

Beyond what clinicians see: missed diagnosis and misdiagnosis of a woman with autism spectrum disorder

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SUMMARY

A young woman with autism spectrum disorder was admitted to the hospital via the emergency care unit. On being admitted, she was improperly diagnosed with a psychotic disorder due to her erratic behaviour and incomprehensible refusal to eat. As a result, the patient was hospitalised against her will. For accurate and correct diagnosis and treatment, it was necessary to collect the patient's detailed clinical history, while being hospitalised.

BACKGROUND

Adult and child psychiatrists mostly still misdiagnose autism spectrum disorder (ASD) while often diagnosing it as other disorders that have similar phenotypical presentations. Due to this, there are a significant number of patients with ASD that reach adulthood without ever being properly diagnosed, most of them with 'high functioning' autism.¹

This fact is even more prominent when considering the diagnosis of female patients with ASD.^{1,2} Underdiagnosis or even missed diagnosis takes place very often in these patients, most likely due to their ability to mask social difficulties, known as camouflaging, and thus, not meeting the current diagnostic criteria for autism.^{2,3}

Missed diagnosis and subsequently the lack of appropriate treatment and support for highly functioning women, occurs due to the lack of appropriate screening tools.^{2,3} The Autism Diagnostic Observation Schedule 2nd Edition, Module 4 (ADOS-2) is so far considered the gold-standard semistructured scale among clinicians to diagnose ASD in adults.⁴ The scale possesses lack of adequate screening sensitivity which in turn requires the need for healthcare professionals to be aware of this fact and therefore be alert in order to perform the correct clinical diagnosis.

More than half of these patients present with coexisting psychiatric comorbidities.⁵ The trigger to seek support from a mental healthcare professional is a negative event, which results in depressive and/or anxiety symptoms. Major depression or anxiety disorders often manifest themselves atypically in adults with ASD,⁶ leading to unnecessary, unsuitable, or even harmful treatments and interventions.

Through this case report, we aim to underline the importance of an accurate diagnosis and early intervention in patients with ASD. An enhanced prevention of psychiatric comorbidities results in improved social and living outcomes. Furthermore,

we point out the challenges of diagnosing an individual with an atypical presentation of ASD and the potential risks of failing to do so.

CASE PRESENTATION

We present the case of a young woman, single and with no children, who lived with her mother. This patient had no current academic or professional occupation. She had no psychiatric history until moving from middle to high school, which prompted her difficulties in social interaction, preventing her from starting and maintaining friendships which led to sadness, anxiety, loneliness and school absenteeism. The patient was prescribed 50 mg sertraline resulting in clinical improvement. However, she dropped out of high school and started to spend most of her time at home reading and tidying up, mostly her room. As an adult she tried to work and failed to perform as required. Afterwards she experienced depressive symptoms and was seen by psychiatrists at the emergency room. She was diagnosed with unipolar depression. Once again, she was prescribed 50 mg sertraline and referred to her family doctor. She went back to her previous routines, spending most of her time alone at home, going out sporadically and exclusively with her mother.

A couple of years later, after an infatuation which went unresponded, the previous depressive symptoms recurred. Isolation at home occurred more than ever, with rituals such as aligning clothes and books on shelves as well as organising the house, throwing out mattresses and bed sheets for no apparent reason except the sense of self-relief.

The week before the patient was hospitalised, she stopped eating for 3 days, which led her mother to take her to the emergency room. The patient had no medical history, previous hospitalisations or any history of substance misuse. On initial evaluation she had extremely low body weight (body mass index (BMI) 13.5 kg/m²). She presented herself with poor self-care, an inexpressive face and an abnormal eye gaze. During the clinical assessment, the patient changed her seating place several times and mentioned that 'she couldn't explain why'. Her memory was preserved. Speech was provoked, laconic, monotonous and decreased in rate with her language presenting no significant changes in semantics or syntax. No formal thought pattern changes were observed. The patient also presented a reduced emotional resonance.



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Blood and urine analysis which included complete blood count, basic metabolic panel, liver, kidney and thyroid panel, infectious serologies, urinalysis and urine toxicology screening, were all negative. A brain CT scan and ECG were performed without significant changes.

