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Childhood Disintegrative Disorder: A Century of Hellers's Syndrome

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Abstract

"Childhood disintegrative disorder" (CDD) now known, reported first as "dementia infantilis" by Theodore Heller in 1908, a century ago, and its research not kept pace with related disorders even though they reported late (autism first reported in 1943 and Rett's syndrome in 1966). Presently, we have few data on epidemiological findings, onset, course, clinical features, very few etiological findings, established validity, and mainly non-pharmacological management with pharmacotherapy targeted for only behavioural control. Future research should focus on etiology and treatment. It is an attempt to review comprehensive the available literatures of CDD, at the end of a century from its first report.

Keywords Childhood disintegrative disorder; Heller's syndrome; Evolution of concepts; Nosology

Introduction

Childhood Disintegrative Disorder (CDD) first described a century ago in 1908 by Theodore Heller as "dementia infantilis". Over the years, this condition described mostly as case reports in literatures and called with various names as 'Heller's syndrome', 'progressive disintegrative psychosis', 'disintegrative psychosis', 'pervasive disintegrative disorder', as "Other CDD" in ICD 10 and as "CDD" in DSM-IV [1]. However, the research of CDD not kept pace and reported long before than infantile autism extensively studied disorder in child psychiatry today and Rett's syndrome (reported first in 1966) [2,3]. Hence, it is worthwhile to review CDD at the end of century from its first report.

Methods

A thorough computerized search in Pubmed/MEDLINE performed up to September-2008 for all the articles in English using the following combinations and/or individual terms: Childhood disintegrative disorder, Heller syndrome, and dementia infantilis. Subsequently, bibliographies of articles selected via the first strategy searched. Full-text articles retrieved with the help of institutional online access. Cross-references of the outstanding articles provided an additional source of papers for the review.

Evolution of Concepts

Theodore Heller, a Viennese educator, first reported a severe developmental regression in six children of 3 to 4 years of age after apparently normal development with prominent mood changes, loss of speech, and complete regression with limited recovery [4]. Heller called it as 'dementia infantilis', as it resemble senile dementia.

Theodore Heller proposed a diagnostic guideline for 'dementia infantilis' [5]. These consists of onset between 3 to 4 years of age, progressive intellectual and behavioural deterioration with loss/marked impairment of speech at onset, associated with behavioural/affective symptoms (fear, over-activity) and possible hallucinations, and an absence of obvious signs of neurological dysfunction or apparent 'organicity' (e.g., normal facial appearance).

Rutter et al. coined a term 'disintegrative psychosis of childhood' for this condition and described as normal or near normal development for first few years of life, onset after 2 and a half years, and severe disintegration involving a severe disorder of emotions, behaviour, and relationships and often a loss of speech and other functions [6].

Corbett et al. suggested a minor change in name as 'progressive disintegrative psychosis of childhood' to differentiate from psychiatric illnesses due to non-progressive encephalopathy, since such children had the presence of organic brain disease [7].

Burd et al. termed this condition as 'pervasive disintegrative disorder' with diagnostic criteria-(a) a period of relatively normal development from birth to 30 months of age (b) rapid regression from relatively normal development that last for 1 to 3 years leading to the following impairments (i) gross and sustained impairment in reciprocal social interaction, (ii) almost total lack of verbal and non-verbal communication, and (iii) profound mental retardation with corresponding functioning in adaptive behaviour, (c) almost no measurable growth in cognitive, linguistic, social, or adaptive functioning from the period of regression (d) maintenance of the good fine and gross motor skills (e) the presence of compulsive and/or stereotypic behaviours, and (f) regression should not be due to storage disease, organomegaly, or a diagnosable neurological disease [8].

Comparative Nosology

ICD-9 for the first time in official classification included a category for 'disintegrative psychosis' or 'Heller's syndrome' in the category of 'psychosis with origin specific to childhood' (Code-299.1) [9]. ICD-9 stressed on 'normal or near normal development' in first year of life, followed by a loss of social skills and the loss of speech with a severe disturbances in emotion, behaviour and relationships.

DSM-III introduced a new category as 'childhood onset pervasive developmental disorder (COPDD)' to the children with an autistic-like condition developed after 30 months of age. DSM-III did not accord a

formal diagnostic status to CDD, since it thought to have an organic basis, and treated as a prototype of dementia. The distinction between COPDD and autism based only on age of onset; this concept not validated later and dropped in DSM-III-R [10]. CDD included in DSM-III-R under the category of 'autistic disorder-onset in childhood', which is equivalent to 'disintegrative psychosis' of ICD-9.

