Apply your psychiatric skills to managing rheumatoid arthritis

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Joint disease is the most common cause of disability and the source of considerable psychological distress. In the United States, 50 million adults complain of joint pain; in 2007, 1.5 million people suffered from rheumatoid arthritis (RA). A chronic inflammatory autoimmune disease of joints, RA can involve almost all organs.[1]

The link to mental illness

Mental illness in RA patients often is underdiagnosed and undertreated. These missed opportunities contribute to poor compliance with medical therapy, suboptimal therapeutic response, greater disability, and diminished quality of life.[2]

Limited mobility, chronic pain, sleep disturbance, fatigue, and immunological factors predispose RA patients to depression and anxiety.[3] The proinflammatory cytokines, tumor necrosis factor-α (TNF-α), interleukin 1 (IL-1), IL-6, and interferon-g have a role in inducing affective symptoms. There also is a relationship between an elevated IL-17 level and anxiety.

Research substantiates a relationship between RA and depression.[3] The prevalence of affective illness is approximately 6% among the general population, and 13% to 30% among RA patients.[4] In arthritic populations, 52% exhibit depression and anxiety; joint discomfort contributes to insomnia in 25% to 42% of cases.[4]

Arthritic pain persists despite suppressed inflammation, which suggests involvement of the CNS.[5] Increased levels of IL-6 and TNF-α can cause insomnia and affect pain perception.[6] Decreased conditioned pain modulation, a lower pain threshold, and pressure pain intolerance lead to increased pain awareness and heightened discomfort.

How can you help your patient who has RA?

Because the focus of care in RA is on the disease's physical attributes, psychiatric symptoms sometimes receive less attention.[7] And because arthritic symptoms overlap with anorexia, weight loss, fatigue, pain, and insomnia, affective illness can go unrecognized.

Depression rating scales can overestimate affective illness, but a history and follow-up questionnaire can facilitate an accurate diagnosis of depression and help determine the need for, and type of, intervention.

Selective serotonin reuptake inhibitors (SSRIs) are considered first-line treatment of depression associated with RA.[7] Although SSRIs for RA can be administered to the maximum recommended dosage, titration is advised in accordance with patient response and tolerance.

Tricyclic antidepressants are not as well tolerated in RA, especially in older patients; however, they have more of an analgesic effect, even at lower dosages.

Joint disease activity and mood are associated with sleep disturbance, and vice versa.[5] Insomnia calls for patient education about sleep hygiene, avoiding caffeine and other stimulants, and an individualized appraisal of options for pharmacotherapy.

Alleviating RA pain is important for psychosocial health.[8] Although the medical team's emphasis should be on controlling inflammation to minimize joint damage and pain, be sure to address your RA patients' mood symptoms to improve the quality of their life.

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References

1. Centers for Disease Control and Prevention. Arthritis-related statistics. http://www.cdc.gov/arthritis/data_statistics/arthritis_related_stats.htm. Updated August 1, 2011. Accessed January 4, 2013.
2. Shih M, Hootman JM, Strine TW, et al. Serious psychological distress in U.S. adults with arthritis. J Gen Intern Med. 2006;21(11):1160-1166.
3. Sato E, Nishimura K, Nakajima A, et al. Major depressive disorder in patients with rheumatoid arthritis. Mod Rheumatol. 2013;23(2):237-244.
4. Wolfe F, Michaud K, Li T. Sleep disturbance in patients with rheumatoid arthritis: evaluation by medical outcomes study and visual analog sleep scales. J Rheumatol. 2006;33(10):1942-1951.
5. Fragiadaki K, Tektonidou MG, Konsta M, et al. Sleep disturbances and interleukin 6 receptor inhibition in rheumatoid arthritis. J Rheumatol. 2012;39(1): 60-62.
6. Lee YC, Lu B, Edwards RR, et al. The role of sleep problems in central pain processing in rheumatoid arthritis. Arthritis Rheum. 2013;65(1):59-68.
7. Dickens C, Creed F. The burden of depression in patients with rheumatoid arthritis. Rheumatology (Oxford). 2001; 40(12):1327-1330.
8. Courvoisier DS, Agoritsas T, Glauser J, et al. Pain as an important predictor of psychosocial health in patients with rheumatoid arthritis. Arthritis Care Res (Hoboken). 2012;64(2):190-196.

