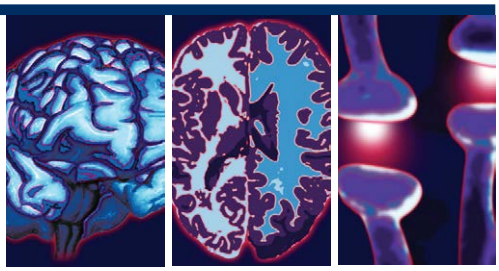

# Between Autistic Spectrum Disorder (ASD) and Childhood Onset Schizophrenia (COS): A Proposal for a Passerella Syndrome

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## ABSTRACT

### Background

Even if childhood-onset of schizophrenia is described in the literature, and there are several case reports of concomitant autism spectrum disorders (ASD) and childhood-onset schizophrenia (COS), early diagnosis of comorbidity remains less the norm than the exception. The definition of a specific syndrome – which we propose to call Passerella – describing this comorbidity condition can help focusing diagnosis and initiate early treatment avoiding dangerous delays in care.

### Method

We report the detailed clinical history of 4 patients, 2 women and 2 men. The case of one of the women has been previously reported. The evolution of the clinical state of the patients is reported together with the diagnosis provided by the caregivers, the pharmacological and psychological treatment and the patient's clinical evolution.

### Results

The delay in formulating a diagnosis of concomitant ASD and COS, as well as the emphasis on the achievement of school or social results, have been an aggravating factor for the patients' sequel of crisis and relapses. The clinical status of the patients has presented a marked improvement when the comorbidity has been acknowledged and properly treated, both pharmacologically and via an appropriate reduction of the stressful demands for school or social performance.

### Conclusion

Early diagnosis of psychiatric comorbidities in ASD allows a more effective therapeutic strategy and the adoption of a psychopedagogic approach adapted to the vulnerability of these patients with respect to stress. The definition of a specific syndrome can help orienting caregivers toward earlier diagnosis and more appropriate intervention.

### Keywords

Children onset schizophrenia (COS), Autistic spectrum disorder (ASD), Psychopedagogic approach, Early diagnosis, Passerella syndrome

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## Introduction

Four cases of patients with ASD and childhood-onset schizophrenia are reported, with a common clinical profile and a shared pattern of difficulties to establish early diagnosis and introduce appropriate therapy [1].

The precocious onset of psychotic symptoms, around 5-8 years, concomitant with explosive tantrums, choleric behaviour and withdrawal are often underestimated because of a misleading focus on "reassuring" school results. This hinders early diagnosis and treatment of COS. To aggravate this situation, even if childhood-onset of schizophrenia is described in the literature, peculiar psychotic symptoms as hallucinations can sometimes be confused with nightmares and fears relatively common in infancy.

Behaviors such as withdrawal accompanied by tantrum, choleric behaviour and aggressive outbursts are present both in autism and psychosis, and it is very difficult to distinguish if they are symptomatic of ASD or COS [2-4]. According to some authors, three underlying symptoms – unusual fears, thought disorders and bizarre anxiety reactions – are related to psychosis in ASD [5]. Also in our sample, we find precocious but misleading psychotic symptoms, making timely diagnosis difficult, and delaying proper treatment.

Our cases show the common treat of being affected by paranoid schizophrenia and are characterized by relatively constant – often persecutory – delusions, often accompanied by hallucinations, particularly paracusias (hearing voices), and perceptual troubles. The psychotic symptoms are surreptitious, and the young patient can suffer, sometimes for years, from a chronic state, without a clearly identified acute episode, before the illness is formally diagnosed [2,6]. These symptoms gravely affect the patient's school and social performances and can degrade the quality of life. Paranoid schizophrenia is a chronic affection, but adequate and timely care can markedly improve the patients' quality of life [7].

Degraded social interactions are typical effects of developmental disorders. Some authors [8,9] report that COS can be accompanied by developmental impairment, affecting particularly language. Even if the speech delay is not always present, verbal communication is impaired and social interaction degraded [1]. In all the 4 patients described in this work, we have found a delay in speech or a difficulty to verbally communicate in social exchanges. Another common element is extreme tantrum crises or choleric behaviour that started in childhood and persisted during the whole life of the patients. If we consider these as COS symptoms, they were more precocious than reported by Rapoport et al. [10]. On the other hand, consistently with Vourdas et al. [11], in some of our patients there was speech impairment preceding the COS onset.