There was an agreement on certain key features of CDD, despite highly divergent diagnostic approaches in ICD-9, DSM-III, and DSM-IIIR. Those are, the onset after the age of 2 years of normal development, and absence of organic or neurological illness. The concept of the 'psychosis of childhood' replaced during this stage by the 'concept of disintegration of mental functions' (similar to senile dementia), and earlier concept of an 'acquired condition' due to some neurological disorders replaced with concept of 'developmental origin' [3].

CDD in ICD-10 and DSM-IV

The term 'CDD' formally introduced in both ICD-10 as well as in DSM-IV and efforts made to bring these two systems in greater convergence [11,12].

Diagnostic criteria of CDD in ICD-10 are similar to Heller and Zappert [11,13,14]. These includes a distinctive pattern of the syndrome onset (a period of several years of normal development before marked deterioration), the progressive deterioration (either gradual or abrupt), once the syndrome had its onset, with loss of skills in multiple areas, behavioural and affective symptoms, and an absence of gross neurological dysfunctions. ICD-10 termed this as 'other CDD', the term 'other' to differentiate it from Rett's syndrome, since regression is present in both conditions and added the term 'symbiotic psychosis' [15,16].

Inclusion of CDD in DSM-IV influenced by results of DSM-IV field trial for autism and related condition [12,17,18]. The criteria of CDD in DSM-IV TR are similar to DSM-IV [12,19].

Why is CDD Placed in PDD?

CDD is placed under the broad rubric of PDD in both ICD-10 and DSM-IV, despite the debate over term PDD itself. Term PDD coined in DSM III to a groups of disorders in which autism is present. There are two reasons to choose term PDD [20]. First, PDD share some general similarities with autism. Second, the term PDD meant to emphasize that development was disturbed over a range of different domains in autism and the related conditions.

The term 'pervasive' in PDD meant to imply the scope of disturbance, in contrast to specific developmental disorders and 'primary' mental retardation. According to Happe and Frith, the term 'pervasive' is misleading and aroused more controversy since there is some autistic individual whose test scores in normal range and no appropriate alternative test developed yet [21]. Researchers questioned the use of term 'developmental' since at least two years of normal development before the onset of illness should be present [8,22]. Volkmar et al. suggested to categorize as 'atypical autism' whenever any difficulty in timing of onset of regression [23].

Epidemiology

Prevalence rates

There is very few community-based epidemiological survey and few clinic based prevalence rate of CDD available in published literatures. Five epidemiological survey of the CDD published till now and included in Table 1.

Investigator	Country (region/state)	Target population	Age group (years)	Assessment criteria	Prevalence rate (per 100,000)	95% CI (per 100,000)[a]
Burd et al. [24]	USA (North Dakota)	1,80,986	Feb-18	DSM-III	1.11	0.13; 3.4
Spoheim and Skjeldal [25]	Norway (Akershus county)	65,6 88	Mar-14	ICD-10 criteria	1.52	0.04; 8.5
Magnusson and Saemundsen [26]	Iceland (Whole island)	85,556	May-14	Mostly ICD-10	2.34	0.3; 8.4
Chakrabarti and Fombonne [27]	UK (Staffordshire, Midlands)	15,500	2.5-6.5	ICD-10 / DSM-IV	6.4	0.16; 35.9
Chakrabarti and Fombonne [28]	UK (Staffordshire, Midlands)	10,903	2.5-6.5	ICD-10 / DSM-IV	9.2	0-58.6
Fombonne [29]	Pooled estimates	3,58,633			1.9	0.87; 4.15

Table 1: Prevalence rates of CDD in various epidemiological studies. [[a] 95% CI derive from exact binomial calculations. Source: Fombonne]

The five surveys of CDD yielded the estimates ranges from 1.1 to 9.2 per 100,000 subjects [29]. The result of pooled estimate by Fombonne's across these five surveys is 1.9 per 100,000 [95 % Confidence Interval (CI): 0.87; 4.15 per 100,000] [29]. The upper limits of associated CI (4.15/lakh) indicate that CDD is a rare condition with one case occurs for every 65 cases of autistic disorders [29]. The upward trends in prevalence rates observed in recent decades may be because of the difference in the case definition and improved awareness. However, available epidemiological surveys do not provide an adequate test of hypothesis of change in prevalence of PDDs [28,30].