When confronted with the possibility of being hospitalised the patient became agitated and physically aggressive, refusing medical assistance. This disruptive behaviour aroused suspicion of a psychotic disorder resulting in forced admittance to the psychiatric ward against her will.

Once admitted to the psychiatric ward, she progressively became more collaborative and as a result, her admission transitioned from compulsory to voluntary on the third day. The patient recognised and accepted the benefits of an inpatient environment, following the nutritional and pharmacological plan that was established.

At the ward admission time, it was possible to assess the presence of depressed humour with death rumination but no plans or intention, factors that were assumed by the patient as the main explanation for her behaviour change in the last weeks. It was also possible to exclude, during the clinical interview, the presence of psychotic symptoms.

During the inpatient period, detailed data were collected both from the patient and her mother.

Developmental, psychosocial and sociocultural history

As a small child the patient had trouble playing by herself as she seemed not to know how. Her mother gave the following example: 'I would give her a doll and she did not want to take it out of the box...I would show her how to play and she would reply that I ruined the doll by unboxing it'. The patient also enjoyed mimicking her mother's mundane affairs such as tidying up her clothes, with a fixation for books that started even before learning how to read ('She would spend hours leafing through a pile of books'). Tactile hypersensitivity ('She would refuse to wear tight pieces of clothing such as tights') and acoustic hypersensitivity ('She could listen to my own voice better than myself') started during her preschool days and have persisted till now.

During elementary school the patient walked on her toes and had a physical tic ('chewing her tongue'). The patient has since outgrown both. Her mother pointed out she also suffered from onychophagy in reaction to stressful events, which remained with her throughout adulthood. During the preschool period the patient also manifested excessive separation anxiety.

She never had learning difficulties and finished middle school without ever falling behind, but in her mother's words, she always had trouble making friends and was a victim of bullying. Her difficulties in socialising worsened during her adolescence whenever she tried interacting with teenage boys ('She tried to get closer to teenage boys, but they soon began to notice she wasn't normal ... She got sad and isolated herself even more'). She only had one boyfriend for a brief period of time and dropped out of high school, before graduating.

After that, her life was entirely devoted to household chores. The patient tried to get a job and was accepted as a waitress in two different restaurants, being let go shortly after. Her co-workers quickly understood 'she wasn't normal'. Her mother, when confronted with the recurrent use of the expression 'She was not normal' explained she meant that her daughter 'barely spoke, had trouble adapting to new tasks and looking other people in the eye'. Also, nobody believed she was an adult woman, given her appearance and behaviour.

Family history

Her mother was diagnosed with autism as a young child and was described by the patient as her best friend ('We are very much alike'). There was no relevant history on the father's family side. Her parents divorced when she was a young child, and the patient never developed any bond with him. Her brother was also diagnosed with autism as a young child. As an adult he was able to get a job and lived on his own. The patient described him as 'just the same as me and our mother... shy and quiet and never had more than a couple of friends during his entire life'. When they were children, they wouldn't play with each other ('He was obsessed with balls...He would spend hours watching snooker games on TV just to watch the balls go around'). He also had a movement tick 'rocking back and forth'.

Our patient was treated with 50 mg/day sertraline and 5 mg/day olanzapine and after 15 days of hospitalisation, she was discharged from hospital with a BMI of 15.8 kg/m². There was an improvement in mood, behaviour and eating patterns. The choice of serotonin reuptake inhibitor was based on its previous efficacy and good tolerability. The antipsychotic was chosen to sedate, given the first hypothesis of a psychotic disorder, and to increase the patient's appetite. However, metabolic side effects are more frequent with olanzapine than other antipsychotics. Therefore, during follow-up the pharmacological treatment should be revised.