The chronology of symptoms encountered in our patients is characteristic. They start at pre-primary school age with "mild" developmental problems such as poor comprehension of social situations, often with some level of language impairment, and difficulty to adapt to new situations. From late childhood to adolescence we encounter "mild to severe" psychotic symptoms similar to the negative and positive symptoms of schizophrenia, accompanied by explosive tantrum crises, choleric behavior, outbursts, withdrawal, loneliness, increasing social adaptive impairment but also delusion (above all of the paranoid kind) and hallucinations. In early adulthood we report few, if any, sexual relationships. In adulthood, we have persistence of psychotic symptoms, severe impairment of social interactions, low quality of life and progressive reduction of autonomy.

While psychiatric comorbidity is often reported for individuals with ASD and Intellectual Disability [10], the connection between ASD and psychosis is still debated in the literature [11-13]. In the context of this discussion, Rapoport et al. [14] consider that the introduction of the distinction of ASD and COS, notably schizophrenia, is an advance in the field of childhood psychopathology. Watkins, et al. and Alaghband-Rad, et al. note that ASD and COS are different in the onset age, differential diagnosis, and treatment [15,16]. Several works underline the effectiveness of this distinction at the clinical level, noting however that there are extensive reports of high COS – ASD comorbidity levels, connected with the presence of common family, genetic and imaging evidence [17,18]. Known psychosis vulnerability factors include birth complications [19] and family history of schizophrenia [20,21]. A recent and extensive review by Takara et al. [15] refers most authors as setting the lifelong presence of schizophrenia in ASD below 4%, in contrast to previous studies that reported a wider range (0% to 28). We note here that the severity level of symptoms used as a threshold to define the ASD population may largely influence the statistics.

The objective of this paper, which builds on a previously published case report [1] is to propose the definition of a specific syndrome describing the COS and ASD comorbidity, for which we propose the name Passerella Syndrome. Our clinical experience leads us to believe that the identification of this specific co-morbidity as a Syndrome may help focusing the attention of the medical professional on this kind of psychopathological affection, allowing them to take timely and appropriate care measures. In particular, a personalized modulation of the demands in the fields of school and social performances may go a long way to improve the prognosis for these patients, in spite of their low level of social interactions.

ASD is a developmental disorder, which implies stable (over time and situations) patterns of behaving, feeling and thinking. In this, ASD is equivalent/comparable to a personality functioning. Taking into account the theoretical framework proposed by Widiger, and Widiger and Smith [22,23], on the relationships between personality and psychopathology, there may be at least three ways to conceptualize the connection between autism (considered as a personality functioning) and Passerella Syndrome (considered as a collection of symptoms/disorders): etiological (causal) relationship, spectral relationship, and pathoplastic relationship. The etiological relationship implies that

Personality has a direct effect on the symptom/disorder/psychopathology or that a symptom/disorder/psychopathology can be the origin of a personality modification. A spectral relationship suggests the idea that personality and psychopathology share a common etiology and are organized on a dimensional continuum. From this perspective, a symptom is a maladaptive form of a personality trait. In a pathoplastic relationship, personality can influence the expression of a disorder as well as a disorder can influence the expression of a personality trait. Thus, a similar symptom will express itself differently according to the personality profile of the patient, as well as a disorder may influence the way a personality trait express itself whether this disorder is highly present or not. Obviously, there may be a combination of the use of these models for the explanation of a relationship between a personality profile and the development of a syndrome. In the specific case treated by this work, the presence of ASD induces an extreme vulnerability to stress, above all when the verbal skill is poor and the social interactions become unavoidable as for children in pre-scholar and scholar situation, sometime also in early childhood or for adults in institutions or adapted workshops. The explosive tantrums, choleric behavior with withdrawal reported for these patients could represent different strategies to escape anxiety and fear, which are exacerbated by the stress of realizing to be incapable to cope with the demands of the environment. Galli Carminati G, Tagan C, Zecca G, Carminati F. between Autistic Spectrum Disorder (ASD) and Childhood Onset Schizophrenia (COS): a proposal for a Passerella Syndrome.

