Letters to the editor

‘Development of parainfectious opsoclonus in an infant by a non-humoral immune mechanism’

Opsoclonus, an unusual but characteristic neurologic sign characterized by non-rhythmic horizontal and vertical oscillations of the eyes, is a rare consequence of viral and neoplastic conditions and can occur after exposure to some drugs. Development is immuno-mediated, but while humoral mechanisms have been suggested, and circulating anti-neuronal antibodies are often detectable, a primary pathogenetic role for such antibodies remains disputed.

We report the development of opsoclonus as a post-viral phenomenon in a female child with severe combined immunodeficiency (SCID) early after successful bone-marrow engraftment, when T cell responses were developing, but before antibody responses could be mounted.

At 9 weeks she was admitted with a persistent dry cough, failure to thrive, anaemia, and alymphocytosis. Bone marrow examination confirmed erythrocyte aplasia with cytologic and immunohistochemical evidence of parvovirus B19 infection. Immunological and metabolic studies confirmed adenosine deaminase deficiency, a rare autosomal recessive form of congenital SCID. Analysis of maternal antenatal booking and other stored serum sampled confirmed congenital parvovirus B19 infection in an immunodeficient child. Treatment with intravenous immunoglobulin (IVIG) was commenced and she underwent an unconditioned whole bone marrow transplant from her parvovirus B19 IgG negative, HLA identical brother.

Nine days after the transplant (day +9) she became encephalopathic, coinciding with a rise in peripheral lymphocyte count. Serum was parvovirus B19 polymerase chain reaction (PCR) positive but CSF was negative. Subsequent lumbar taps confirmed a raised CSF protein and lymphocytosis, but remained parvovirus B19 PCR negative. Opsoclonus, first unequivocally recognized on day +32, may have been present earlier. CSF indices began to normalize following treatment with methylprednisolone (2 mg/kg) and acyclovir commenced on day +9. Her clinical condition was slower to respond and seemed partially steroid-dependent. At times of good control she demonstrated developmental progress, but with good social interaction, but relative gross motor delay. The clinical and electrographic picture were consistent with a subcortical pathology. A late MRI showed bilateral pulvinar changes (Figure 1). No evidence of coincidental neuroblastoma was found.

The patient’s serum, maternal serum, and a sample of the IVIG batch used were negative for non-specific neuronal nuclear and Purkinje cell IgG antibodies by immunofluorescent screening on monkey brain sections.

Recognized viral antecedents of opsoclonus include Epstein-Barr virus, mumps, Coxsackie B3, St Louis encephalitis, and enteroviruses including oral polio vaccine. To our knowledge this is the first documented association with parvovirus B19.

The association of opsoclonus with neuroblastoma is well recognized and is the only well-characterized paediatric paraneoplastic neurologic phenomenon. In adults, opsoclonus is one of a number of paraneoplastic syndromes. In some, a humoral immune pathogenesis due to the presence of neoplasia has been clearly demonstrated. A number of specific anti-neuronal antibodies that react simultaneously with neuronal and neoplastic tissue are detected in these patients. Their primary pathogenetic role is however disputed on the basis of poor specificity. The antibodies are not specific for the type of malignancy, or type or presence of neurological syndrome.

Unidentified IgG and IgM antineuronal antibodies directed to cerebellar Purkinje and granule cells in association with paediatric opsoclonus were found. The target antigens recognized by these antibodies remain unidentified, leaving questions over the specificity of the serological findings. Indirect support for the humoral hypothesis comes from the observation of improved outcome for children with opsonus-related neuroblastoma, implying that the antibodies that recognize tumour epitopes control tumour size. Preliminary studies suggest however that the neuroblas-tomas associated with opsoclonus have primary favourable biological characteristics.

Our patient’s neurologic deterioration and opsoclonus occurred during T-lymphocyte engraftment, before efficient antibody production occurs. We did not detect antineuronal antibodies in the patient, her mother, or the IVIG using a similar immunohistochemical screening technique to that described by Connolly and colleagues. While the clinical context strongly supports post-infectious, or ‘graft-versus-virus’ encephalitis secondary to congenital parvovirus B19 infection as the cause of the neurologic syndrome, the opsoclonus is likely to have been secondary to direct lymphocytic action, rather than antibody-mediated.

The MRI appearances resemble those recently described in variant Creutzfeld-Jakob disease (vCJD) and underline...
that while of considerable value in the diagnosis of vCJD in an appropriate clinical setting, these appearances can have other causes.

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References

‘When chronic disability meets acute stress: psychological and functional changes’

In the mid 1980s a surgical intervention, selective posterior rhizotomy (SPR) or functional rhizotomy, was established as a viable treatment option for many children with spastic cerebral palsy (CP). SPR is a neurosurgical intervention that decreases spasticity by severing dorsal nerve rootlets. A child has undergone SPR, muscle tone is significantly reduced throughout the child’s extremities, necessitating a course of physical rehabilitation. Recent critics suggest that the surgery may be of questionable value, presenting evidence that the surgery itself may offer only marginal benefit over the intensive physical therapy involved. The debate regarding the efficacy of this procedure continues, but there is no doubt that surgery of any kind creates added stress for the child and family.