Clinic based prevalence rate of CDD with all cases of child psychiatric clinic over a period of 5 years is 0.22% and in 10 years period in the same centre was 0.45% [22,31]. This higher prevalence shows the actual number of cases could be higher in India considering its higher population. Other clinic based prevalence of CDD with broader diagnosis of childhood psychosis, autistic disorders, and so forth, ranges from 1.64% to 6% [17,32].

Sex ratio

The equal or lower male-female ratio observed in earlier studies [33]. However, in recent studies noted male preponderance similar to autism [34]. The male: female ratio is 3:1 (before 1977) and 5.5:1 thereafter [35,36]. One reason for lower or equal sex ratio in earlier studies is that the CDD might misdiagnosed with Rett's disorder, which described much later in 1966 [37]. In recent studies, males outnumber females by 4:1 [23]. Malhotra and Gupta [22] report clinic based male: female ratio of 5:1 in India.

Clinical Features

Age of onset (AOO)

AOO, a key defining feature of CDD, linked with evolution of its concepts. 'Development' prior to regression (especially for loss of previously acquired skills) is relatively prolonged (several years) and reasonably normal for e.g. child has the capacity to speak in sentences by the age 2 years [38]. The minimum age at onset described as 2 ½ years and 2 years in both ICD-9 and ICD-10 [6,11]. In a review of 106 cases, Volkmar et al. found the mean AOO is 3.6 years similar with Heller's original description [13,23]. In contrary, the age range in various literatures also varied from 1.2 years to 9 years [7,39,40]. Malhotra and Gupta reported the AOO in the range of 2 ½ - 7 years (mean AOO-3.7 years) in Indian population [22].

Difficulty in AOO of CDD

AOO of CDD in Heller's original description is 3 to 4 years that supported further by reviews [23]. Both ICD-10 and DSM-IV, CDD require a normal development up to 2 years of age and for typical autism, symptoms should arise before three years of age [20]. When autistic symptoms occur after two years of age but before three years, it may misdiagnose as CDD, as onset of typical autism between 2 to 3 years of age is quite uncommon. This problem compounded when CDD has onset before 2 years [18,22,39]. This confusion is detrimental in research of CDD. ICD-10 and DSM-IV allows diagnosing typical autism up to 3 years, even though, Kanner's original concept of AOO of typical autism was before two years [2]. Hence, researchers echoes AOO of CDD should be at least 3 years of normal development [20,22,41].

Characteristics of onset

Authors observed different patterns of onset in CDD. An abrupt onset (days to weeks) seen in some cases, whereas a more gradual (weeks to months) observed in others. There may be a premonitory phase of nonspecific agitation, anxiousness, or dysphoric symptoms preceding severe regression. Malhotra and Gupta reported the acute/sub-acute onset (days to weeks) in 66.6% of cases of CDD, in contrast, with insidious onset (weeks to months) of other studies [22,23,35].

Precipitating event

Precipitating event (psychosocial stress/medical illness) prior to onset of regression frequently and consistently noted in CDD [22,39,42]. Association of medical/psychosocial events with onset of CDD may be a chance factors, but needs careful examination [22,43]. Types of stressors reported is diverse, but all share the feature of being relatively common to pre-school children, e.g. birth of a sibling or death of a grandparent, hospitalization for elective surgery, or immunizations, it may be due to older age of onset of CDD experiences more events. Case studies observed that the presence of psychosocial events is common than medical events, but contrary in Indian study - 50% of cases has medical event [fever (16.5%), seizure (16.5%), vaccination (8.25%), acute gastroenteritis (8.25%)] and psychosocial event present only in 8.25% (scolding) [22,32,35,39]. Significance of stressful events in pathogenesis of CDD is unclear. One possible hypothesis could be that the medical events acted as a form of stress that triggered the illness; the most common event was seizures, which led to maximum degree of insult in the shortest time-period [31,44]. Stress, whether psychosocial or biological, can lead to impairment in functioning of the pre-frontal cortex manifest as hyperactivity, disorganized, impulsive behaviour and even cognitive deficits [44]. Contrary to previous studies, seizures observed at onset in 33% of cases rather than during the course of illness [22]. Attributing some etiological significance to an associated medical/psychosocial event is common in children with autism who regress as compared to those who do not [45].

