Psychological characteristics of children with Shwachman syndrome

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Abstract

Twelve children and young adults with Shwachman syndrome were compared with their unaffected siblings and with controls suffering from cystic fibrosis in terms of intellectual ability, motor skills, and behaviour. There were highly significant differences in intelligence quotient between those with Shwachman syndrome and the other two groups. Four of the index subjects but none of the control subjects were below the normal range. The differences between groups on other tests of cognitive and motor skills were not significant, though those with Shwachman syndrome tended to have the lowest scores. There was no evidence that those with Shwachman syndrome had more behavioural difficulties than the control subjects. We suggest that the intellectual difficulties of patients with Shwachman syndrome may be of neurological rather than social origin and that they may originate before birth.

Shwachman syndrome is a rare multiorgan disease of unknown cause first described in the 1960s.^{1 2} In infancy the condition presents with failure to thrive, bulky offensive stools as a result of pancreatic exocrine insufficiency, intermittent thrombocytopenia and neutropenia, and growth and bone abnormalities (metaphyseal dyschondroplasia). Shwachman syndrome is the second most common cause of pancreatic insufficiency in well nourished North American and European children, with an incidence of 1:200 000,³ and a possible autosomal recessive mode of inheritance.⁴

Symptomatic treatment with pancreatic enzymes and a low fat diet alleviates the problem of maldigestion, but poor growth often persists. Most patients remain below the third centile for height and weight into adult life⁴ and administration of growth hormone does not improve growth.⁵ Some early studies reported that affected children have adequate psychological development with normal motor milestones and mental abilities within the reference range.¹ Others reported that patients were occasionally grossly retarded (one child of four described by Shmerling *et al*⁵ and two of 20 described by Bodian *et al*²), and one mentioned more subtle developmental delays (in milestones and intelligence quotient (IQ)).⁴ The psychological characteristics of children with Shwachman syndrome, however, have not been studied systematically.

In this study we have examined intellectual ability and achievement in a group of 12

children and young adults with Shwachman syndrome. We compared them with their unaffected siblings (who share the family environment but not the disease) and with matched controls with cystic fibrosis (who share many similarities in illness and hospital treatment, but not family environment).

Subjects and methods

All children and young adults with Shwachman syndrome who were between 4 and 20 years old at the time of the study and who had been diagnosed or treated, or both, at the Hospital for Sick Children were invited to enter the study. Many had also been included in the study by Aggett *et al*.⁴ Seventeen children were identified but one had died, the parents of two refused (in one case because they thought that the diagnosis was incorrect), and two were lost to follow up, leaving a possible 12 children. At the time of the study, one of these 12 was too ill to take part, but a further child was identified in Birmingham whose family agreed to participate, making 12 children in all. Eight of the 12 children also had unaffected siblings who agreed to take part for comparison (table). When there were several unaffected siblings, the one nearest in age was asked to participate in the study.

A second control group, of children matched for age, sex, and social class, was selected from the London register of children with cystic fibrosis. All those approached agreed to participate.

PROCEDURE

Index and control subjects were normally assessed at the hospital that they usually attended, on the same day as their routine outpatient appointment. Siblings were asked to accompany the affected child and were tested on the same day. One subject no longer attended hospital and was seen in the local health centre instead.

On assessment the parents were interviewed to provide developmental, social, and medical details (for example, developmental milestones, time off school because of illness, and peer relationships) and the Connors parent questionnaire was administered.⁶ Subjects and controls were given age appropriate IQ tests (McCarthy scales of children's abilities; Wechsler preschool and primary scale of intelligence; Wechsler intelligence scale for children, revised edition; and Wechsler adult intelligence scale, revised edition). They also completed the Annett and Kilshaw pegboard (a test of manual motor skill)⁷; an immediate and delayed visual recall mem-

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Age, sex, and IQ of patients with Shwachman syndrome, control subjects (siblings), and control subjects with cystic fibrosis