Numerous studies over the last 30 years have shown that parents of children with disabilities, including parents of children with CP, experience higher levels of stress than those caring for non-disabled children. Coping strategies used by such parents have also been investigated. Effective coping strategies, active coping strategies (i.e. problem-focused coping) have been consistently associated with the well-being of these parents. Two emotion-focused coping strategies, seeking social support and positive reappraisal, have also been shown to be effective when used by these parents. On the other hand, there have been consistent reports of the deleterious effects of other emotion-focused strategies such as avoidance, wishful thinking, self-controlling, and self-blaming coping for these parents. Nevertheless, the experiences of parents whose children have a chronic disability and are also encountering a significant acute stressor have received very little research attention. More specifically, the experiences of parents whose children have CP and are to undergo SPR have not been studied.

The aims of this study then were twofold. The first was to compare measures of child functioning and parent stress at two points in time (before surgery and follow-up). It is predicted that before surgery ratings of parenting stress would be significantly higher than those at follow-up, while ratings of children’s functioning will be higher at follow-up than those before surgery. The second aim was to compare the coping strategies used by parents in a stressful medical situation to those used in a stressful family situation. A repeated measures design was used to assess parent variables (stress and coping) and child variables (capability and performance) at two points in time: one week before surgery (T1) and one year after surgery (T2). All of the children had been diagnosed with spastic CP by a physician before their presentation at the rhizotomy clinic of a major metropolitan hospital. Each child was examined and his/her medical records were reviewed by a team of four pediatric specialists (neurologist, physiotherapist, neurosurgeon, and physical therapist) with the goal of confirming the diagnosis of spastic CP and evaluating the child’s candidacy for SPR. The SPR was to be followed by in-patient rehabilitation.

Forty-two mothers completed the before-surgery test packets, and 17 of these completed the follow-up packets. Wilcoxon signed rank statistic and χ² analyses were used to test for differences between those who responded and those who did not. There were no significant differences between the groups on demographic characteristics or on T1 measures of child function or parenting stress. This cannot be taken to mean that there were no differences in children’s functioning or parents’ stress scores at follow-up. Differences were found on two coping subscales at T1. Responders used less escape-avoidance coping and less positive reappraisal.

Children’s before-surgery mobility levels were rated using the New York University Mobility Classification scheme. No children were in Category I: independent (community) ambulators with no devices; one was in Category II: independent (community) ambulators with hand-held assistive devices; none were in Category III: quadraped crawlers with some independent therapeutic ambulation; nine were in Category IV: commando (belly) crawlers with some therapeutic ambulation with or without therapist assistance; and seven were in Category V: no independent means of locomotion. Average length of children’s in-patient rehabilitation admission was 15.1 weeks (SD 6.75). Mean age of the children at T1 was 4.4 years (SD 1.90). Mean age of the mothers was 34.6 years (SD 1.90). Mothers were predominantly Caucasian (n = 13), married (n = 10), unemployed outside the
home \((n=11)\), and without hired help \((n=12)\). Four families received the services of a personal care aid for the child. There was greater variability in family income (median, $30 000–$49 000), number of children (median 3), and the mother’s education (median, high school diploma or some college).

The Parenting Stress Index-Short Form\(^{10,11}\), a self-report instrument, was used to assess three dimensions of parents’ stress. Scaled scores of the Pediatric Evaluation of Disability Inventory\(^{12}\) were used to measure the children’s capability and performance in the areas of self-care and mobility. The raw scores of the Ways of Coping Questionnaire\(^{13}\) were used to assess behavioral and cognitive coping strategies that parents used in two stressful situations: during their initial visit to the rhizotomy evaluation clinic \((T1)\) and during the most stressful family conflict that had occurred since the child’s surgery \((T2)\).

The first aim of this study was to investigate changes in the children’s function and in parenting stress scores. Descriptive statistics for \(T1\) and \(T2\) ratings and \(z\)-scores are reported in Table I. Children’s function scores showed a statistical increase on each of the four scales. Although the children showed significant functional limitations at the time of the initial assessment as well as at follow-up, certain domains showed significant clinical improvement. Clinically improved mobility domains included chair/wheelchair transfers, bath transfers, in- and outdoor locomotion, and stairs. For example, 12 children were able to sit supported in a chair at follow-up versus five before surgery, 10 children could crawl versus five before surgery, 13 children could walk indoors with a device versus five before surgery, and six children could crawl or walk up and down stairs versus 1 before surgery.

Parents showed statistically and clinically significant increases in total parenting stress and in the parent–child dysfunctional interaction subscale. However, it is important to note that parenting stress scores were already in the high average range at \(T1\) (79th percentile), and increased slightly to the borderline range at follow-up (81st percentile). Four of the parents were experiencing clinically significant levels of stress (90th percentile or higher) at \(T1\) and seven at \(T2\). It was suggested that parents whose scores fell in the clinical range be referred for closer diagnostic study and for professional assistance\(^{19}\). Physicians and other health care providers may want to consider screening for clinical levels of distress as part of their intake procedure.

