

Clinical picture and duration of prodromal period of schizophrenia in adolescents

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The aim of the study was retrospective estimation of clinical picture and duration of prodromal period in 150 adolescents with the first episode of schizophrenia

Key words: adolescents , schizophrenia, prodromal period

Introduction

The stages of schizophrenia symptomatic progress are highly variable in each individual case. A prodromal period may be markedly expressed and it may last for a long time, with slow, insidious symptomatic progress without evident changes in behavior and emotions that might be recognized by relatives. Schizophrenia onset may also be rapid with entirely developed psychotic symptoms within several hours or days.

Many investigators think that the onset of schizophrenia is in majority of patients preceded by the prodromal period (that may extend for several days, or even, years), which is characterized with: 1) psychopathologic symptoms, as: disordered stimulus selection, disturbance of speech production as well as its understanding, attention disturbance, thought blocking, fear, anxiety, hostility, aggressive behavior, disturbed motor coordination and lack of spontaneous activity, loss of interests, passive behavior, withdrawal from social life, diminished ability to play social roles, neglecting order and personal hygiene, flattened or inappropriate affect, unclear, digressive speech, with overdeveloped structure or dependent on circumstances, poor structure or essence of statements, odd beliefs, not characteristic for the social group a patient belongs to, or magic thinking, thought supremacy value, evaluations with extraordinary perception (recurring illusions, „telepathy”, recurring *deja vu* symptoms, feeling the presence of an absent person), disabled initiative, decreased activity, interests, loss of energy, decreased ability of appropriate understanding of social situations, particularly those requiring abstract reasoning, 2) psychopathological syndromes, such as depressive,

anxio-depressive, obsessive-compulsive, hypochondriac, dysmorphophobic, anorexia nervosa, with mixed characteristics, 3) altered, unusual behavior, non characteristic before of a given person, often odd behavior (for instance, antisocial, of paragnomen type, social withdrawal, isolation, talking with oneself, collecting things) [4, 5, 11, 13, 16, 17].

According to some authors, the prodromal period may include combined picture - with temporal dynamics - of the symptoms mentioned above, but symptoms characteristic for subsequently developed schizophrenia are always present as primary symptoms, such as disorders of perception and thinking described above. Other symptoms and psychopathologic syndromes or sometimes difficult to classify behavioral disorders are secondary reaction to the primary symptoms [2, 13, 14, 20].

It is difficult to describe a definite drawing line between the prodromal period and the occurrence of schizophrenia symptoms, especially if one considers, as already mentioned, the ambiguous nature of the term "prodromal" symptoms. The similar problem relates to the differentiation of the beginning of prodromal period from the previous period that, despite what many investigators think, can also be quite abundant in symptoms in some patients with later schizophrenia diagnosis. It seems that this phenomenon is particularly specific for patients with early schizophrenia onset (during childhood and adolescence) and predominant negative symptoms [7, 9, 10]. As revealed in some studies, the differences in psychomotor development, personality profiles, adaptation skills and social functioning between this group of patients and their healthy peers appears very early [12]. However, it is not clear whether the described symptoms and types of behavior prove only a predisposition to schizophrenic disorders or whether they constitute a nonspecific, long lasting prodromal period. Perhaps, it may be necessary to consider some types of schizophrenia (neurodevelopmental?) as a process including non psychotic, intermittent and psychotic periods. The period we termed „intermittent”, would be equivalent to the prodromal period and would be characterized by the presence of both the earlier symptoms with enhanced intensity and single symptoms associated with schizophrenia (as specific disorders of thinking, perception, attention, memory) as well as symptoms and syndromes secondary to their occurrence [3, 19].

Because there is no single, generally approved definition of prodromal period, there is also no consensus indicating the symptoms that may still be attributed to the prodromal period and which symptoms apparently prove the onset of schizophrenic process. Literature reports on clinical picture of prodromal syndromes and their duration provide variable data. The situation resembles difficulties with the identification of early symptoms of probable psychotic symptoms relapse in the course of schizophrenia. There is evidence, supported in literature, that some of these relapse indicating symptoms may correspond to those of the prodromal period, for instance, fear, irritation, decreased mood, social withdrawal, decreased activity, disordered cognitive function, suspiciousness, referential attitude, delusional attitude, as indicated in the majority of studies [18].