Neurocognitive impairments (e.g. executive dysfunctions and theory-of-mind deficits) are considered vulnerability factors for psychosis according to several works about prodromal psychosis in ASD [21,24]. The distinction between the beginning of endogenous comorbid psychosis and the psychotic reaction to a stressful situation is important in the diagnostic process for ASD individuals. This complex intertwining of causes and effects has brought a lot of attention, both theoretically and clinically, to the "differential diagnosis" between COS and ASD, and has had the concomitant effect to reduce the attention to the co-morbidity cases, in spite of them being clearly reported by the literature. For instance, as reported by Selten et al. [21], the impairment in the understanding of social relations by ASD individuals can be mistakenly attributed to psychosis, as well as the social difficulties introduced by psychosis can be attributed to ASD. The consequence is that a carefully conducted "differential diagnosis" process may lead, unfortunately, to a missed comorbidity diagnosis. Spontaneous psychotic disorders in school -age individuals, including schizophrenia, should therefore be considered in the wider context of the subject's vulnerability, above all if ASD is present, particularly in relation to the demands on scholastic and or social performances, which often induce a "toxic" stress for these fragile patients. We want to stress that it is not our intention to diminish the importance of the work done to establish a differential diagnosis between COS and ASD, but rather to suggest that a "triple" differential diagnosis should be considered, between COS, ASD and COS-ASD co-morbidity (the proposed Passerella Syndrome). In these cases, a marked improvement in the cognitive evolution can be achieved by a reduction of stress due to the school and social requirements. For example,

the school year could be split into two and moments of rest can be introduced into the daily routine (e.g. listening to music, watching non-exciting video, introducing moments of pause with a nap, a quiet walk, a pet therapy session). Parents and caregivers may be worried by the consequent delay in the achievement of the school curriculum, but in reality, this adaptation of the schedule avoids losing much more time in a sequel of crisis and relapses. The reduction of stress, which is central to the treatment of this syndrome, is better achieved via a precise structuring of the daily activities, low achievement demands and the introduction of pauses expressly dedicated to rest and relaxation.

## Case Reports

In the present study, we obtained the consent from the 4 patients (2 women and 2 men) and from their legal tutors. In our Cabinet of Diagnosis and Care in Geneva we treat a population of 265 patients (December 2017: 154 women, 111 man), out of which 26 patients (9.8%, 17 men and 9 women) present ASD, included Asperger. Among these, 7 patients (3 girls and 4 boys, 26.9% of the ASD population and 2.6% of the total), which present the specific clinical profile discussed in this work.

### ■ Case of SF

SF is a 22 years old woman. She is the first of 3 siblings, with one brother and one sister. There is no reported psychiatric case in the parents' families. During the pregnancy, a small blood loss is reported at 8 months. The delivery required induction and forceps. The baby had a weight of 4.190 kg and a length of 52.5 cm. The APGAR is not reported. There is no reported delay in sitting and walking. Early childhood is without reported difficulties apart from a speech delay. The parents (and the preschool the professionals too) record the impression that their daughter "is living in her own world".

Starting from pre-school age she shows a choleric behavior, altered with withdrawal, probably related to the difficulties in comprehension of social interactions. Speech therapy starts at 5 years. Neuropsychological evaluation 7 (WISC-III) finds borderline intelligence, severe memory impairment, difficulties in verbal and non-verbal communication, lack of concentration and difficulties in social communication. At 8 she is diagnosed with ASD. No X-fra is detected and the IRM does not show any anomaly. An IQ test scores verbal at 84 and performance at 62. She attends specialized school from childhood to 18. Menarche is at 12, with no reported sexual intercourse to date. At the beginning of the adolescence she has tantrum crises with aggression against objects or persons, above all when her routine is altered, showing a clear need for repetitive and previsible activities. She lives in an institution offering a special program for young adults with high level of autonomy, working in an adapted workshop. At 17 the patient consults with our practice because of the importance of her anxiety episodes, accompanied by tantrum and aggressiveness, with an attitude of reverie and withdrawal. The evaluation of the presence of auditory delusions is hampered by the lack of confidence in the therapists and by the refusal or difficulty to describe the symptoms. Treatment with Aripiprazole-Abilify 5 mg/j and Escitalopram - Cipralex 5 mg/j reduced the anxiety and the withdrawal attitude. From the psychoeducative point of view, the activities were centered on a relaxed exchange with other persons working in an adapted occupational workshop, e.g. weaving and pottery. Regular moments of rest are introduced in the daily schedule to allow the patient to spend a moment alone, taking a drink and a snack. The clinical evolution is positive, with a reduction of the symptoms that led her to consult, and the patient is stable with a very good level of autonomy (use of public transport, walk in the town, week-ends with the family once a month, regular sport activities). There has been no need of hospitalization.

