3968 g. (8½ lb.), and birth length 56 cm. (22 in.). She was the second child, the first having died at a few days of age from cerebral birth injury. Development was retarded from the first few weeks; she did not smile until 4½ months, could not maintain a sitting position until 9 months, and was paying little attention at 10 months, when fits started. These were typical salaam spasms; when sitting she would suddenly flop forward with arms outstretched and eyes turned upwards, and the spasms were repeated in runs many times a day. At 12 months she had three major convulsions.

She was first seen by us at 13 months of age. It was clear that she was mentally subnormal and her development quotient (DQ) on the Griffiths scale was 40. Her

face was broad, with an unusual appearance, at first glance reminiscent of a mongol. Brushfield's spots were marked. Her EEG showed symmetrical, synchronous, 2-2.5 c/sec. spike and wave activity. Blood urea, calcium, sugar, and electrolytes were normal. Amino acid chromatography of the urine was normal.

A four-week course of prednisolone (30 mg. daily) brought about a reduction and finally abolition of spasms and the EEG improved, but the DQ was little changed (43). Two weeks after prednisolone was stopped she had some right-sided focal fits which were controlled with phenobarbitone. Over the next two years she had occasional bouts of flexor or extensor spasms, mainly when a tooth was erupting, and she made slow mental progress. Ethosuccimide was started at 3 years of age and has been continued ever since. At 3 years she started to laugh frequently for no reason, and periods of causeless laughter have been a prominent feature ever since. Now at 7 years she attends a day training centre. She cannot talk but appears happy because of her almost continual smile and her frequent laughing and giggling. Her tongue is often protruded and her mandible is large (Fig. 1). Her gait is stiff and jerky, for which the term 'puppet-like' is appropriate. Her limbs, however, are hypotonic rather than spastic or rigid, and the reflexes are normal. Occasional major and focal fits occurred until the age of 7, when chlorthalidose (Librium) was started. Her head circumference is only 51 cm. (20½ in.), and there is a depression below the occiput. Skull x-ray film shows a mesocephaly with a reduction in the basal angle (122°, normal 135°). Chromosome analysis of the lymphocytes of peripheral blood (Dr. John Edwards) shows a normal female karyotype. An ophthalmological examination (Mr. M. Roper Hall) showed deficiency of iris pigmentation, Brushfield's spots, and a deficiency of choroid pigment.

Case 2. This boy, unrelated to Case 1, is the 4th child in an otherwise normal family. He was born at full term of a normal delivery with a birthweight of 4053 g. (8 lb. 15 oz.). Development was slow from a few weeks of age; he did not smile until about 4 months and could not maintain a sitting position unsupported until 10 months. At 12 months he first pulled himself to the sitting position. He was first seen at hospital when aged 20 months; he could stand with support only, and would reach out and grasp an object but had no pincer grip; he recognized his parents, smiling and vocalizing, but had

Received August 18, 1966.

* Present address: Radcliffe Infirmary, Oxford.

FIG. 1.—Case 1, age 7 years.

FIG. 2.—Case 2, age 7 years.

no words. He laughed and chuckled to an unusual degree. His motor development was assessed as that of a 12-month child, but his personal-social development was only at the 6-months level. Head circumference was 46 cm. (18½ in.). At 22 months he started to have infantile spasms of extensor type. When sitting he would suddenly fall backwards with stiff arms; after he was sitting up again, the jerk would be repeated and he would have 5 or 6 in about 10 minutes. In the next two months occasional major fits also occurred. His EEG at 20 months showed high amplitude symmetrical synchronous 5-6 c/sec. activity unaffected by eye opening. Amino acid chromatography of the urine was normal. A tryptophan load test gave an abnormal result (28 mg. xanthurenic acid excretion following a dose of 0.2 g./kg. body weight 1-tryptophan), and he was therefore treated with pyridoxine 50 mg. daily, with no effect. Control of his fits was, however, achieved with ethosuccimide. After two years a severe relapse with status epilepticus necessitated the addition of mepacrine, which has, with the exception of a further episode of status, maintained freedom from spasms up to the present. He still has occasional left-sided clonic fits, but these have responded to sodium phenytoin.

Now, at 7 years, he is severely subnormal but is continuously smiling, laughing, and protruding his tongue (Fig. 2). His gait is stiff, jerky, and flat-footed, like that of Charlie Chaplin. His face is reminiscent of Case 1, and very similar to Case 3 of Angelman. There is occipital flattening but no depression. Skull x-ray film showed mesocephaly with a basal angle of 121° (normal 135°). Ophthalmological examination showed fine pigmentary mottling of the retina and deficiency of choroidal pigment peripherally.

Electroencephalographic Findings

Case 1. Samples of the EEGs at different ages are shown in Fig. 3 and the EEG findings in relation to age, fits, and therapy are shown in Fig. 4.