Patients with Shwachman syndrome				Sibling control subjects			Control subjects with cystic fibrosis		
Case No	Sex	Age (years)	IQ	Sex	Age (years)	IQ	Sex	Age (years)	IQ
1	Male	3.9	(48)	Female	6.4	106	Male	4.7	132
2	Female	4.8	76	No sibling			Female	5.08	114
3	Female	4.8	105	Male	8.5	125	Female	5.08	119
4	Male	10.3	105	No sibling			Male	11.4	116
5	Female	12.3	68	Male	9.3	102	Female	12.3	88
6	Female	13.3	69	Male	11.0	90	Female	14.2	80
7	Female	14.08	61	Male	11.7	92	Female	14.8	92
8	Male	15.3	88	No sibling			Male	15.3	112
9	Female	18.2	76	Female	20.08	99	Female	17.5	90
10	Female	18.7	90	No sibling			Female	18.6	96
11	Female	19.9	71	Female	13.0	91	Female	20.0	93
12	Female	11.0	82	Male	8.2	113	None available		
Mean (SD)		12.5 (5.5)	81 (14.6)*		11.0 (4.2)	102.3 (12.2)		12.6 (5.5)	102.9 (16.3)

*Excluding case 1.
Case 8 and case 10 were siblings.

ory test from the British ability scales⁸; a test of visuomotor skill (the Bender-Gestalt test of visuomotor development)⁹; the Bruininks-Oseretsky motor skills test,¹⁰ and a word reading test from the British ability scales.⁸ The large age range meant that not all these tests were suitable for all subjects; numbers of subjects reported as completing the tests in the results section therefore vary accordingly.

Statistical analysis was by the Student's paired *t* test using two tailed probability estimates.

The children and young adults with Shwachman syndrome were exactly matched for sex and social class with those with cystic fibrosis (four were social class I or II, and the remaining eight were social class III). The mean (SD) ages for the two groups were similar, being 12.5 (5.5) years and 12.6 (5.5) years, respectively. Three of the siblings of the patients with Shwachman syndrome were older than the affected children, and five were younger (mean age of siblings 11.0 years); two sibling pairs were girls, but the other siblings were opposite sexes to the affected children (three girls and five boys altogether).

Results

PSYCHOMETRIC TESTS

The results are shown in the table. One child (case 1) was severely handicapped and could not achieve a score on the appropriate IQ test. He was therefore assessed on the Griffiths's mental development scale.¹¹ His developmental quotient is given in parentheses in the table as this scale has a different mean (SD) from the other scales and his developmental quotient was not included in the statistical analysis. Patients with Shwachman syndrome had significantly lower IQs than their siblings, differences ranging from 20 to 34 (mean 25.7) *t*=11.25, *df* 6, *p*<0.0002 (excluding case 1) and the control patients with cystic fibrosis (differences ranged from 6 to 38 points (mean 19.1) *t*=6.08, *df* 9, *p*<0.0005) (excluding case 1). The control patients with cystic fibrosis, however, did not differ from the siblings in IQ (*t*=0.31, *df* 6, *p*>0.05). No particular pattern of deficits was found among the subtest scores of the patients with Shwachman syndrome.

In terms of motor skills (for those who were able to complete the Annett pegboard) those with Shwachman syndrome were slower than their siblings but faster than those with cystic fibrosis as measured by *z* scores. This was true for both right and left hands but none of the differences was significant. Only five with Shwachman syndrome, four with cystic fibrosis and five siblings completed the Bruininks-Oseretsky test of motor development (age range 4 to 14 years). The results showed that although those with Shwachman syndrome did less well than their siblings (*t*=1.85, *df* 4) and those with cystic fibrosis (*t*=2.17, *df* 3), these differences did not reach significance, perhaps because of the small numbers studied. The scores on the Bruininks-Oseretsky test and the IQ test were strongly positively correlated (Pearson *r*=0.73, *df* 12, *p*<0.002), as might be expected.

The results of the British ability scales visual memory test showed that the patients with Shwachman syndrome scored less well (in terms of *T* scores) than their siblings on both immediate and delayed memory, but the index cases and those with cystic fibrosis had similar scores for both immediate and delayed recall. None of the differences in memory testing were significant. The group with Shwachman syndrome also made more errors on the Bender-Gestalt test (using the Koppitz scoring system) than those with cystic fibrosis, though this did not reach significance on a paired *t* test (*t*=2.29, *df*=6, *p*=0.06). The scores of the group with Shwachman syndrome on the Bender-Gestalt test could not be compared with those of their siblings because of the age differences (error scores on the Bender-Gestalt test are age related).

Finally, comparison of the subject's reading skills (by *T* scores) on the British ability scales word reading test indicated that those with Shwachman syndrome were doing only a little less well than their siblings and the cystic fibrosis controls, and none of the differences were significant.