### ■ Case of AN

AN is a 27 years old woman. She is the first of two siblings, with one brother. There is an occurrence of alcoholism in the family of the mother, and a cousin of the father suffers from schizophrenia. She was born at full term by vaginal delivery after a normal pregnancy but with several wraps of the umbilical cord around her neck and a broken collarbone. Weight and length are not reported, and the APGAR score is not recorded. No delay is reported in sitting and walking. As a child, she shows little emotions when separated from her parents and she is often hyperactive with agitation and some difficulties to stay in the arms of adults, with poor gaze fixation. At 4 the patient is able to follow some courses of gymnastic and music but she shows a lack of concentration. At 5 the teacher remarks a bizarre behavior characterized by a lack of socialization with the other children and a lack of verbal communication, even if no speech

delay was previously recorded. The parents (and also the preschool professionals) refer the impression that their daughter "is living in her own world". Between 5 and 7 the occasional tantrum episodes intensify; the patient presents difficulties to integrate groups and to develop an appropriate social behavior. At 9 the patient admits to the parents that she hears threatening voices, at particular in the morning. At 12, an endocrinologic investigation shows a delayed puberty. At 14 a neurological examination reveals that blood, metabolic balance and EEG are within the standard, likely excluding a neurometabolic cause; genetic analyses are performed to search for a 22q11 microdeletion or a fragile X syndrome, with negative results. A brain MRI fails to detect any anomaly. At 14 WISC-III and CMS Memory Scale for Children reveal borderline intelligence. She attends private school with special programs from childhood to 18. Menarche at 15, no sexual intercourses to date. At 18 the symptomatology is compatible with paranoid schizophrenia. At 20 she moves without difficulties from the family house to an institution. At the institution, she lives in an apartment with five other young persons under the supervision of teachers, following tailored organized activities, often alone with an educator or in small groups with a few residents. At 22 the patient arrives at our practice with a demand of normal psychiatric care for ASD and COS disorders, notably anxiety episodes, accompanied by tantrum. The treatment is: Biperidene retard 4 mg per day, Valproate- Chrono 750 mg per day per os, Hydroxyzine 100 mg per day, Atenolol 25 mg 1 times per day, Clozapine 250 mg per day, Haloperidole 1 mg once per day, Baclofene 25 mg per day, Lorazepam 1 mg per day. From the psychoeducative point of view, personalized activities in an adapted occupational workshop have been elaborated, e.g. notably at the bakery. The patient performs regular sport in the institution where she lives. Regular moments of rest are introduced with music, non-exciting videos, and quiet moments alone where she can have a drink and a snack. The clinical evolution is positive and the patient is stable. There have been no relapses or hospitalization during the last 5 years and she can spend every other week-end with the family.

## ■ Case of FB

FB is a 40 years old man. He is the second of two siblings, with one sister. There is no reported psychiatric case in the parents' families. During the pregnancy, there is a small blood loss at 4 months with a risk of miscarriage, but cervical banding is not necessary. Delivery is normal, with weight, length and APGAR not reported. Soon after the birth, the presence of a small pocket of cephalorachidian fluid is detected, but it quickly disappears. A tooth is extracted at 3 week and half. Vomiting is frequent till 15 months. Sitting occurs at 7-8 months, walking at 15 months. There is a very mild speech delay, but the patient can say small phrases at 3. The parents (as well as the preschool professionals) report the impression that the child "was living in his own world". Tantrum crises start at 3, biting other children, with an intense sense of "fear of everything". Social exchanges with other children and then adolescents and young adults are problematic. He is described as hyperactive (ADHD is confirmed at adult age, but with a total refusal of the treatment due to its side effects). Verbal therapy is introduced at 6 and continues till 11 with poor results. From 15, cognitive therapy is introduced and continued till 18. Sexual development is normal with reported heterosexual intercourses. This is the only patient with a reported sexual activity. At 18 the WAIS-III test scores a borderline intelligence. The patient attends private school with special programs from childhood to 9, then specialized school till 18. At 18, antidepressant (non-specified) is introduced accompanied by clonazepam, but it is stopped abruptly and epileptic crises appear. At this time, there is a concomitant utilization of cannabitol. Genetic evaluation excludes X-fra. First hospitalization in psychiatry is at 18, with several other episodic hospitalizations following, with clastic crises, paranoid delusions. Auditive hallucinations are also very likely, but of very difficult appreciation because the patient often refuses to communicate with the therapists. An antipsychotic treatment is introduced. The patient has lived in different institutions, then in a protected apartment, and for the last 10 years in a normal apartment. From 18 to 40 the patient works in several adapted workshops and from 40 he has only episodic activities in specialized programs. At 39 the patient arrives at our practice for treatment of schizophrenia and ASD. The present treatment is: Zuclopenthixol depot 225 mg per 2 weeks, Venlafaxine 112.5 mg per day, and Lorazepam 2.5 mg per day. The consequent improvement of the clinical situation has allowed elaborating a project to integrate a protected apartment with adapted activities in an occupational and recreational structure, the life in an apartment alone and without structured activities being too stressful.

