Autism and Autistic Symptoms Associated with Childhood Lead Poisoning

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ABSTRACT

Autism is a developmental disorder that impairs both nonverbal and verbal communication and reciprocal social interactions and is seen in association with an abnormally restricted range of interests. Although symptoms typically develop without clear etiological cause, some cases are associated with disorders or conditions that negatively impact brain development. Lead is a neurotoxin to which the developing brain is particularly vulnerable. Moreover, lead poisoning in children is known to negatively affect brain systems implicated in cognitive, communication, and social functioning. The present paper presents two case histories of children who, during periods of severe lead poisoning, developed autism or autistic symptoms. These cases underscore that there are multiple causes of autism and the importance of environmental influences in some cases.

INTRODUCTION

The key features of autism, first described by Kanner in 1943,[1] are impairments of the development of both nonverbal and verbal communication and reciprocal social interactions seen in association with an abnormally restricted range of interests.[2] Current diagnostic schema indicate an onset of symptoms before the age of 3 years. Although Kanner generally excluded cases with known brain dysfunction, it is now recognized that, in addition to the idiopathic form, autistic disorder can also be caused by a number of conditions that negatively impact brain development (eg, tuberous sclerosis, neurofibromatosis, postnatal herpes).[3,4]

One of the most common causes of neurodevelopmental impairment is childhood lead poisoning. Pediatric lead poisoning has deleterious effects on the development of widespread brain areas including those implicated in cognitive, communication, and social functioning.[5] In several cases, a temporal association was noted between elevated blood lead levels and the emergence of autistic symptoms.[6,7] The present paper describes two children who, during periods of elevated blood lead levels, displayed the symptoms of autistic disorder. Several unique elements of these cases differentiate them from idiopathic autism and indicate that

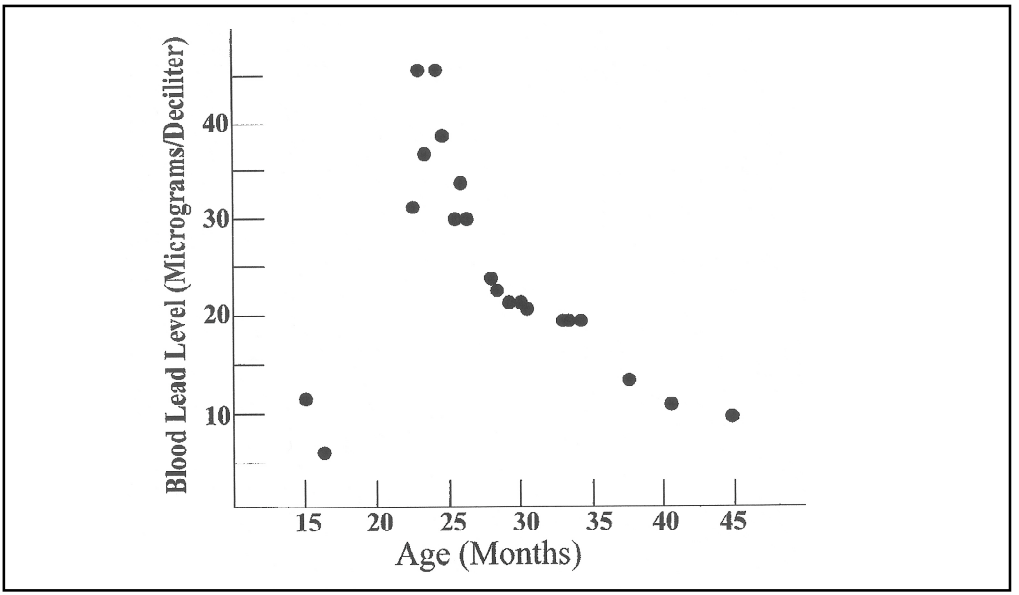

Figure 1. Blood lead levels of patient 1 as a function of age.

brain damage from plumbism can cause the symptoms of autism.