Given the long-term deficiencies in communication and social interaction, with emotional difficulties and overload of sensory processing, the primary diagnosis of ASD appeared to be the most plausible. Concomitantly, the patient had other symptoms that lasted for more than 2 weeks and caused impairment in her normal daily functioning, characterised by the feeling of sadness, loss of appetite with a refusal to eat with weight loss, obsessions and repetitive behaviours among other described signs, and symptoms compatible with a comorbid depressive episode.⁷⁻¹⁰

GLOBAL HEALTH PROBLEM LIST

- ▶ ASD might easily go under and/or misdiagnosed, especially among women and given their heterogenous presentation.
- ▶ The diagnosis of ASD is far more challenging in adulthood than childhood.
- ▶ Individuals with ASD are often diagnosed with a comorbidity. The comorbidity might be the cause that leads the patients and/or their families to ask for professional help.
- ▶ Improperly diagnosing these individuals with a psychotic or other disorder might happen, particularly in an emergency setting.

Global health problem analysis

ASDs are characterised by persistent deficits in social communication, including non-verbal behaviours and social interaction in multiple contexts, namely with difficulties in developing and maintaining relationships. In addition to deficits in social communication, the diagnosis requires the presence of restricted and repetitive patterns of behaviour, interests or activities. Considering that the symptoms change with the development, which enables them to be masked by compensatory mechanisms, the diagnostic criteria can be fulfilled based on retrospective information, although the current presentation should cause significant impact.^{7-9,10} According to DSM-5, within the spectrum are included the autism disorder (AD), Asperger syndrome (AS) and pervasive developmental disorder not otherwise specified (PDD-NOS). Previously, they were subcategorised on the DSM-IV, with their differences residing in severity. AD is the

most severe as it is commonly associated with speech delay and intellectual disability, besides social and communication difficulties, as well as abnormal interests. Less severe situations correspond to individuals suffering from AS presenting difficulties mostly on social interaction and circumscribed interests, most of the time without learning or language disability. Individuals with PDD-NOS present with an even milder form of the disease, usually with only social and communication challenges. The DSM-5 grouped all these categories into one spectrum and specified their gravity and behavioural domains, namely social and communication challenges, and unusual, repetitive and restricted interests.^{7 8 10 11} Women can easily go underdiagnosed or even misdiagnosed as their clinical presentations may be more subtle and they are more likely to be able to mask social difficulties, known as camouflaging, and thus, not meeting the current diagnostic criteria. Socially speaking, women tend to internalise their problems. Introspection, shyness or even a particular interest such as literature could easily pass unnoticed as accepted behaviour within them.¹⁻³

It is fundamental to note that diagnosing ASD is far more complex in adulthood than during childhood as it is based on detailed developmental history.¹¹ Also, the less evident the symptoms, the harder it is to diagnose ASD. The ADOS-2 was not performed. However, ASD was the most likely diagnosis as our patient fulfilled all five symptom clusters according to DSM-5. The patient exhibited poor social communication and interaction skills in all the subdomains, having trouble with social reciprocity and non-verbal communication. She also lacked capability in developing, understanding and maintaining relationships. Since childhood she had difficulties in forming and maintaining friendships, rather showing preference for solitary activities. In fact, the inability to relate and integrate with her peers during middle school was the reason for her to drop out. Her social impairment kept with her through adulthood. She was incapable of forming intimate relationships and only socialised with her closest family members. Stereotyped and repetitive behaviours, insistence on sameness, and hypersensitivity in sensory inputs were present since early development, fully manifesting later in life and causing significant impairment in her current functioning. A special interest, although not peculiar, in books was reported, as well as an increase in obsessive-like behaviours at home during stressful and negative periods of her life. Changing and adapting to new routines was very challenging, with a greater need for predictability and control in all situations. The transition from elementary to middle school and getting a job proved to be quite difficult. She ended up being fired from both of her two waitressing jobs, shortly after starting them. These series of events prompted her to stay at home depending on her mother. There were other elements from her childhood that supported this diagnosis, such as motor stereotypies. Tactile and acoustic hypersensitivity were also described by the patient and her mother, ever since she was a child, without remission. The symptoms were also not better explained by intellectual disability or global developmental delay. She most likely had AS while preserving verbal fluency and having no difficulties in acquiring language or any other learning disabilities. Additionally, she had a family history of ASD, with her own mother and brother having been diagnosed with it. As a disorder that aggregates in families, our patient had a higher probability of inheriting ASD. Both the mother and two children share the same diagnosis in different ranges of severity. The mother, on the milder end of the spectrum, managed to hold a stable job and raised two children from a previous relationship. Her brother was also able to complete school, get a job and live

