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U sjeni terapijske promjene: distonične reakcije tijekom križne titracije atipičnih antipsihotika u djeteta s poremećajem iz spektra autizma – prikaz slučaja

/ In the Shadow of a Therapeutic Switch: Dystonic Reactions During Cross-Titration of Atypical Antipsychotics in a Child With Autism Spectrum Disorder – A Case Report

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Poremećaj iz spektra autizma (PSA) obilježavaju teškoće u socijalnoj komunikaciji te prisutnost ograničenih i repetitivnih obrazaca ponašanja, interesa i aktivnosti. U kliničkoj praksi psihomotorički nemir, razdražljivost i agresivna ponašanja često zahtijevaju farmakološko liječenje. Prikazujemo devetogodišnjeg dječaka koji je u višegodišnjem ambulantnom praćenju dječjeg i adolescentnog psihijatra pod dijagnozama autizma u djetinjstvu i hiperkinetičkog poremećaja. Dominantne tegobe bile su

Autism spectrum disorder (ASD) is characterized by difficulties in social communication and the presence of restricted and repetitive patterns of behavior, interests, and activities. In clinical practice, psychomotor agitation, irritability, and aggressive behaviors often require pharmacological treatment. We present the case of a nine-year-old boy who had been followed for several years on an outpatient basis by a child and adolescent psychiatrist with diagnoses of childhood autism and hyperkinetic disorder. His predominant difficul-

psihomotorički nemir, impulzivnost i poteškoće emocionalne regulacije, uz narušeno svakodnevno funkcioniranje. Zbog opisanih poteškoća započeto je liječenje niskim dozama aripiprazola uz postupnu titraciju. Tijekom praćenja zabilježeno je pogoršanje psihomotoričkog nemira te je indicirana zamjena aripiprazola risperidonom metodom križne titracije. Nekoliko dana nakon uvođenja risperidona roditelji su zamijetili epizode nevoljnih pokreta u trajanju od nekoliko sekundi, obilježene lateralnim kretnjama vrata u oba smjera te generaliziranim grčenjem tijela uz ekstenziju laktova i koljena, fleksiju šaka i retrofleksiju vrata. Dječak je otprije pokazivao stereotipne pokrete, što je uz nemogućnost verbalnog opisivanja simptoma bilo izazov u razlikovanju distoničnih reakcija od pogoršanja stereotipija. Zbog sumnje na ekstrapiramidne nuspojave započeto je postupno ukidanje antipsihotične terapije te je učinjen pregled neuropedijatra uz elektroencefalografiju. Nalazi nisu upućivali na neurološku podlogu simptoma, a nekoliko tjedana nakon ukidanja terapije opisani fenomeni u potpunosti su se povukli. Iako vremenska povezanost pojave distoničnih reakcija s razdobljem križne titracije upućuje na moguću ulogu promjene dopaminergične neurotransmisije, ostaje nejasno bi li se razvile i tijekom sekvencijske zamjene antipsihotika. U obzir treba uzeti i farmakogenetske čimbenike jer je pokazano da varijacije gena *CYP2D6* utječu na izloženost antipsihoticima, a novija istraživanja u djece s PSA-om pokazuju da i druge genetske varijante mogu utjecati na izloženost risperidonu. Prikazan slučaj naglašava važnost individualiziranog pristupa u liječenju djece s poremećajem iz spektra autizma.

ties were psychomotor agitation, impulsivity, and problems with emotional regulation, accompanied by impaired everyday functioning. Because of these problems, treatment with low-dose aripiprazole was initiated and gradually titrated. During follow-up, a worsening of psychomotor agitation was observed, and replacement of aripiprazole with risperidone using a cross-titration method was indicated. Several days after risperidone was introduced, the parents noticed episodes of involuntary movements lasting a few seconds, characterized by lateral neck movements in both directions and generalized body stiffening with elbow and knee extension, flexion of the hands, and retroflexion of the neck. The boy had previously exhibited stereotyped movements, which, together with his inability to verbally describe symptoms, made it challenging to distinguish dystonic reactions from an exacerbation of stereotypies. Due to suspicion of extrapyramidal side effects, gradual discontinuation of antipsychotic therapy was started, and the boy was examined by a child neurologist, including electroencephalography. The findings did not point to a neurological basis for the symptoms, and several weeks after discontinuation of therapy, the described phenomena completely resolved. Although the temporal association between the onset of dystonic reactions and the period of cross-titration suggests a possible role of changes in dopaminergic neurotransmission, it remains unclear whether they would also have developed during a sequential switch of antipsychotics. Pharmacogenetic factors should also be considered, as *CYP2D6* gene variants have been shown to affect antipsychotic exposure, and more recent studies in children with ASD indicate that other genetic variants may influence risperidone exposure as well. The presented case underscores the importance of an individualized approach in the treatment of children with autism spectrum disorder.