Case 1

Patient 1 is an Hispanic child raised in an English/Spanish bilingual household. He has two older brothers who were described as developmentally normal and doing well in school. When pregnant with him, his mother began prenatal care during the latter part of the first trimester. The patient was born full term via normal spontaneous vaginal delivery without complications; Apgars were 9 at 1 minute and at 5 minutes, reflexes and cry were described as good, and physical examination showed all systems to be normal. The nursing assessment noted adequate bonding between the mother and her child. The patient was admitted to the Neonatal Intensive Care Unit (NICU) due to poor feeding and sepsis. He was treated and discharged home to his parents. Subsequent medical records show that early developmental milestones in all areas were attained in an age appropriate fashion. For example, he sat unassisted at 8 months, stood at 9 months, walked at 10 months, and spoke single words at 12 months. He was noted to show normal interactive behavior at 9 months and to indicate his wants at 15 months.

The patient was found to have an elevated blood-lead level at about 15 months of age; elevated levels continued to be reported for at least 26 months. He underwent chelation treatment at about 24 months of age. The available records concerning his blood lead levels are summarized in Figure 1.

According to his mother, he had a vocabulary of about 10 words when 16 to 20 months of age, but lost the ability to speak around the time that lead poisoning was detected. She expressed her concerns about his communication problems, and also the emergence of temper tantrums, to his pediatrician, who subsequently referred the patient for assessment.

A speech and language evaluation,

when the patient was 27 months of age, described severe delays in both expressive and receptive oral communication. Reevaluation about 5 months later noted similar impairments and observed: "Deficits are found in both English and Spanish, which are not attributable to bilingualism." Educational evaluations at both 27 months and 34 months noted delays in all areas except gross motor functioning. Psychological evaluation also indicated expressive and receptive language delays as well as decreased attention span and increased motor activity and impulsivity. Pediatric evaluations documented a deterioration toward autistic disorder noting, when the patient was 3 years 5 months of age, Pervasive Developmental Disability (PDD) tendencies and, at 4 years 1 month of age, autism. However, several observations by his teacher during this period indicated behavioral characteristics that are unusual in autistic children. For example, he was described as "...a curious child with a short attention span for his age who can be very active at times. He makes more eye contact than in the past, his temper has improved, he is using some words... is affectionate and plays with others but does not like to be hugged or touched by anyone other than his mother." [The preceding is a quote from his teacher.]

The patient was first evaluated by the authors of this paper, aided by a Spanish/English translator, when he was about 4 years 5 months of age and, at that time, met *DSM-IV* criteria for autistic disorder (marked impairments in communication, social interactions, restricted interests, and activities).[2] He presented as a neatly dressed boy who appeared quite at ease with his surroundings. Although he was alert, it was not clear if he was oriented to time and place since, for the duration of the evaluation (.3 hours), the patient did not engage in comprehensible speech with either examiner or the translator. He only occasionally made eye contact with either the examiner or translator and it was not clear, based on his unchanging facial expression, whether he understood what was being said to him. He never engaged in conversation with either the examiner, the translator or his mother. His only speech consisted of echolalic repetition of whatever was said to him, whether in Spanish or English.

In contrast to his lack of responsiveness to speech, he was overly reactive to visual stimulation. While he never turned his head toward the person who was addressing him, he quickly turned to face and focus upon any movement in the testing room. For example, a slight movement of the window blinds due to air currents or a pencil that rolled when placed on the table instantly evoked an orienting response from the patient followed by an obvious and prolonged visual concentration on the eliciting stimulus.

Throughout the evaluation, the patient was unable or unwilling to remain seated for more than a few minutes. He repeatedly left his chair and would only remain seated if physically restrained. The patient appeared continuously cheerful and hummed a short tune that he incessantly repeated throughout the evaluation. He only deviated from his happy mien on one occasion when he was prevented from getting out of his chair during testing. At that time, he mercurially became tearful and, just as quickly, resumed his previous good mood when he was permitted to get up.

Although formal cognitive testing was initiated, the attempt was aborted due to both an inability to communicate with the child and also his behavior, including his inability or unwillingness to remain seated. Moreover during testing he would frequently avert his gaze from the test materials and focus on

some other area in the room; attempts to refocus him were futile.

The *Childhood Autism Rating Scale* (*CARS*) was used to evaluate his behavior. The *CARS* is a standard instrument that quantifies behavior with respect to relating to people, imitation, emotional response, body use, object use, adaptation to change, visual response, listening response, taste, smell, and touch response and use, fear or nervousness, verbal communication, nonverbal communication, activity level, level and consistency of intellectual response, and general impressions. The patient's overall score was in the range of severe autism.