In an effort to better understand the mothers’ experiences, different types of parenting stress were examined. The parent–child dysfunctional interaction subscale scores were in the average range at \(T1\) (75th percentile), but showed a dramatic increase to the clinical range at \(T2\) (90th percentile). This subscale measures the extent to which mothers believe their child does not meet her expectations, and the extent to which the interactions with her child are not reinforcing to her as a parent. High scores suggest that the parent–child bond is either threatened or was never adequately established. Given

<table>
<thead>
<tr>
<th>Measure</th>
<th>(T1)</th>
<th>(T2)</th>
<th>(z)-score</th>
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<tr>
<td>PSI-SF ((n=17))</td>
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<td>Parent–child dysfunctional interaction</td>
<td>24.0</td>
<td>20.0-32.0</td>
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<td>Parental distress</td>
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<td>Difficult child</td>
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<td>Total</td>
<td>81.0</td>
<td>61.0-111.0</td>
<td>83.0</td>
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<tr>
<td>PEDI Function scale ((n=17))</td>
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<tr>
<td>mobility</td>
<td>33.4</td>
<td>15.2-49.7</td>
<td>41.4</td>
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<tr>
<td>self-care</td>
<td>43.6</td>
<td>21.4-55.6</td>
<td>46.0</td>
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<td>Caretaker assistance scale ((n=15))</td>
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<tr>
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<td>WOC-R ((n=11))</td>
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<td>Confrontive</td>
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<td>0.0-16.0</td>
<td>5.0</td>
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<td>Distancing</td>
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<tr>
<td>Taking responsibility</td>
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<tr>
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<td>Positive reappraisal</td>
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<td>0.0-15.0</td>
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\(T1\), 1 week before surgery; \(T2\), 1 year after surgery; PSI-SF, Parenting Stress Index-Short Form; PEDI, Pediatric Evaluation of Disability Inventory; WOC-R, Ways of Coping-Revised.

\(^{a}\)\(p<0.05\); \(^{b}\)\(p<0.01\); \(^{c}\)\(p<0.001\).
the fact that the mothers in this study scored in the average range at T1, it might be concluded that the bond had indeed been established for most of them, but had been threatened in the one year between surgery and follow-up.

The difficult child subscale scores were also in the average range at T1 (75th percentile), but increased only slightly to the 80th percentile at follow-up. In contrast, the parental distress subscale scores were only in the 50th and 55th percentile at T1 and T2, respectively. Taken together, the scores suggest that the parenting stress experienced by these mothers is more closely related to changes in the relationship with their children than it is a response to personal factors in the mother’s lives.

The second aim was to compare parental coping strategies in two stressful situations (Table I). Mothers used more social support, positive reappraisal, self-controlling coping, and problem-solving when faced with the stressful family event (T2), than the stressful clinic visit (T1). None of the strategies were associated with total stress at T1 or T2. These results support the situation-specific model of stress and coping. This model suggests that distress is the result of the interaction of a stressful event, coping resources, cognitive appraisals, and coping strategies. Mothers’ use of strategies in a medical situation was different than their use in a family situation. This is not to say that the strategies used in the family situation are not also used in the medical situation. In fact, three of the four (i.e. social support, problem solving, self-controlling) were the most frequently used strategies in both situations. However, they were used more often in the family situation than in the medical situation. However, there is one strategy which is used somewhat infrequently in the medical situation (relative to the other strategies, and relative to its use in the family situation). This strategy is positive reappraisal. Its increased use at T2 raises at least two questions: is the difference in use accounted for by the differences in the situation or is the difference reflective of progress in the process of coping?

More specifically, has the passage of time between T1 and T2 allowed the mother to reflect on her experiences, making ‘positive reappraisal’ a more viable coping strategy at T2?

Results of this study indicate that children demonstrated statistically significant increases in functioning at follow-up. Although functional gains in specific domains were achieved, the children still had significant functional limitations at the time of follow-up and remained dependent on their caregivers for many self-care activities and mobility. Parents reported higher levels of stress at follow-up, with the most significant increases being experienced in the parent–child dysfunctional interaction subscale. Mothers also reported on the coping strategies they used in two different situations, and results showed greater use of social support, positive reappraisal, self-controlling coping, and problem-solving during a stressful family situation than during a stressful medical situation.

Several limitations should be discussed. First, the findings in this study should be interpreted with caution due to the limited number of participants and the absence of a control group. The latter makes it difficult to identify the unique contributions of treatment beyond that of maturation over the one year follow-up period. Second, the homogeneity of the disability group limits the generalizability of this study. Finally, the attrition rate also raises the question of the degree to which this sample is representative of all families whose children undergo SPR. This study examined the experiences of mothers as they were the ones to respond when questionnaires were provided to the ‘parents’. Soliciting the participation of both mothers and fathers should be encouraged in future studies.

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References