Behavioral clinical features

Once diagnosed, CDD resembles autism in its phenomenological manifestations. Typically, social skills are markedly impaired but degree of impairment may slightly less than autism [2,36,46]. Parents usually report the loss of social interaction skills is dramatic, great concern to them, and typical striking picture of development of total mutism/marked deterioration in verbal language in a child begun to speak full sentences. It does not typically return to previous levels of communicative ability, even in individuals who subsequently regain speech.

Unusual behaviours including stereotyped behaviours, problems with transitions, and non-specific over-activity typically observed [31]. Various affective responses often observed inexplicable at the time of onset and a general loss of interest in the environment present in 25% of cases [22]. Deterioration in self-help skills, notably in toileting skills, is striking, in contrast to autism where such skills often acquired somewhat late but are not typically lost [35,36].

Studies consistent reported a differential pattern of regression - regression of acquired skills is not uniform in all the spheres, i.e., regression in motor skills is least affected in comparison with other areas [3,31,32]. Reasons for such pattern is not been commented in the literature. It is known that language and bowel/bladder skills have cortical control (via autonomic pathways), while motor skills are coordinated complex efforts arising out of inputs from the cerebral cortex, cerebellum, and basal ganglia. Hence, it could be possible that children with CDD experience patchy cortical insult rather than generalized insult of brain. This hypothesis of CD is speculative only, as there is no information of biological correlates of CDD and that requires further study (Table 2) [1].

Cases			
Years	1908-1975	1977-1995	1996-2004
Variables	N=48	N=58	N=67
	Male / Female		
Sex ratio	35/12	49/9	53/14
Age at onset (years)	**Mean SD**		

	3.42 1.12	3.32 1.42	3.21 0.97
	Mean SD		
Age at follow-up	8.67 4.14	10.88 5.98	10.25 4.81
Symptoms	**% of N cases**		
Speech deterioration/loss	100 (47)	100 (58)	100 (54)
Social disturbance	100 (43)	98 (57)	100 (54)
Stereotypy/resistance to change	100 (38)	85 (54)	68 (54)
Over-activity	100 (42)	77 (37)	59 (54)
Affective symptoms/anxiety	100 (17)	78 (38)	55 (54)
Deterioration/ self-help skills	94 (33)	82 (49)	66 (54)

Table 2: Characteristics of CDD cases over a century.

Atypical presentations of CDD

Agarwal et al. reported many atypical features in their case report such as abrupt onset after 9 years of normal development presented as acute psychosis initially along with hallucinatory behaviour [40]. This is first hallucinatory behaviours reported in available literatures after Heller [13].

Etiology

Following paragraphs described briefly on evidences on etiology of CDD currently exist in literatures, despite initial Heller's impression of absence of organicity.

Seizure and Electroencephalography (EEG)

Although data are few, the rates of seizure disorder and EEG abnormality appear to be similar to those observed in autism and suggest EEG should routinely indicated in clinical assessment [1,43,47]. EEG data in recent reports of 45 cases shows abnormalities [18,31,48]. Onset of seizures correlated temporally with onset of developmental deterioration [31]. Shinnar et al. reported relatively high rates of seizures in a large cohort of children with language regression in autism spectrum disorder, despite regression with autistic spectrum disorder reported equally in individuals with/without seizures [49,50].

Neurochemistry

One study reported changes in cerebrospinal fluid beta-endorphin [51]. Recent study suggests a previously unrecognized interaction between the immune system and Brain Derived Neurotrophic Factors [52].

These neurotrophins, neuropeptides or autoantibodies may contribute to the pathogenesis of CDD or may be serological markers for children may go to develop CDD. Even though, these findings are not specific to CDD, their presence prior to clinical diagnosis may permit the early diagnosis and earlier treatment intervention but further replication is required.

Genetics of CDD

Overall, there is limited information on genetics of CDD in only few epidemiological studies and case reports and lack of direct evidence from population genetic or molecular studies [1].

Case report of a boy by Mouridsen et al. found an inversion of chromosome 10 (46xy, inv (10) (p11, 21q21.2) and anomaly found in boy's mother who was a successful professional [48]. Zwaigenbaum et al. [53] reported on two half-brothers one with autism and the other with CDD.