on his own. There was little information regarding his interpersonal relationships. However, our patient seemed to be on the most severe level of the ASD spectrum. Till the present, she had not been able to complete education, or maintain a job. Her only source of communication and affection came from her mother. Mothers with ASD can be highly resilient and are able to overcome their difficulties to put their child's needs first; however it is a field of study that has been little researched. During her hospitalisation a brain MRI scan was not performed as the brain CT showed no abnormalities and the patient refused repeating other imaging examination. A brain MRI would have been more appropriate as there is literature centred on the use of structural MRI (sMRI) and functional MRI (fMRI) to identify variations in patients with ASD. An sMRI might have presented an increase in total brain volume, an increase in intrahemispherical white matter volume and a decrease in interhemispherical (ie, corpus callosum) white matter volume. An fMRI might have presented an underconnectivity in distributed cortical networks promoting symptoms of ASD. However, future research in this field is required with larger sample sizes and less heterogeneity in the chosen methodology.¹²

As a neurodevelopmental disorder, its expression develops continuously throughout life. In most cases, the onset of a medical, neurological or psychiatric disorder can be the first feature that one should be aware of when making the differential diagnosis between signs and symptoms related to autism and those related to a comorbidity.⁹ In the presented case, we considered a psychiatric comorbidity as the precipitant factor for the patient's breakdown. Hence, our first hypothesis was the presence of a depressive recurrent episode, as she had two previous episodes, without any history of hypomanic or manic episodes. They occurred during her adolescent and adult years, lasting for months until she was treated with an antidepressant. Both seemed to have been triggered by negative life events. The following and current depressive episode happened almost a decade later. It is important to mention that the less severe presentations of ASD have a higher risk of depressive episodes, generally happening during negative or stressful periods. Behavioural problems are, quite often, the visible expression of mood disorders.^{9 11} Yet, instead of manifesting common symptoms of depression, she was irritable, restless and aggressive when interviewed in the emergency room. The behavioural maladjustment was interpreted as the way she found to express her grief and sorrow. Other signs and symptoms favouring this hypothesis were collected from her mother and included seeking refuge in her bedroom, poor self-care and anorexia leading to weight loss. The patient's cognitive ability was not necessarily protective but a possible risk factor for depression.¹³ She could easily fall into comparison with her peers. She also had a good insight into her own limitations, such as her professional failure and inability to establish and maintain satisfying relationships. An eating disorder (ED) as a comorbidity was considered a second hypothesis given the high prevalence of autistic traits and ASD among women suffering from anorexia nervosa.¹⁴⁻¹⁶ In this case, a pre-existing extremely low BMI (13.5 kg/m²), associated with food refusal for several days in a row, resulted in significant weight loss and favoured the diagnosis of an ED. However, she complied during inpatient treatment with the prescribed meal plan as well as the frequent recordings of her weight, without resistance or avoidance. The patient denied fear of gaining weight and, allegedly, thought she was too underweight, demonstrating awareness. Therefore, this hypothesis was excluded. The possibility of an obsessive-compulsive disorder (OCD) was also considered as a comorbidity, considering the patient history of compulsive-like behaviours. That condition is

more frequent among patients with ASD than in the general population. The high comorbidity between OCD and ASD is suggestive of overlapped aetiological mechanisms. To distinguish between ASD and OCD it is important to note that in OCD, the obsessions are intrusive, unacceptable, uncontrollable and egodystonic, hence the expected resistance towards them. However, in ASD such behaviour is not verified, unless OCD appears as a comorbidity. Themes such as contamination, pathological doubt, sexual fantasies, aggressive thoughts and superstitions are most frequent among patients with OCD. On the other hand, showing a particular interest towards collecting things; reading specific literary themes, playing with, or hitting objects are most frequent among patients with ASD. The role of compulsion in OCD is to prevent or reduce the uneasiness caused by the obsession. However, in ASD, repetitive behaviours are pleasurable or distressful.^{17 18}