The authors of this paper reevaluated the patient when he was 6 years 10 months of age. In the interim, he was enrolled in a special school for developmentally disabled children, though there was no program specifically designed for remediation of autistic symptoms. At this second assessment, he no longer met *DSM-IV* criteria for autistic disorder. [2]

His mother, brother, and his brother's friend accompanied the patient to the evaluation. He never engaged in conversation with either examiner and, as in the previous evaluation, his speech was echolalic. However, he was able to respond appropriately to simple commands.

During the entire evaluation the patient was not observed engaging in motor stereotypies or self-stimulatory behavior. In addition he was affectionate, not only with his mother, but also his brother and his brother's friend. In addition, during several of the rest breaks, when he was in the waiting area, he was seen happily engaging in reciprocal play behavior with his brother and his brother's friend. At one point, he clearly solicited a hug from his brother's friend and was visibly pleased when he received it.

Limited cognitive testing, compatible with the patient's communication deficiencies, was attempted. He was able to do the simplest designs (16th percentile) from the *Block Design* subtest from the *Wechsler Intelligence Scale for Children, Third Edition* (*WISC-III*). When asked to copy the design from the *Rey Complex Figure Test*, he did so, making an accurate reproduction that was scored at the 32nd percentile for children of his age. However, when subsequently asked to reproduce the figure from memory, the patient was either unable to do so or simply could not comprehend what was being asked of him. Unfortunately, his verbal communication impairments were so severe as to preclude accurate assessment of other aspects of his neuropsychological performance including verbal and visual memory as well as executive functioning.

The *Vineland Adaptive Behavior Scales* was administered to evaluate general functionality in communication, daily living skills and socialization. T. Lidsky, who was aided by an English/Spanish translator, interviewed the patient's mother. The patient was severely delayed in all domains (communication, daily living skills, socialization, low adaptive level; percentile rank < 0.1). However, the pattern of standard scores typical of autism, wherein the daily living score is significantly superior to both communication and socialization scores, was not observed in this child. The *CARS* was again used to evaluate his behavior. Unlike the previous rating, the patient's overall score was incompatible with a diagnosis of autism.

Case 2

Patient 2, a male, was born by normal spontaneous vaginal delivery following an uneventful full-term pregnancy. Apgar scores were 8 at 1 minute and 9 at 5 minutes. No delivery or postpartum problems were noted and he was judged