Volkmar et al. described the possibilities of various known genetic mechanisms in CDD such as sporadic mutation of chromosome, mutations of single molecules in the DNA chain like encoding Methyl-CpG-Binding Protein 2 (MECP2) gene of Rett's syndrome and unlikely to have mendelian inheritance [1,22,50,53,54].

In the absence of compelling evidence, CDD is hypothesized as a complex disorder resulting from either a chance accumulation of a number of rare genetic events, from some unknown environmental precipitant that alone or in combination with a genetic predisposition results in the apparently sporadic emergence of the syndrome, or from a novel genetic mechanism" [1]. Those interested in genetics of CDD referred to Volkmar et al. [1].

General medical conditions and CDD

General medical conditions such as tuberous sclerosis, neurolipidoses, metachromatic leukodystrophy, Addison-Schilder's disease, and subacute sclerosing panencephalitis along with hundreds of other possible causes including metabolic, infectious, genetic, immunopathic, environmental, and epileptogenic causes associated with CDD [15,55]. It is possible to identify a specific general medical condition accounts for child's deterioration, in that case, the diagnosis of CDD to made, and presence of associated medical condition to be noted [35,56].

There is no data on neuropsychology of CDD. There are no striking differences in brain morphology/structures observed in computed tomography scan of head [8,32,48].

Course and Prognosis

Detailed data on course and outcome of CDD is available from 1977 onwards [35]. Follow-up period varied from 1.2 years to 32 years [15,35]. Developmental regression leading to severe to profound mental retardation (MR) seen in more than 75% of all cases [23]. Nearly 75% cases, course is static after deterioration to much lower level of functioning [39]. On the one hand, no further deterioration occurred, but there will be limited improvement, e.g. a child regains the capacity to speak although usually only in a limited way [1,32]. In a small number of cases, the developmental deterioration is progressive and does not plateau, especially in presence of some identifiable organicity [7,15]. If the process is progressive, death may be the eventual result and there may be increased mortality if other medical conditions are present [3,57]. Two children were severely impaired, had seizure disorder, were non-verbal, and in residential treatment in follow-up data of 14 years [58]. Death at the ages of 9 years with subacute sclerosing pan encephalitis (SSPE) and at age of 31 years with tuberous sclerosis reported [15]. One adolescent case apparently died following a seizure [1].

Life expectancy appears normal in some cases with significant degree of improvement [23]. Those who live longer tend to be more mute and in residential placement in comparison with infantile autism [18].

Mouridsen et al. compared CDD with infantile autism on numerous outcome variables and reported of lower functioning, aloofness, and greater co-morbid epilepsy in CDD suggestive of poorer course with death rate of 15% in CDD in comparison with 3% in autism [15].

Validity of CDD as a Diagnostic Category

The validity of CDD as a separate diagnostic category has been issue of considerable debate and that depends on whether they have distinctive clinical presentation or course [59].

CDD and Autism

Kanner original thought that autism is congenital but in some cases, parents reported some period of normal development before symptoms of autism are developed and referred as 'late onset autism' or 'setback autism' in Japanese literatures sometimes [2,41,60-63].

By definition, CDD requires a period of at least two years of normal development despite some studies reported an earlier age of onset [17]. The studies of internal and external validities of CDD in Tables 3 and 4 demonstrate that CDD warrants a separate diagnosis.

Variables	Findings	Studies
Epilepsy	No difference in the incidence of epilepsy	Volkmar and Cohen [32]; Malhotra and Gupta [22]
	Significantly higher in cases of CDD	Mouridsen et al. [15]
Genetic factors	No evidence of a genetic factor	Volkmar and Cohen [32]; Malhotra and Gupta [22]; Kurita et al. [63]
Computed Tomography	No abnormality	Volkmar and Cohen [32]; Burd et al. [58]; Kurita et al. [64]
Development outcome	Poorer outcome	Volkmar and Cohen [32]; Malhotra and Gupta [22]
	No differences at least in short-term outcome	Mouridsen et al. [15]; Kurita et al. [64]

Table 3: Studies on the internal validity of CDD.

Studies	Findings
Malhotra and Gupta [22]	These studies demonstrated the internal validity of CDD on its core features i.e., a period of normal development followed by marked regression.
Volkmar and Cohen, [32]	
Volkmar and Rutter [18]	
Volkmar and Rutter [18]	More 'autistic' symptoms than autism
Malhotra and Gupta [22]	No difference in core autistic symptoms but CDD cases had less repetitive/restrictive play in comparison to autism
Kurita et al. [64]	Stereotypy was more common in CDD and resistance to change was less common in comparison to autism

Table 4: Studies on the external validity of CDD in comparison with autism.

