BACKGROUND
The risk of abnormal bleeding with serotonin reuptake inhibitors (SSRIs) has been recognized since a landmark British study demonstrated the association between upper gastrointestinal bleeding and SSRIs. The risk of bleeding is directly correlated with the affinity of the antidepressant for the serotonin transporter, with adjusted odds ratios varying from 9.4 for Clomipramine to 1.8 for Maprotiline. Furthermore, the risk of bleeding is increased when SSRIs are used concomitantly with antplatelet drugs. It has been suggested that serotonin reuptake inhibitors induce subsequent depletion of intra-platelet serotonin which in turn, interferes with platelet aggregation to increase the risk of bleeding. The duration of SSRI treatment leading to bleeding such as hematemesis, epistaxis, and petechiae has been found to be between 26 and 40 days. There is insufficient evidence to guide the pharmacological treatment of anxiety in patients with underlying hematological conditions resulting in platelet dysfunction, which makes the following case significant.

AIM
To describe the management of a complex patient diagnosed with generalized anxiety disorder, social phobia, obsessive compulsive disorder, and alcohol abuse who required anxiolytic therapy concomitant with platelet dysfunction.

discase description
50-year-old divorced Caucasian female and mother of two grown-up children, who had been working as a government employee for 27 years, presented with anxiety symptoms. The initial onset of her anxiety symptoms occurred when she was approximately 9 years of age. The patient complained of excessive worrying about "something dreadful happening all the time," tension, inability to relax, and irritability. These symptoms were accompanied by neck and shoulder muscle aches, teeth clenching, sleep difficulties and impaired concentration. The patient also reported longstanding anxiety in social settings where she described feeling self-conscious and scrutinized. The patient reported a fear of public speaking and described significant anxiety symptoms including palpitations, sweating, and "butterflies in my stomach" when she had to speak at staff meetings. In addition, the patient avoided eating in restaurants unaccompanied due to anxiety. The patient also reported a compulsion to do things in a certain order (e.g., she had to open curtains first, let the dogs out, turn on the radio, and then have her breakfast). The patient had an underlying fear that if the order was not followed, then "something will go wrong, I will be testing fate." The patient would avoid stepping on the cracks while walking on the pavement as she was concerned this would result in harm to her family. The patient also felt compelled to count the holes in the ceiling as she believed this would protect her family from harm. These symptoms were egodystonic; the patient felt distressed by them but unable to resist them. Since the age of 14, the patient reported consuming alcohol on a regular basis. She was presently drinking 2-3 glasses of wine daily, but there were occasions where the patient would drink excessively leading to recurrent blackouts. The patient acknowledged that the drinking led to relationship difficulties but denied any impairment at work. The patient acknowledged her drinking to be a problem and was receiving addiction counselling. The patient reported attempting suicide at 44 years of age, by means of a drug overdose following the breakup of her marriage. The patient was treated for depression by her family doctor with venlafaxine but she denied any inpatient treatment. She was also treated with thyroid for hypothyroidism. At this time, the patient’s thyroid stimulating hormone was within the normal range. Of note in her past medical history, was bruising resulting from treatment with venlafaxine for which the patient was seen by a hematologist. She had tested negative for VonWillebrand’s disease, Factor VIII, IX and X deficiencies. The patient also tested negative for antiphospholipid and antinuclear antibodies. The patient’s INR and platelet count were within the normal range. The patient reported receiving a stimulant as an adjuvant to her platelet aggregation studies suggested a qualitative platelet defect due to "absence of release of ADP and Epinephrine." In the report, the hematologist suggested that the venlafaxine was contributing to the platelet dysfunction to result in bruising. It was unclear from the report whether the effect on platelet aggregation was confined to venlafaxine or other antidepressants could cause the same effect. We prescribed cilostazol (20 mg daily) for the management of her anxiety symptoms. At the 4 week follow-up, she reported that her anxiety symptoms had subsided and she was feeling “very calm”. The patient had also reduced her alcohol consumption from 2-3 glasses of wine daily to the same amount per week. The patient reported headache but no bruising. Two weeks later, the cilostazol was discontinued by the family physician due to significant bruising, and the patient was switched to escitalopram (10 mg daily). The patient remained on escitalopram for approximately 4 weeks before its discontinuation, as the bruising was spreading all over the patient’s body. However, the patient reported improvement in anxiety to the point that she was able to stop drinking alcohol. The patient was instructed to remain medication-free for 2 weeks during which time, the bruising subsided.

case management
She was then started on clomipramine (25mg BID) to see if she would respond any differently to tricyclics compared to the newer antidepressant medications. At the 3 week follow-up and on a relatively low dose of clomipramine, the patient reported a reduction of her anxiety symptoms without a recurrence of bruising. However, at a subsequent follow up 4 weeks later, the patient was again, all covered with bruises with a subgluteal hematoma resulting from a fall. The patient’s anxiety symptoms and alcohol abuse were still in remission but the clomipramine was immediately discontinued. The patient was again advised to remain medication-free for 2 weeks to allow the bruising to subside. The patient was concerned that she would relapse on alcohol as a self-medication strategy if her anxiety symptoms were to recur. Following the medication free period, she was started on buspirone (10 mg BID) and followed bi-weekly. Buspirone was considered a safer anxiolytic compared to benzodiazepines in view of patient’s active alcohol addiction. The patient’s anxiety symptoms showed an initial response to buspirone, but the dose was gradually increased to 30 mg BID to treat residual anxiety. The patient tolerated the medication well without any recurrence of bruising. She was followed in clinic for 6 months while on buspirone before being discharged to her family doctor. During this time, the patient’s anxiety symptoms and alcohol abuse remained in remission.

conclusion
Buspirone may be a safer anxiolytic alternative to benzodiazepines in patients with substance use disorders due to its apparent lack of abuse liability. Just as substance abuse may be a “self-medication” strategy in some patients with untreated anxiety disorders, the presence of untreated anxiety disorders may increase the risk of substance abuse disorders. As such, successful pharmacological treatment of underlying anxiety symptoms could help with comorbid substance use as demonstrated in the current case.

references

The case described above was published and can be accessed & cited as follows: