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Prolonged Use of Fluoxetine, Multiple Skeletal Fractures, and Some Gene Mutations

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Dear Sir,

We had previously reported the case of a 33 year old female patient, who was suffering from depression and remitted with fluoxetine 20mg/day(1). At the end of 8 years of using fluoxetine 20 mg/day, three spontaneous fractures occurred within short intervals. The first fracture appeared on the right radiusand distal third of the ulna. After 8 months, the second fracture occurred at the distal third of the os cruris on the spinal cord. One and half years later a fragmented fracture was seen at the collum chirurgicum and tuberculum majus of promiximal third of the right humerus. During the operations there were no biochemical abnormalities other than slight elevations of LH and FSH. The bone densitometry was within normal limits. The densitometry was measured (-1.5) only for the corpus of the femur. The patient was diagnosed with initial osteopenia(1). We now have performed gene analysis of the same patient and have found that there was COL1A1, heterozygote (adult form transporter) and vitamin D receptor resistance, heterozygote.

Discussion

In the previously presented case the patient was relatively young and three spontaneous fractures appeared within short intervals at the eighth year of using SSRIs. Ziere et al (2008) and Williams and Insogna (2009) have reported that osteoporosis could occur due to the administration of SSRIs (2,3). SSRIs and TCAs can lead to bone fractures especially in the older patients (4). Fractures appear in bones other than vertabra with longer durations of SSRI use,but not with TCA use.

Depression and antidepressant treatments are relevant with regard to bone pathologies. SSRIs have been associated with lower bone mineral density (BMD), increased rates of bone loss, and increased rates of fracture after falls (5).

We propose that there might be a relationship between the prolonged use of fluoxetine and mutations of the related genes which may interfere with normal bone remodelling causing both decreased BMD and also structural changes that causes decreased bone strength and an increased susceptibility for fractures.

There is a study including the relationship between 5-HT2 receptor polymorphism, response to antipsychotic medication, and vitamin D receptor variants (6). We think that SSRIs should also be included in this relationship because antipsychotic medications have effects on serotonin similar to those of SSRIs.

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References:

1. Ceylan ME, Maner F. Long-term use of fluoxetine and multiple skeleton fractures. Eur J Clin Pharmacol 2010;66(12):1279
2. Ziere G, Dieleman JP, van der Cammen TJ, Hofman A, Pols HA, Stricker BH. Selective serotonin reuptake inhibiting antidepressants are associated with an increased risk of nonvertebral fractures.J Clin Psychopharmacol 2008;28(4):411-7
3. Williams BO, Insoqna KL. Where WNTS went: the exploding field of Lrp5 and Lrp6 signaling in bone. J Bone Miner Res 2009; 24(2):171-8
4. Ziere G, Dieleman JP, van der Cammen TJ, Hofman A, Pols HA, Stricker BH. Selective serotonin reuptake inhibiting antidepressants are associated with an increased risk of nonvertebral fractures. Evid Based Ment Health 2009;12(1):26.
5. Haney EM,Warden SJ, Bliziotes MM. Effects of selective serotonin reuptake inhibitors on bone health in adults: time for recommendations about screening, prevention and management? Bone 2010;46(1):13-7
6. Tanigawara Y, Iketani O, Yamayoshi Y. Variability in drug response caused by the genetic polymorphisms of receptors Nippon Rinsho 2002;60(1):51-7