### Case of LF

LF is a 45 years old man. He is the first of two siblings, with one brother. There is no reported psychiatric case in the parent's families. At 3 months of pregnancy there is a risk of miscarriage and cervical banding is performed. The mother is confined to bed for several months with a premature delivery at 35 weeks. The baby weights 2.580 kg, with a length of 47 cm. The APGAR score is not reported. An inguinal bilateral hernia requires surgical reduction at 2 months. The sitting age is not reported, but he walks at 18 months, and there is a delay in motor coordination in early childhood. A speech delay is recorded, accompanied by poor verbal communication that persists to date. Speech therapy is not possible because of lack of compliance. No IQ evaluation is recorded. The patient attends specialized school from childhood to 18. Starting from adolescence, he lives in specialized institutions. The parents (as well as the preschool professionals) report the impression that the child "was living in his own world". At 5 serious tantrum crises appears where the patient breaks everything around him. Hay fever and eczema are present from childhood. There is no information about sexual development, and, as far as we know, he has had no sexual intercourse till now. At 16 he attends psychiatric day hospital because of challenging behavior and cannabis addiction. At 37 comes the first psychiatric hospitalization, where auditory delusion and severe persecutory feelings are reported. A diagnosis of paranoid schizophrenia and ASD is proposed. During the hospitalization, a WAIS-III test detects a mild intellectual disability. Several hospitalizations in psychiatry follow the first one, above all because of aggressive behavior. He attends specialized school from childhood to 18. He lives in Institutions from adolescence till now, where he works in several specialized workshops. From 40 he has episodic activities in specialized programs. At 40 the patient arrives at our practice for psychiatric care for ASD and schizophrenia causing the repeated hospitalizations. The present treatment is Zuclopenthixol depot 200 mg every 2 weeks, Lorazepam 1 mg per day, Hydroxyzine 50 mg per day, Baclofene 20 mg per day, Valproate chrono1500 mg per day, Biperidene retard 4 mg per day, Clotiapine 40 m per day, Sertraline 50 mg per day, Méthylphénidate 40 mg per day, Melatonine 3 mg per day. From the psychoeducative point of view a schedule of personalize activities has been elaborated, such as the distribution of fruits and vegetables to the different apartments of his institution, some work in the garden and regular sport activities at his residential institution. Regular moments of rest have been introduced with non-exciting videos, music, and pauses where he can have a drink and a snack. The clinical evolution is positive and the patient is stable, with no relapses or hospitalization during the last 3 years. He spends a weekend with the family every 2 months.

In Table 1 we summarize some common characteristics of the cases reported.

## Discussion

The objective of this work is to bring to the attention of psychiatric practitioner the existence of a specific ASD and COS comorbidity in order to improve the opportunities of early diagnosis and increase the opportunities to introduce a more effective treatment and psychoeducational strategy. In this context, it is very important to