INTERVIEW WITH THE PARENTS

Interviews with the parents suggested that in terms of early history the largest difference

between the groups was that of birth weight. All but one of the children with Shwachman syndrome were lighter at birth than their siblings (the exception was a sibling who had been born prematurely), and this difference was significant by the paired *t* test ($t=2.91$, *df* 7, $p=0.02$). The children with Shwachman syndrome were also significantly lighter at birth than those with cystic fibrosis (paired *t* test, $t=2.89$, *df* 10, $p<0.02$); those with cystic fibrosis did not differ from the siblings ($t=0.25$, *df* 6, $p=0.8$).

There was some indication of delayed speech and motor milestones among the children with Shwachman syndrome. For instance, four of them had not sat up unsupported until they were more than 9 months old, according to their parents, whereas none of the other children had started sitting so late. The age of walking did not differ across the groups. Five of the children with Shwachman syndrome said their first words after 12 months of age, whereas only one other child started talking so late. In view of the age of some of the other subjects, however, and the effect this may have on the accuracy of parental recall the milestone data have to be treated with caution.

Children's scores on the Connors parent questionnaire varied greatly in all groups and the differences between groups did not approach significance. In terms of absences from school, parents of children of school age with Shwachman syndrome reported that some had had more than a week off school during the previous three months. Two children and one young adult were off work for this time. Children and young adults with cystic fibrosis had rather more time off on the whole (four had had more than two weeks off, and three had had one to two weeks off school or work). Siblings of the children with Shwachman syndrome had also sometimes had more than one week off school or work ($n=3$), suggesting that in general those with Shwachman syndrome were not missing undue amounts of schooling when compared with their siblings, and were missing less schooling than children with cystic fibrosis.

Discussion

The mean IQ for the children and young adults with Shwachman syndrome was more than one standard deviation below the mean for the general population and was significantly lower than the mean IQ of both their siblings and matched controls with cystic fibrosis. Four of those with Shwachman syndrome scored less than 70 for full scale IQ and this fell below the accepted reference range (that is, more than two standard deviations below the mean of the general population). One of the four fell into the range of severe learning difficulties (case 1). None of the siblings and none of the patients with cystic fibrosis scored outside the normal range, and the mean IQ of the two control groups was close to the mean for the general population.

Other psychometric tests almost always showed poorer performance by children and young adults with Shwachman syndrome when compared with siblings and with those with cystic

fibrosis. The restricted age ranges of many of the tests meant that the numbers in each group were sometimes small, and none of the differences were significant. The poorer motor skills of those with Shwachman syndrome may have been a function of IQ and this kind of general correlation of test scores with IQ may also have accounted for other differences in test results among groups.

There are a number of reasons why children and young adults with Shwachman syndrome may be less able than their siblings and than those with cystic fibrosis. Firstly, it could be argued that when children have a chronic illness they will inevitably miss some schooling and this, together with the stress associated with the illness, may depress their scores on psychometric tests. If this is the case, it would be predicted that children with Shwachman syndrome would score as well as those with cystic fibrosis (or even better, given our evidence of rather more time off school for those with cystic fibrosis). The children with cystic fibrosis were doing better than those with Shwachman syndrome, however, though admittedly the two group's scores were most alike for 'attainment' tests, such as reading. Thus absence from school cannot explain the findings on IQ.

Secondly, it might be that the small size of the children with Shwachman syndrome meant that they were treated as much younger children, thus retarding their emotional and cognitive development.¹² Again, children with cystic fibrosis would be expected to be similarly affected, as their growth is also poor. This explanation, therefore, is also inappropriate.

Finally, it may be that in Shwachman syndrome there is some subtle neurological damage that does not occur in cystic fibrosis. This explanation fits the findings of the study best, as it would follow from this that there would be significant differences between the children with Shwachman syndrome and their siblings and between those with Shwachman syndrome and those with cystic fibrosis, but no differences between those with cystic fibrosis and the unaffected sibling group. Moreover, it would be expected that measures of intellectual potential would be more affected than attainment, as was indeed the case. There was no evidence of an increasing deficit with increasing age in this study for those with Shwachman syndrome, though whether the children's IQ declines over time can only be answered satisfactorily by a prospective longitudinal study. It is possible that any neurological damage may occur within the uterus, however, and this would not necessarily increase after birth. The significant differences between the children with Shwachman syndrome and the other groups in birth weight suggests that prenatal adversity may well be an important factor.

The reasons for intellectual difficulties in children with Shwachman syndrome will probably remain unclear for some years. It is now certain, however, that these children should be considered at risk of developmental delay and early intervention programmes should be made available to them.

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