Finally, the diagnosis of psychosis was considered in the emergency setting. Individuals with ASD seem to be at greater risk of developing psychotic disorders than those in the general population.¹⁹ Even for an experienced psychiatrist, it might be difficult to clinically distinguish between ASD and schizophrenia spectrum disorders.¹⁸ Schizophrenia can easily be misdiagnosed in adults suffering from ASD.²⁰ The disruption in verbal communication, especially receptive or expressive language, as well as the worsening of 'bizarre' and 'incomprehensible' behaviours in stressful contexts, might be noted in both disorders.^{19 21} At the emergency room, the patient had difficulty in explaining her behaviour at home and her lack of compliance with the assessment prompted the suspicion of a psychotic disorder. When told about the need to be subjected to diagnostic testing, she initially refused to leave her mother and later on became agitated and physically aggressive. The patient's low weight and refusal to eat for several days could have been related to a persecutory delusion (poisoning). Deficits in social interaction and reduced emotion resonance overlap between both disorders, making it once again difficult to attribute the patient's avolition, social disconnection and emotional impairment to either schizophrenia or an ASD. Our research revealed no evidence of psychotic symptomatology, both in the past and present. However, at the emergency room it would have been difficult not to consider the diagnosis of a psychosis given her lack of compliance, poor self-care, abnormal eye gaze and food refusal that could have signalled a delusion of poisoning.

It must be noted that to date no 'cure' for autism has been found, despite claims in that direction. A comprehensive assessment of a patient should take all different levels, aspects and interactions into account in order to tailor an individualised treatment plan.⁹ As previously noted, co-occurring mental health disorders are common among the ASD population. Therefore, treatment is directed at symptoms of co-occurring disorders, rather than the symptoms of ASD directly. Risperidone and aripiprazole are atypical antipsychotics approved by the Food and Drug Administration (FDA) to treat irritability and by the European Medicines Agency to treat agitation in children and adolescents. However, both are associated with side effects, such as sedation, increased risk of movement disorders and weight gain, limiting their use. Methylphenidate and atomoxetine are also approved by the FDA to treat *attention deficit hyperactivity disorder* symptoms. Sleep disruption, nausea and anorexia are commonly reported side effects. Serotonin reuptake inhibitors are prescribed for the treatment of depression, anxiety and OCD symptoms in the general population. However, their efficacy in the ASD population is poorly established.

A very heterogeneous presentation is the hallmark of ASD, ranging from extremely severe phenotypes (usually recognised

up until 2 years old due to the severe difficulties in language learning), to the less severe ones (that present mostly with subliminal signs and symptoms that could easily go unnoticed). Women, whose peculiarities associated with the diagnosis are most often socially acceptable, might easily go underdiagnosed and misdiagnosed, even when evaluated through the lens of a mental healthcare professional. It is not infrequent to reach adulthood without a single diagnosis, especially when these features are combined with an average or above-average cognitive capability that allows them to camouflage, learn by social imitation and behave as expected by society. The diagnosis is usually made many years after their first contact with mental health services. The inability to form or initiate new relationships and to deal with changes or significant losses are key to diagnosing these individuals. When confronted with their innate difficulties and limitations to surpass adult milestones, they might suffer from other psychiatric comorbidities such as depressive disorders, possibly recurrent and of substantial gravity. In fact, the presence of psychiatric comorbidities during all stages of life within these groups of individuals are also the rule and not the exception, which makes both the diagnosis and treatment even more of a challenge. Hence, a recovery plan and individual treatment care throughout life are imperative.⁹

Learning points

- ▶ The risk of delayed, misdiagnosed and, consequently, mistreated autism spectrum disorder (ASD) is increased among high-functioning women.
- ▶ There could be catastrophic consequences related to the missed, late or wrong diagnoses among people who suffer from ASD.
- ▶ Patients with ASD have a higher prevalence of psychiatric comorbid conditions compared with the general population.
- ▶ The inability of patients with ASD to express their emotions and thoughts makes the psychiatric diagnosis more challenging.
- ▶ It is imperative to increase the suspicion and alertness for ASD and to better screen these patients.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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