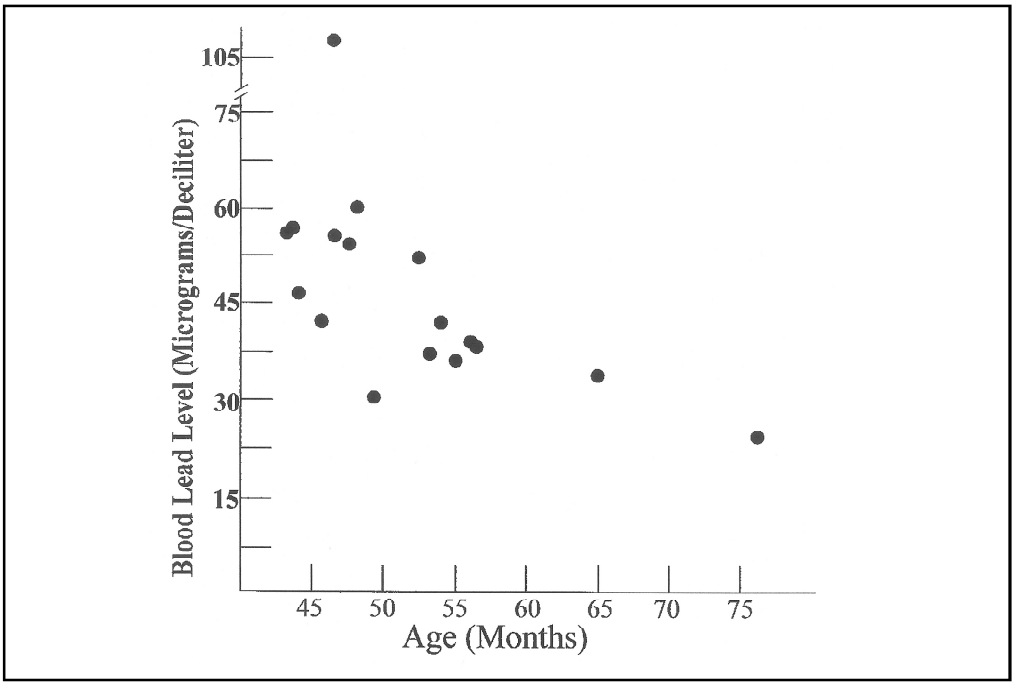

Figure 2. Blood lead levels of patient 2 as a function of age.

appropriate for gestational age. There was no maternal history of alcohol, drug or tobacco use during pregnancy. Prenatal vitamins and iron supplements were taken during the pregnancy, which was monitored with standard prenatal care. Physical growth and development were normal; early developmental milestones in all areas were met in an age appropriate fashion.

The patient's medical history is remarkable for severe lead poisoning that was first detected at approximately 3 years, 4 months of age and which lasted at least 5 years. Several months after poisoning was detected, his blood lead levels increased to 110 µg/dL prompting hospital admission for intravenous chelation therapy. He was discharged home with a blood lead level of 52 µg/dL and received outpatient chelation therapy. The patient's history of lead poisoning and blood lead levels are shown in Figure 2.

Clinic notes from his hospital admission indicated that his intake examination was "unremarkable". There were no descriptions of behavioral or neurological problems, although the child's mother expressed concern about his high level of activity. It was reported that there was a "paucity of speech" and a "decrease in following of commands" although it was thought that this might be attributable to sleepiness. At discharge the patient was described as "alert, playful" and as a "cute, well-developed, well-nourished boy". No mention was made of any concerns about the patient's cognitive status.

Problems concerning the patient's cognitive abilities or behavior were not described until he began kindergarten. A history taken at that time (age 5 years 11 months) reported that his development up that point was within normal limits. The school's student support team administered the *WISC-III* and the child

attained a verbal IQ of 79 (8th percentile), performance IQ of 79 (8th percentile) and full scale IQ of 77 (6th percentile), each in the borderline range. Difficulties were noted in the "areas of memory, processing information, and spatial reasoning". In addition, the patient was described as being "aware of his academic difficulties in the classroom and he displays feelings such as insecurity in terms of his academic skills." Notably, with respect to his future "autistic like behaviors" (see below), the patients "highest score was in the area of practical social judgment" and he was also noted to respond well to praise and positive reinforcement. The child was recommended for special educational services.

The patient's cognitive functioning progressively deteriorated over the next two years with most significant declines in speech and communication. A speech/language evaluation performed at the age of 7 years 9 months indicated that both receptive and expressive language skills were at a 2 to 2 1/2 year-old age level. The *Stanford-Binet Intelligence Scale, Fourth Edition* was administered and the patient's composite score (54, < 1st percentile) had decreased to the mentally retarded range. Areas of impairment were verbal reasoning (< 1st percentile), quantitative reasoning (2nd percentile), and short-term memory (< 1st percentile); abstract/visual reasoning was relatively preserved (19th percentile). In addition, the patient was unable to sustain attention. A psychoeducational review at this time indicated his teacher's concern about the child's "autistic like" behaviors viz: "He does not communicate or interact with peers and adults appropriately and efforts to communicate with him often produce blank stares. (The child)...also runs out of the room whenever possible, and he frequently "twirls in the hall." A subsequent report also noted that the child "...often stares blankly when others attempt to communicate with him", that he "...makes squealing noises, lays on the floor and cries, and runs away from adults. A teacher noted an incident in which [the child] vomited and exhibited no interest in removing the vomit from his hands and clothing." The *CARS* was used to evaluate the patient's behavior and his score was in the clinically significant range for mild to moderate autism. The child was placed in a small classroom with one-on-one instruction and modeling prompts that emphasized the use of language in functional settings.