It seems that determination of prodromal period clinical pictures may be easier and more precise in case of adolescent patients. More credible data may be obtained with fewer difficulties if compared with those obtained from children and more detailed

data are usually supported by their parents or family members than those in case of adults with first psychotic episode.

Considering the costs and methodological problems, there are still few prospective studies on persons with the so called increased risk of schizophrenia (for instance children of schizophrenic patients); the majority of existing studies applied retrospective investigation methodology with various study schemes for data acquisition, what makes any comparisons difficult.

The aim of the study

The aim of the study was the retrospective evaluation (based on medical record data) of clinical picture and duration of prodromal period in adolescents with the first episode of schizophrenia. Further, we intended to establish the time period between the onset of psychotic symptoms and the beginning of antipsychotic therapy.

The study was based on medical records prepared by physicians and it should be assumed that some of them were not complete or contained mistakes associated with incorrect interpretation. It should be emphasized that we also aimed to determine, based on previous experience, the proper way of structured questionnaire preparation that would allow to acquire complete and objective information from patients, parents or family members.

For the purposes of this study the following, own definition of prodromal period had been adopted: it is recognized by patient and/or the family or family members behavioral changes, psychopathological symptoms or syndromes, or all described symptoms or their combined form, occurring prior to psychotic symptoms in such a number, intensity or configuration that allows for schizophrenia diagnosis according to DSM-IV or ICD-10 criteria [6, 15].

Material

Medical records of 150 patients aged 15-19 (mean age 16.7 ± 0.3) - boys and girls - with the first schizophrenia episode, hospitalised in 1984-1996, at the adolescent ward of 2nd Psychiatric Clinic of Medical University in Łódź or treated in ambulatory Therapeutical and Consulting Department at Psychiatric Clinics, were analyzed.

Methods

Data available in medical records (interviews with patient, family, family members, and sometimes with home-room and other teachers, relatives) on symptoms preceding the fully developed clinical picture of schizophrenia, were analysed. In some cases (21 persons) additional information obtained from medical records prepared in other medical centers before the psychotic symptoms onset, were also analysed. If an identified symptomatic complex had been equivalent to psychopathological syndrome, it was then qualified according to DSM-IV and ICD-10 standards [8, 15]. The data were analyzed statistically. Student t-test was applied for comparison of difference significance.

Results

Clinical symptoms of prodromal period in adolescents with the first episode of schizophrenia.

Table 1

Clinical picture of prodromal period prior to the onset of schizophrenia

Clinical picture of prodrom	Adolescents with schizophrenia						Statistical significance
	All N=150		Boys N=72		Girls N=78		
	N	%	N	%	N	%	
None (rapid onset)	33	22.0	14	9.3	19	12.6	n.s.
Symptoms of „negative” type	74	49.3	39	26.0	35	23.3	n.s.
Depressive or mixed	25	16.7	10	6.3	15	10.0	n.s.
Obsessive-compulsive disorder	11	7.3	6	4.0	5	3.2	n.s.
Anorexia nervosa	4	2.7	1	0.7	3	2.0	*p<0.005
Conduct disorder	3	2.0	2	1.4	1	0.7	*p<0.005

The retrospective analysis revealed that the schizophrenic disorder appeared rapidly (within several hours or days) in approximately 1/4 of studied persons (22.0%) and usually it was not possible to identify any evident symptoms or behavioral changes proceeding the onset of psychotic symptoms. In individual cases, patients or their family reported short term sleep disturbances, the feeling of being lost, psychomotor agitation. In most cases this data were provided by the patients, however, patient families, did not usually notice any remarkable changes in behavior or disabled functioning. The period, in some patients directly preceding distinct, prodromal symptoms lasting for several days, was essentially asymptomatic.