**Table 1: Summary of some common patients' characteristics.**

| Patient | Gender | IQ | Age of tantrum crises/choleric behavior | Delay/impairment in verbal communication | "Living in his own world" in childhood | Delusional symptoms/ hallucinations |
|---|---|---|---|---|---|---|
| SF | F | Borderline intelligence | Pre-school age | Yes | Yes | Yes |
| AR | F | Borderline intelligence | Pre-school age | Yes | Yes | Yes |
| FB | M | Borderline intelligence | 3 years | Yes | Yes | Yes |
| LF | M | Mild intellectual disability | 5 years | Yes | Yes | Yes |

assess the patient with rating scales such as CARS or AAPEP [25-27] or if possible with ADOS-2 [28] and ADI-R [29] Once the comorbidity diagnosis is established, it is possible to define a personally tailored therapeutic and socieducational path. For this particular comorbidity, that we propose to define as a specific new syndrome (Passerelle), an essential therapeutic step is the establishment of a predictable and regular daily routine and a reduction of the stressful situations or activities, which can have a literally toxic effect on these fragile patients, increasing the symptoms and hampering the recovery process.

Birth complications are present in all the cases reported, and these should not be underestimated as a vulnerability element for psychosis [21]. If we regard the serious and violent tantrums as effects of a psychotic anguish, the debut of schizophrenia onset is too early even for COS. But we must not forget that the choleric episodes present in the patients considered in our report, could be the expression of social stress in the pre-scholar and scholar age, when the interaction with peers is unavoidable.

For patients still in the school age, appropriate measures include the reduction of the academic demands and a managed deferral of the academic curriculum, possibly even splitting the academic year in two by repeating a class. These measures allow a better cognitive development and markedly improve the prognosis for the patient.

In adulthood, the same stress-reducing balanced approach has to be adopted, privileging regularly scheduled occupational and recreational activities over productive work, even in adapted workshops. It is fundamental to introduce regular pauses in the daily routine, where the patient can relax, listen to music, watch non-exciting videos and enjoy a drink and a snack. It is useless and dangerous impose school and social performances or challenges which can produce exactly the contrary of the desired effect, impairing more than improve cognitive development.

In our precedent case report [1], the impairment in verbal communication and the difficulty in the social contact are relatively mild for a classical ASD, while in the other cases reported in the present work, there is a delay in speech development, even if the important element is more the social use of language than the language level itself.

Following Widiger and Smith, the combination of their three models (etiological/causal relationship, spectral relationship, and pathoplastic relationship) suggests that the presence of ASD induce an extreme, stable and constitutional vulnerability to stress, above all when the verbal skill is poor and the social interactions become very problematic for children in prescholar and scholar situations, sometimes also in early childhood. The explosive tantrums, choleric behavior and withdrawal could represent different strategies to escape anxiety and fear, but could also express a disruption of psychotic symptomatology with estrangement from reality [6,7].

An important common element is that the parents and, when pre-school begins, the professionals, report the impression that the patients are "living in their own world", with an important withdrawal from real situations and social interactions. This attitude is present in ASD, but probably, in case of the comorbidity described here, another reason for this attitude is the presence of acoustic/visual hallucinations, which could be easily underestimated since these are rarely reported by the children themselves because of timidity and shame, and also due to the often-concomitant poor verbal skills. Another common observation is the presence of acoustic/visual hallucinations at adult age, corresponding to the typical symptomatology of paranoid schizophrenia. In general, the evaluation of this pathology is hampered by the combined effect of ASD and the difficulties in social communication, since the patient tends to express minimal complaints and does not want to talk to the therapists.

In **Table 2** we summarize some common symptoms of the proposed Passerella syndrome.

A major negative effect of a delayed diagnosis of the comorbidity is the belated pharmacological treatment and adoption of adapted psychoeducational measures. The consequence of this is a reduced social insertion and an increased likelihood of psychiatric hospitalization, often after a long and painful sequence of often ineffective pedopsychiatric and psychoeducational interventions.

We should add to this picture the high occurrence of epileptic episodes in patients with ASD. The lack of compliance of the patients (e.g. for EEG or imagery exams) hinders a precise characterization of the epileptic syndrome [30], even if such investigations should be performed as far as feasible for these "Passerella" patients.