CDD found to be a valid diagnosis at least in its internal validity. Volkmar and Rutter [18], in their review of CDD for DSM-IV field trial, observed that the major differences present in the dramatic clinical presentation and course.

They also feel that a separate diagnostic entity of CDD would increase its research potential to clarify basic mechanisms of pathogenesis; however, Hendry questioned the utility of CDD as a diagnostic concept since CDD resembles autism in course, outcome, and overlap of symptoms in both once established [64,65].

She raises questions a limited research data available in comparison with autism and reliance on parental data to draw conclusions.

CDD and Rett's syndrome

Rett's syndrome is a progressive condition develops after some months of apparently normal development and may resemble CDD. Characteristic feature of Rett's syndrome are normal head size at birth, head growth begins to decelerate between six months to one-year of age, losing purposeful hand movements and development of characteristic hand wringing, and hand-washing stereotypies. Expressive and receptive language skills become severely impaired and associated with marked mental retardation. The presence of some symptoms suggestive of autism is the major rationale for placement of Rett's syndrome in the PDD in both ICD-10 and DSM-IV.

Both CDD and Rett's disorder are regression conditions differ from typical autism [66]. Rett's disorder is most prominent during pre-school years especially when autism-like symptoms develop. Rett's syndrome earlier thought to occur only in girls, but now described in boys [67]. Genetic advances in understanding of Rett's syndrome have some similarities with CDD, but preliminary screening of MECP2 gene not shown success so far [68].

CDD and childhood schizophrenia

Category of Childhood schizophrenia is only available condition to describe autism and related disorders in first (1952) and second (1968) editions of the American Psychiatric Association's Diagnostic and Statistical Manual. Kolvin and Rutter noticed the bimodality of onset of these two conditions and pioneered in separating the autistic spectrum disorders from schizophrenia [41,69]. Still there may be confusion between autism and very early onset schizophrenia, where the degree of regression and deterioration suggests CDD, and characteristic finding of schizophrenia may reduce confusion [70].

CDD and organic brain pathology

The association of neurological disorders with CDD appears as exception rather than the rule. Epileptic conditions can mimic autism or CDD [31,71]. One area of controversy has been with respect Landau-Kleffner syndrome. The presence of a neurological disorder is usually associated with a more abrupt onset, rapid progression and later onset [23]. Both the ICD-10 and DSM-IV classificatory systems allow any diagnosable neurological condition to be separately coded, however, CDD should be diagnosed on basis of behavioural features, irrespective of the presence or absence of any associated medical condition.

A question also arise whether to separate CDD into primary and secondary subtypes? The line of management different in two subtypes especially when the cause of secondary to a treatable condition such as seizure, then the prognosis could be far better.

Assessment

A careful, proper and thorough history has no substitute in the assessment of CDD, as the information on the pattern and age of onset of the condition is central [3]. Examination of videotapes of birthdays or family functions will reliably document the child's early development [1,72]. Examination/observation of child in clinic is crucial, preferably in more and less structured activities such as during developmental assessment or while interacting with the parents. Observation of child's play is also helpful to document the levels of language, cognitive and social organizations, and to observe the gross and fine motor skills [1]. Assessment of family/parents is essential to understand the degree of engagement, knowledge of illness and family burden to ensure the compliance to treatment [31].

Psychological assessment of child is required that includes the current levels of functioning and to document the subsequent developmental change to helps for educational and rehabilitative programming of parents. The use of developmental and other tests typically given to younger children may be appropriate [73]. Modifications and flexibility in usual assessment procedures may consider according to the need of the patients. Leiter International Performance Scale may helpful in higher functioning and non-verbal children [74]. To assess the communication skills, the Receptive-Expressive Emergent Language Scale; the Sequenced Inventory of Communicative Development; and the Reynell Developmental Language Scales are appropriate [75-77]. Checklist for Autism in Toddlers a screening instrument for autism spectrum disorders may be helpful in reducing chance of misdiagnosing autism as CDD [78]. Pervasive Developmental Disorder Behaviour Inventory (PDDBI) is an informant based rating scale designed to assess responsiveness to intervention of both adaptive and maladaptive behaviour [79]. Vineland Adaptive Behaviour Scales should administer to document levels of adaptive behaviours [80]. This instrument provides useful information both for diagnostic and programming purposes [1].