Nearly a half of the studied patients (49.2%) demonstrated slow progression of symptoms resembling „the negative” schizophrenia symptoms: disturbances of attention, memory, verbalization difficulties, problems with understanding words, „overflow of thoughts”, thought blocking, poverty of speech and thoughts, decreased activity and lack of interests, different degrees of social withdrawal (including complete isolation), diminished or flattened affection, desensitization, anhedonia, apathy, the loss of expressive abilities, diminished or lack of care for own appearance [1]. The patients, in majority (5/6 of the subgroup), since their early childhood differed from peers and schizophrenic patients with prodromal period of different clinical demonstration. The abnormalities in prenatal, neonatal and perinatal periods were significantly more common in these patients, than compared with healthy persons. Their psychomotor development varied from both the normal course in healthy persons and schizophrenic patients with predominant positive symptoms. The differences usually related to at least several discrete developmental malfunctions and did not have the character of evident pathologic characteristics. They were associated with delayed abilities of walking and constrictor muscle control, delayed speech development, speech disorders, poor

physical skills as well as school problems and diminished social skills. The psychosocial functioning of these persons was remarkably poorer since their childhood and difficulties in coping with social life challenges increased with age [1, 12]. Clinical patterns, formerly called „pseudoneurotic” - depressive, mixed (anxiety-depressive, hypochondria-depressive, dysmorpho-depressive), obsessive-compulsive, conduct, and anorexic disorders was much less common. Conduct disorders were significantly more common in boys, anorexic disorders were more common in girls ($p < 0.005$), the remaining psychopathological syndromes were diagnosed with equal frequency in adolescents of both genders.

Various other symptoms preceding prodromal period such as tics during childhood period, ADHD - motor hyperactivity with disturbed concentration as well as symptoms, signs and abnormal behavior equivalent to those spotted in persons with symptoms resembling „negative ones” in prodromal period were found in nearly a half of the patients included among the subgroup of prodromal period with obsessive-compulsive disorder characteristics. Obsessive compulsive symptoms in most of patients (in 8 out of 11) in this subgroup appeared early, usually during childhood period, and their intensity increased with patient age.

Both in the case of patients with „negative” prodromal symptoms and in the case of obsessive-compulsive disorders, it was difficult to determine evident onset of the prodromal period.

The length of the prodromal period

The determination of the prodromal period length in schizophrenia is extremely difficult and only in a case of prospective studies on schizophrenia high risk groups there are no substantial doubts on the duration period of prodromal symptoms. These data, however, may be obtained indirectly, by estimation of time period of prodromal symptoms - psychotic and non-psychotic - present until the time of schizophrenia diagnosis (tab. 2)

Table 2

The period of prodromal symptoms until schizophrenia diagnosis in adolescents

Time of prodrom until schizophrenia diagnosis	Clinical picture of prodrom										All	
	Symptoms „negative” type		Depressive symptoms (total)		OCD		Anorexia nervosa		Conduct disorder			
	L	%	L	%	L	%	L	%	L	%	L	%
≤3 months	0	0	1	0.8	0	0	0	0	0	0	1	0.8
3-6 months	0	0	11	9.4	0	0	2	1.8	2	1.8	38	32.6
7-12 months	0	0	9	7.8	3	2.5	1	0.8	1	0.8	41	35.0
13-24 months	4	3.4	2	1.8	0	0	1	0.8	0	0	20	24.8
>24 months	50	42.7	2	1.8	8	6.9	0	0	0	0	8	6.9
Total	74	63.2	25	21.3	11	9.4	4	3.4	3	2.5	117	100.0

The symptoms of the prodromal period resembling „negative” symptoms lasted from 6 to 24 months (mean 13.4 months) in majority of patients before the development of completely symptomatic schizophrenia picture. „Pseudoneurotic” symptoms lasted from 3 to 12 months (mean 5.6 months), obsessive-compulsive disorders - 6 months to 12 years (mean 9.3 yr.), conduct and anorexic disorders - 3 to 6 months (mean 5.2 months). However, it is noteworthy that single, less expressed symptoms resembling „negative” ones appeared in most patients (in 50 out of 74) much earlier (several years, mean 9.6 yr. before diagnosis). The large differences in duration of similar symptoms were evidently associated with their intensity, effects on worsening of social functions (at school, in family life) and parent or family member interest in patient problems, their education and professional awareness as well as medical specialist care availability.