| Table 2: Summary of some common symptoms present in the proposed Passerella syndrome. |
|---|
| In the definition of the Passerella Syndrome, the major diagnostic elements that we suggest are: |
| • Possible presence of pregnancy and or birth complications (often underestimated). |
| • Impaired verbal communication and degraded social interaction. Possible presence of concomitant speech delay. |
| • Precocious onset of psychotic symptoms, around 5-8 years, concomitant with explosive tantrums, choleric behaviour and withdrawal. |
| • At pre-school age, parents and professionals report the impression that the patients are "living in their own world. |
| • Paranoid schizophrenia characterized by relatively constant, often persecutory, delusions, frequently accompanied by hallucinations, particularly paracusias (hearing voices), and perceptual troubles. |
| • Psychotic symptoms are surreptitious, and, before the illness is formally diagnosed, the young patient can suffer, sometimes for years, from a chronic state without a clearly identified acute episode. |
| • Few, if any, sexual relationships in early adulthood. |
| • Persistency of psychotic symptoms in adulthood, with severe impairment of social interactions, low quality of life and progressive reduction of autonomy. |
| • Degraded social interactions. |

It is our opinion that one of the compounding difficulties in the identification and treatment of this comorbidity has to be found in the historical developments of the psychopathology of ASD and psychoses. The existence of a connection between these two affections has been long and, at times, hotly debated. The generally accepted conclusion of a clear distinction between ASD and COS, in particular schizophrenia, orientates professional caregivers toward a differential diagnosis, downplaying the fact that there is a below 4% prevalence of COS – ASD comorbidity [15]. We do not want to reopen the COS versus ASD debate, and we consider that the accepted wisdom of the need of a differential diagnosis between COS and ASD is per se clinically correct. However, we believe that any such differential diagnosis should also take into account the possibility of the presence a COS-ASD comorbidity that we consider not just a mere superposition of the two conditions, but a clinical condition per se, that we propose to identify as a separate syndrome called Passerella. When this syndrome is present, timely recognition of the situation allows the adoption of an adapted therapeutic strategy, specifically in the psychopedagogic approach, giving particular relevance to stress-reducing measures that take into account the sensitivity of these patients to stressful situation.

This is very important for the well -being of the patients, since ASD – COS comorbidity is a very serious situation and prognosis varies dramatically according to when it is recognized and diagnosed and how it is therapeutically addressed. The definition of a specific syndrome with the accompanying diagnostic, therapeutic and prognostic specifications would be of great help, both for professionals and for families to enhance early diagnosis and treatment. Beyond improving prognostic perspectives for the patients, this would allow the establishment of family therapy and interdisciplinary exchanges to improve the coordination of the various actors of the therapeutic process.

## Conclusions

Although we realize the limitations of the present work, given the varsity of the field of COS and ASD comorbidity, we believe that both the existing literature and our clinical experience justify the definition of a new syndrome, for which we propose the name of "Passerella Syndrome" to help recognizing and targeting the specific COS-ASD comorbidity clinical condition and orienting the treatment.

Our experience shows that a belated or partial diagnosis results in a degraded quality of life for patients and families, often causing a difficult and exhausting therapeutic history for patients, families and professionals alike.

As we have suggested in our previous single case report, the timely diagnosis of COS comorbidity in ASD facilitates the introduction of early and appropriate treatment and the adjustment of the daily schedule and of the various activities, be them scholar or work-related according to age, taking into account the sensitivity of these patients to stress-related situations.

Cases similar to the ones described here are reported in the literature, but we contend that they are not merely the superposition of a COS and an ASD situation, such in comorbidity, as they are usually described, but rather a specific syndrome. In our experience, we have noticed a specific regular pattern characterized by an early onset time with the early appearance of COS symptoms followed by ASD. This specific pattern that we found to be reproduced in our cases, often misleads professionals down the path of a "differential diagnosis".

We therefore propose this new "Passerella syndrome" characterized by the observed pattern, in order to underline the specificity of the clinical profile, with the final objective to increase early detection and clinical effectiveness in its treatment. One important element is the assessment by the therapist of the presence of acoustic/visual hallucinations in the young patient. Given the young age and the often-present non-compliance, this can only be accomplished by an attentive observation, looking for clinical signs. We found that a particularly telling clue is when parents and professionals report that the patient seems to be "living in his own world". These hallucinations are the most probable cause of the reported explosive tantrum crisis, choleric behavior accompanied by withdrawal, loneliness, increased social adaptive impairment.

Parents and educators are often concerned, in the interest of the young patient, by the delays suffered by the scholar curriculum. However, it is our experience that an undue pressure on school and social performances may cause a much greater loss of time and a high degree of suffering because of crisis and relapses.

A better understanding of this proposed comorbidity syndrome would require more cases to be reported and further studies would be necessary to better understand this disorder.

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