IQ profile of CDD shows the severe to profound degree of MR, whereas autistic children usually have moderate range of mental retardation [18,22,31,32].

In a case of CDD, medical investigations not routinely indicated and that may not reveal any specific medical conditions or specific neuro-degenerative disorder [1,31]. Investigations like EEG, CT / MRI imaging may be indicated when (a) case is unusual; e.g. in late onset (after the age of 6 years) (b) if deterioration is progressive and does not plateau [1]. Other possible investigations may consider based on clinical condition of child for e.g. phenylalanine assay for phenylketonuria, and thyroid function test in hypothyroidism.

Management

Multidisciplinary approach is most effective way in management of CDD and in similar line with typical autism [1]. There is no specific pharmacological treatment in CDD [1]. Pharmacological treatment offered with various psychotropics with/without hospitalization with target of behaviour control rather than control of underlying process and it is mainly because of expectation of parents for pharmacotherapy. This could also explain high rates of pharmacotherapy offered to retain follow up of patient [22]. Atypical anti-psychotics like risperidone (in prospective open label study) and Olanzapine have shown effectiveness [81,82]. Masi et al. conclude that low-dose Risperidone might positively affect the clinical outcome in young children with PDD not only in the short-term, but also in the long-term period [81]. Double blind, placebo controlled trial of psychotropics is required for further evaluation of its efficacy. Recently, prednisolone (2 mg/kg/day) is found to be effective in two case report presented with seizure with sustained improvement in their motor, behaviour, language and motor regression at 30 months and 48 months follow-up [83].

Trials of benzodiazepines, antidepressants and lithium shown disappointing results [39,58]. Clozapine shown some effectiveness in three children of CDD but leucopenia observed in one case [84]. Anti-epileptic drugs are the main stay of treatment of seizures associated with CDD and carbamazepine is the commonly used anti-epileptic drug [3].

Psychosocial managements in CDD are similar with typical autism. Behaviour modification should be generalizable, consistent, and focus on replacing the maladaptive to adaptive skills. The special education to child may be considered. The behavioural therapy successfully used in autism via training parents and adults to provide structure and reinforce behaviours (i.e., parents training) [85]. Functional behavioural analysis should done with ABC-f approach (A- for antecedents or triggers, B- behaviours of targets, C- consequences, or responses of caregivers, f- frequencies of target behaviours) to each maladaptive behaviour and assess the motive behind the maladaptive behaviours. Parents should be educated about the differential reinforcement schedules. Here, PDDBI may be helpful in monitoring intervention [78]. Behavioural therapy should be focused on (a) development of a regular routine with as few changes possible, (b) structured class room training, aiming at learning new material and maintenance of acquired learning, (c) positive reinforcements to teach self-care skills, (d) speech therapy and/ or sign language teaching and (e) behavioural techniques to encourage interpersonal interactions. Psychotherapy, per se, is not effective in treatment of CDD, but

parental counselling and supportive psychotherapy are useful in reducing the parental anxiety and guilt, and ensuring their active involvement in therapy.

It is essential to inform the families to make use of local, other resources, to get mutual support and government benefits of respective countries [1]. Indian parents should get information about railway travel concessions, and benefits of national trust act in 1999 and 2000 and Persons with Disabilities Act in 1995 and income tax deduction for maintaining handicapped child [86].

Future Directions

The future research of CDD may focus on comprehensive evaluation of the cases based on a structured clinical tool via videotapes and detailed neurological assessment, identification of cause by using modern neuroimaging as well as molecular genetic techniques, and on the development of specific treatment modalities.

Conclusion

Although CDD first described in 1908 (much earlier than autism in 1943 and Rett's syndrome in 1966) a century ago, this condition not frequently reported in the literature in comparison with autism and Rett's syndrome and still not fully understood. It is now clear that once CDD is established; it is behaviourally similar to autism. However, the difference in onset, course and some clinical features and the precise etiological mechanism not yet understood. In future, the discovery of biological correlates, causes, and pathogenic pathways will no doubt change the ways in which CDD diagnosed and may well lead to new oncological approaches that, in turn, will facilitate further scientific progress. Etiological issue and treatment issue mainly pharmacotherapy trial need to be the focus of research for CDD in years to come.

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