A school-based evaluation several years later, when the child was about 12 years old, indicated some progress in language and social skills. For example, although he did not initiate conversations, he would have conversations if approached, would interact with his peers, and he no longer exhibited any maladaptive behaviors. In contrast, his cognitive impairments persisted, as did his attentional problems.

When the patient was about 13 years old, the authors of this paper evaluated him. At the time of this assessment he no longer met *DSM-IV*[2] criteria for autistic disorder. He presented as a neatly dressed, well-groomed, well-nourished boy who was quiet but cooperative during the testing session. He sat with his head facing down for most of the time, making eye contact only briefly and, when the contact was reciprocated, quickly averted his eyes. He showed no emotion and exhibited few spontaneous movements. No unusual behaviors or abnormal body use were observed. He showed an appropriate interest in and use of toys and other objects, such as a pencil. The patient always answered questions when asked, but typically replied with single words or a 2 to 3 word phrase. For example, when asked what he did during the summer, he responded "played". When asked if he

played sports, he responded "yes". When asked which sport, he responded "basketball". The child also clearly had an appreciation for his level of performance on at least some tasks. While performing the computer based *Wisconsin Card Sorting Test*, he quickly learned the rule needed to perform the task correctly. Once the rule was changed, he persisted in using the old rule and had difficulty in learning the new rule. After several wrong answers, he shrugged his shoulders and, gestured toward the computer and said, "something wrong with it".

The *WISC-III* was administered and the patient's verbal IQ (46, < 1st percentile), performance IQ (65, 1st percentile) and full scale IQ (53, < 1st percentile) were in the intellectually deficient range. Neuropsychological testing indicated impairments affecting expressive language, visual attention, visuospatial constructional ability and visuospatial memory, fine motor functioning, auditory working memory, verbal concept formation, planning ability and cognitive flexibility.

The patient's mother was interviewed by J. Schneider to complete the *Vineland Adaptive Behavior Scales*. The child was severely delayed in all domains (communication, daily living skills, socialization, low adaptive level; percentile rank < 0.1). However, the pattern of standard scores typical of autism, wherein the daily living score is significantly superior to both communication and socialization scores, was not observed in this child. The *CARS* was again used to evaluate his behavior and unlike the previous rating, the patient's overall score was incompatible with a diagnosis of autism.

DISCUSSION

This paper described the case histories of two children with severe lead poisoning that, for a period during development following poisoning, presented with the symptoms of autism. The first case met each of the diagnostic criteria for autistic disorder while the second case, due to the age at which symptoms emerged, would be identified as pervasive developmental disorder, NOS.[2] However, in addition to the late onset of symptoms in the second patient, both cases differed from idiopathic autism in another important respect; each child emerged from the autistic phase. Although there have been several cases reported in which autistic individuals were able to emerge from autism,[8] those patients had a high level of cognitive functioning and underwent specialized cognitive rehabilitation. In contrast, both of the children described in this report had very low levels of cognitive functioning and neither was exposed to specialized treatment.

Certain cases of autism have been reported to be caused by disorders that produce structural abnormalities in the brain or space occupying lesions as well as by brain infections. Herpes encephalopathy can produce all of the core symptoms of autism and, similar to the second patient, appear well after the age typically associated with the onset of idiopathic autism. Indeed, there are case reports of herpes-induced autism in previously healthy adolescents[9,10] and in an adult of 31 years[11]. Herpes-induced autism, like the lead poisoning-induced cases described in the present paper, is sometimes reversible.[4]

The two case histories presented here, as well as the reports of autistic symptoms in children with disorders that produce brain lesions or encephalopathy, indicate that there are multiple causes of autism. Further, the ability of brain infections and lead poisoning to produce such symptoms highlights the importance of environmental factors in the etiology of autism.

The ability of lead poisoning to

induce symptoms of autism is also relevant to cases of preexisting pervasive developmental disorders irrespective of etiology. Such individuals have a greater propensity to engage in pica and, as a result, are more likely to become lead poisoned.[12,13] In such cases, lead poisoning can be expected not only to negatively impact neurocognitive functioning,[5] but also to potentially exacerbate the preexisting symptoms of autism. Indeed, one case report describes a decrease in hyperactivity and stereotypies in an autistic child with a blood lead of 42 μg/dL once this level was reduced by chelation with succimer. [6]

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