The first EEG, taken at the age of 13 months, showed a little 5-6 c/sec. activity with superimposed high voltage 2-3 c/sec. waves and spikes. This slow wave and spike activity occupied 65% of the record. During the period of treatment with prednisolone, nine EEGs were taken and the amount of slow wave and spike activity gradually decreased, so that after a month on prednisolone only 10% of the record was occupied by 2-2.5 c/sec. activity and spikes were rare. Relapse occurred, and within 10 days of stopping prednisolone the delta discharges occupied 72% of recording time. Eight more records were taken between the age of 15 months and 4½ years. All but one showed spike and wave activity, mainly at 2 c/sec., occupying up to 95% of the record. It should be noted that even when fits were not occurring, the EEG still showed some abnormal discharges. The most recent record, taken at 7 years of age, showed continuous synchronous symmetrical 5-6 c/sec. activity, uninfluenced by eye opening and closing.

Case 2. The first EEG, at 20 months of age, showed high voltage symmetrical synchronous 5 c/sec. activity, not associated with drowsiness, and unaffected by eye opening and closing (Fig. 5). At 2 years there was high voltage 2.5-3 c/sec. activity with occipital spikes. At 2½ years there was delta rhythm but no spikes, but at 4½ years the record showed continuous 2 c/sec. spike and wave activity. The relation of the EEG to fits and therapy is shown in Fig. 6. An EEG, taken in January

FIG. 3.—Case 1. Samples of EEG records at different ages. The patient was awake on all occasions.

1966 when the child was aged 7 years, showed almost continuous 2 c/sec. spike and wave activity. The last record (in March 1966) was normal; the child had

received chlordiazepoxide for two weeks.

The records of both cases, at the age of 4½ years, are

FIG. 4.—Case 1. Percentage of total EEG recording time occupied by slow wave-and-spike activity at various ages, in relation to fits and therapy.

FIG. 5.—Case 2. Samples of EEG records at different ages. The patient was awake on all occasions.

very similar in appearance as can be seen in Fig. 7. The record of Case 1 at 7 years is very similar to that of Case 2 at 20 months.

Dr. Angelman has kindly allowed us to see the EEGs of his Cases 2 and 3 and these show bilateral spike and wave, but this is mainly around 2-3 c/sec. and is definitely not as slow as in our cases.

Discussion

Our two patients have the following features in common with those of Angelman: facial appearance, protruding jaw, continual tongue protrusion, ataxic jerky gait, and arm movements, frequent smiling and laughing, microcephaly; severe mental sub-normality, history of infantile spasms and major fits, and incomplete development of the choroid. One shows an occipital depression and the other occipital flattening. Although there was a clinical suggestion of brachycephaly as described by Angelman in one of our patients, measurement of skull x-ray film showed both cases to be mesocephalic. However, the skull base was inclined nearer to the vertical than normal in all five cases.

FIG. 6.—Case 2. Percentage of total EEG recording time occupied by slow wave and spike activity at various ages, in relation to fits and therapy. S indicates status epilepticus.

FIG. 7.—Comparison of EEGs of Cases 1 (B.D.) and 2 (C.M.) at 4½ years.

The feature of our two cases which distinguished them from all our other patients showing infantile spasms was a consistent *absence* of hypsarrhythmia and the *presence* of symmetrical synchronous 2 c/sec. wave and spike activity throughout the period of study. A number of patients with infantile spasms initially show hypsarrhythmia but develop 2 c/sec. wave and spike activity later, either during steroid therapy or as spontaneous maturation occurs. This is, in fact, a transitional EEG pattern. However, in our two patients it was seen in EEGs taken between 13 months and 7 years.

Angelman's three patients were similar in showing bilaterally symmetrical synchronous wave and spike activity, and there is no mention of hypsarrhythmia in his paper. They differed from ours, however, in that the wave and spike activity was faster, being mainly around 3 c/sec.

We have already drawn attention to the similarity of the EEGs of our two patients at the age of 4½ years. It is of interest that symmetrical synchronous 5-6 c/sec. activity occurred in Case 2 at the age of 20 months and in Case 1 at 7 years. This pattern is uncommon in infantile spasms. In our series we have seen it once during and after response to steroid treatment. In none of the cases was it associated with drowsiness.

Effect of therapy. In contrast to Angelman, we obtained improvement in each of our cases with drug therapy. Case 1 temporarily improved on prednisolone, and later on ethosuccimide and chlordiazepoxide. Case 2 responded initially to ethosuccimide. Later, after status epilepticus,

there was a dramatic clinical and EEG response to mepacrine.

Apart from the publication by Angelman (1965) there appears to be no published description of this syndrome on infantile epilepsy. It is obviously rare. We have seen over 200 cases of infantile spasms but only the two children described in this paper show the features which, taken together, seem to be specific.

Summary

Two children similar to those described as 'puppet children' by Angelman have been studied over 5 years. The clinical features of this syndrome, which we suggest should be called the 'Happy Puppet' syndrome, are: severe mental subnormality, infantile spasms, easily provoked and prolonged paroxysms of laughter, ataxic jerky movements like those of puppets, a common facial appearance with apparent prognathism, certain ocular features, and a horizontal occipital depression.

The EEGs showed slow wave and spike activity. Hypsarrhythmia was never seen. This contrasts with the EEG findings in nearly all other children with infantile spasms.

We thank Dr. Roy Astley, Dr. John Edwards, and Mr. Michael Roper Hall for their help in the investigation of these patients. We are grateful to Dr. Angelman for allowing us to see EEGs of his patients.

REFERENCE

- Angelman, H. (1965). 'Puppet' children. A report on 3 cases. *Develop. Med. Child Neurol.*, 7, 681.