Without any information from their child, parents were usually alerted by easily noticeable symptoms, such as aggression, antisocial behavior, expressing suicide intentions, isolation, worsening of school results, intense and frequent compulsions. Some of the described symptoms had been considered as manifestation of „bad personality”, laziness or revolt for a long time. This markedly postponed illness recognition and searching for professional assistance (tab.3).

Table 3

Time period following the first psychotic symptoms until hospital admission of adolescents with schizophrenia

Time period before the therapy commencement	Adolescents with schizophrenia N= 50	
	N	%
Up to 6 months	39	26.0
Up to 12 months	79	52.6
Up to 24 months	118	78.6

Discussion

Assuming that all abnormal symptoms, features and behaviors among age matched healthy population may be relevant to the beginning of prodromal period of schizophrenia, the prodromal period would last for 12 to 15 years in 50 patients (33.9%). Currently, it is not clear whether they symptoms, features and behaviors are associated with the beginning of mental illness, or, as it is assumed by most investigators, they constitute a characteristic group of features in some persons, who under a certain set of environmental conditions, would develop schizophrenia disorder (usually demonstrating major negative symptoms).

Duration of prodromal symptoms (since the clear behavioral changes until psychotic symptoms) determined in retrospective studies was over 3 years (mean 3.2) in entire study group. Moreover, the diagnosis correlated with the therapy introduction in our study group.

Many authors, especially those who conducted their study on elderly patients with the first schizophrenia episode, claimed even longer prodromal symptom period

(as long as 5 years). However, if one considers the data on a part of patients with prodromal symptoms resembling „negative ones” and of obsessive-compulsive type, then it is evident that the first symptoms appeared over 9 years earlier (mean 9.6). These mean values are known to be misleading. It is important that there is a wide range of prodromal period duration (between several hours or days and several years) that may be associated with its specific picture as well as with the following course of schizophrenic disorders.

The symptomatic pictures of prodromal period found in this study did not differ significantly from those previously described in literature. However, the early onset of a number of features, symptoms, disorders of psychomotor development, social adaptation were much more often described in some patients, mainly in those with prodromal period characterised with „negative” symptoms or obsessive-compulsive disorders with predominant negative symptoms in the course of the illness or in form of schizophrenia with persistent obsessions and compulsions.

The appropriate design of prospective studies on large populations would allow for more accurate description of clinical pictures involved in schizophrenia prodromal period as well as for a precise differentiation of symptoms associated with an increased risk of schizophrenia and those primary, evident onset symptoms. Recognition of these symptoms and determination of particular development disorders, prodromal personality profiles, adaptation disorders, family history of schizophrenia may, at least in some patients, facilitate schizophrenia diagnosis and therefore, accelerate introduction of appropriate therapy. Moreover, it might also be beneficial for the illness course enhanced remissions, improved effects of pharmacotherapy, decreased number of recurrences and hospitalization periods, lesser extent of cognitive malfunction and improved overall performance) [8].

Conclusions

1. Approximately 1/4 adolescents with schizophrenia (22%) experienced sudden onset of the disorder. The preceding period was commonly asymptomatic, in some cases, minor sleep disturbance, undefined psychomotor anxiety, minor attention disturbances and the feeling of loss were present a few days before.
2. In 78% patients mental disorders preceding fully developed schizophrenia were identified as: „negative”-like symptoms (49.3%), depressive and mixed disorders (anxio-depressive, hypochondriac-depressive, dysmorphophobic-depressive), obsessive-compulsive disorder, anorexia nervosa and conduct disorders. Anorexia nervosa was significantly more common in girls, and conduct disorders were significantly more frequent in boys. The remaining syndromes were equally frequent in both genders.
3. It was especially difficult to determine the length of prodromal period in the retrospective study. It was estimated for 3 years in our study group.
4. In 38.6% patients with prodromal period characterised with negative-like symptoms or obsessive-compulsive disorder the first, single symptoms appeared very early (in early childhood), and their intensity increased with their age until entirely

developed schizophrenia symptoms emerged. They most probably prove increased risk of schizophrenia but not the presence of prodromal period.

5. In 1/4 patients schizophrenia diagnosis was established after 6 months of psychotic symptom duration, after 1 year the diagnosis was established in a half of the study patients, and 3/4 patients were diagnosed 2 years after symptom onset.

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