

The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided. The patient described in this column is a composite with characteristics of several real patients.

Refractory social anxiety disorder

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When first seen, our patient was 27 years old and had severe social and performance anxiety dating back to elementary school. She dropped out in grade 11 and was unable to work owing to severe social anxiety. She was housebound unless accompanied, and she avoided speaking with authority figures, including her child's teachers. She had a history of chronic depression, panic disorder, agoraphobia and obsessive-compulsive disorder (OCD). She used marijuana 3–4 times per week, but denied using alcohol.

The patient was initially treated with citalopram, titrated to 80 mg/d, but she stopped after 6 months owing to lack of efficacy. When she returned to the clinic 2 years later with similar symptoms, she was prescribed paroxetine, titrated to 80 mg/d. Paroxetine has the highest pooled effect size in its class for the treatment of social anxiety disorder (SAD; 0.49, moderate efficacy).^{1–3} Doses of 20–60 mg/d are suggested; however, higher doses have been used off-label to treat other disorders.^{4,5} Paroxetine improved our patient's mood but only minimally improved her SAD. Augmentation with quetiapine and risperidone were ineffective. There is good evidence supporting the use of quetiapine for generalized anxiety disorder and OCD augmentation, but it is not recommended for SAD based on negative randomized controlled trials (RCTs).⁶ There is evidence to support using adjunctive risperidone or aripiprazole in SAD.⁶ Our patient remained housebound, her second relationship ended, and her son was removed from her home by Children's Aid owing to poor supervision. She eventually regained custody, but had to attend parenting classes. She began augmentation with clonazepam, which garnered some improvements; however, her avoidance behaviour re-

mained. Although monotherapy with clonazepam is considered a second-line treatment for SAD,⁶ adjunctive clonazepam has demonstrated mixed results.^{7,8}

Pregabalin is structurally related to the anticonvulsant gabapentin, but seems to have a novel mechanism of action. Unlike other anxiolytic agents, it inhibits calcium entry into the nerve terminals, reducing neurotransmitter release of various excitatory neurotransmitters, including glutamate and noradrenalin.^{9–11} Abnormalities in γ -aminobutyric acid and glutamate have been associated with various anxiety disorders, and evidence supporting the use of anticonvulsants to treat SAD is emerging in open-label studies and RCTs.¹² Pregabalin monotherapy has demonstrated efficacy in 3 RCTs^{13–15} at doses of 450 and 600 mg/d¹⁴ and is recommended as a first-line treatment of SAD at these doses.⁶ The onset of action of pregabalin is typically seen within the first week; however, this agent appears to have fewer adverse cognitive effects than benzodiazepines. The most commonly reported adverse events are dizziness, drowsiness, weight gain and peripheral edema.¹¹ According to a recent systematic review, there is little evidence to suggest that pregabalin has the potential for abuse; however, there have been case reports of pregabalin abuse in individuals with a history of substance use disorders.¹⁶

Since our patient's functioning continued to be impaired, adjunctive clonazepam was discontinued. Pregabalin was then added to augment paroxetine, and within 6–8 weeks, the patient's symptoms of social anxiety were noticeably improved. She was able to speak with her child's teachers and completed a high school equivalency program. She then enrolled in a paralegal course. She is now able to more effectively deal with authority figures and social situations.

Given the substantial functional impairment associated with SAD, includ-

ing reduced workplace productivity, increased costs and reduced health-related quality of life, it is essential for clinicians to evaluate and monitor disability and quality of life in these patients, independent of their symptomatic changes.¹⁷ In our patient, significant deficits developed at a young age, including lack of education and poor social interaction skills such that it was difficult for her to initiate and maintain friendships or romantic relationships. Although her pharmacological treatment played a key role in her improvement, facilitating other pieces, such as education, social skills and career development, was also a major component of her treatment.

Typical augmentation strategies have limited effectiveness in SAD, an area where there is little evidence for the treatment of refractory patients. Although there may not be strong evidence in support of pregabalin in refractory SAD, it was quite effective in our patient. Since SAD is a disorder that results in impairment early in life, it is common for patients to have had impaired or delayed social development. In addition to the persistent pharmacotherapy trials, working on functional recovery was a very important component in the eventual good clinical outcome of this case. This case also highlights the need for further clinical evidence and guidelines for next-step treatments in SAD to strengthen the level of care we can provide to these patients.

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