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References

1. Eley TC, Sugden K, Corsico A, et al. Gene-environment interaction analysis of serotonin system markers with adolescent depression. Mol Psychiatry. 2004;9(10):908-915.
2. Haber SN, Rauch SL. Neurocircuitry: a window into the networks underlying neuropsychiatric disease. Neuropsychopharmacology. 2010;35(1):1-3.
3. Frodl T, Bokde AL, Scheuerecker J, et al. Functional connectivity bias of the orbitofrontal cortex in drug-free patients with major depression. Biol Psychiatry. 2010; 67(2):161-167.
4. Woolley CS, Gould E, McEwen BS. Exposure to excess glucocorticoids alters dendritic morphology of adult hippocampal pyramidal neurons. Brain Res. 1990;531(1-2): 225-231.
5. Heim C, Nemeroff CB. The impact of early adverse experiences on brain systems involved in the pathophysiology of anxiety and affective disorders. Biol Psychiatry. 1999;46(11):1509-1522.
6. Isgor C, Kabbaj M, Akil H, et al. Delayed effects of chronic variable stress during peripubertal-juvenile period on hippocampal morphology and on cognitive and stress axis functions in rats. Hippocampus. 2004;14(5):636-648.
7. De Kloet ER, Vreugdenhil E, Oitzl MS, et al. Brain corticosteroid receptor balance in health and disease. Endocr Rev. 1998;19(3):269-301.
8. Philip AM, Kim SD, Vijayan MM. Cortisol modulates the expression of cytokines and suppressors of cytokine signaling (SOCS) in rainbow trout hepatocytes. Dev Comp Immunol. 2012;38(2):360-367.
9. Coplan JD, Lydiard RB. Brain circuits in panic disorder. Biol Psychiatry. 1998;44(12):1264-1276.
10. Anisman H, Merali Z. Cytokines, stress and depressive illness: brain-immune interactions. Ann Med. 2003;35(1):2-11.
11. Crowley JJ, Lucki I. Opportunities to discover genes regulating depression and antidepressant response from rodent behavioral genetics. Curr Pharm Des. 2005;11(2): 157-169.
12. Covington HE 3rd, Vialou V, Nestler EJ. From synapse to nucleus: novel targets for treating depression. Neuropharmacology. 2010;58(4-5):683-693.
13. Videbech P, Ravnkilde B. Hippocampal volume and depression: a meta-analysis of MRI studies. Am J Psychiatry. 2004;161(11):1957-1966.
14. Sandi C. Stress, cognitive impairment and cell adhesion molecules. Nat Rev Neurosci. 2004;5(12):917-930.
15. Hartley CA, Phelps EA. Changing fear: the neurocircuitry of emotion regulation. Neuropsychopharmacology. 2010;35(1): 136-146.
16. Kim DK, Lim SW, Lee S, et al. Serotonin transporter gene polymorphism and antidepressant response. Neuroreport. 2000;11(1):215-219.
17. Ueyama E, Ukai S, Ogawa A, et al, Chronic repetitive transcranial magnetic stimulation increases hippocampal neurogenesis in rats. Psychiatry Clin Neurosci. 2011; 65(1):77-81.
18. Irwin W, Anderle MJ, Abercrombie HC, et al. Amygdalar interhemispheric functional connectivity differs between the non-depressed and depressed human brain. Neuroimage. 2004;21(2):674-686.
19. McEwen BS. Physiology and neurobiology of stress and adaptation: central role of the brain. Physiol Rev. 2007; 87(3):873-904.
20. Gusnard DA, Raichle ME, Raichle ME. Searching for a baseline: functional imaging and the resting human brain. Nat Rev Neurosci. 2001;2(10):685-694.
21. Hulsebosch CE, Hains BC, Crown ED, et al. Mechanisms of chronic central neuropathic pain after spinal cord injury. Brain Res Rev. 2009;60(1):202-213.
22. Gottfried JA, Dolan RJ. Human orbitofrontal cortex mediates extinction learning while accessing conditioned representations of value. Nat Neurosci. 2004;7(10):1144-1152.
23 Arnone D, McKie S, Elliott R, et al. State-dependent changes in hippocampal grey matter in depression. Mol Psychiatry. 2012;1(8):1359-4184.
24. Brunoni AR, Lopes M, Fregni F. A systematic review and meta-analysis of clinical studies on major depression and BDNF levels: implications for the role of neuroplasticity in depression. Int J Neuropsychopharmacol. 2008;11(8): 1169-1180.
25. Maeng S, Zarate CA Jr. The role of glutamate in mood disorders: results from the ketamine in major depression study and the presumed cellular mechanism underlying its antidepressant effects. Curr Psychiatry Rep. 2007;9(6):467-474.
26. Vaidya VA, Fernandes K, Jha S. Regulation of adult hippocampal neurogenesis: relevance to depression. Expert Rev Neurother. 2007;7(7):853-864.
27. Lisiecka DM, Carballedo A, Fagan AJ, et al. Altered inhibition of negative emotions in subjects at family risk of major depressive disorder. J Psychiatr Res. 2012;46(2):181-188.
28. Mayberg HS, Lozano AM, Voon V, et al. Deep brain stimulation for treatment-resistant depression. Neuron. 2005;45(5):651-660.
29. Levkovitz Y, Harel EV, Roth Y, et al. Deep transcranial magnetic stimulation over the prefrontal cortex: evaluation of antidepressant and cognitive effects in depressive patients. Brain Stimul. 2009;2(4):188-200.
30. Schlaepfer TE, Lieb K. Deep brain stimulation for treatment of refractory depression. Lancet. 2005;366(9495):1420-1422.
31. Astrup, J. Energy-requiring cell functions in the ischemic brain. Their critical supply and possible inhibition in protective therapy. J Neurosurg. 1982;56(4):482-497.
32. Fletcher JM. Childhood mistreatment and adolescent and young adult depression. Soc Sci Med. 2009;68(5):799-806.
33. Warner-Schmidt JL, Duman R. VEGF as a potential target for therapeutic intervention in depression. Curr Opin Pharmacol. 2008;8(1):14-19.
34. Clark-Raymond A, Halaris A. VEGF and depression: a comprehensive assessment of clinical data. J Psychiatr Res. 2013;47(8):1080-1087.
35. Alonso R, Griebel G, Pavone G, et al. Blockade of CRF(1) or V(1b) receptors reverses stress-induced suppression of neurogenesis in a mouse model of depression. Mol Psychiatry. 2004;9(3):278-286.
36. Thomas RM, Peterson DA. A neurogenic theory of depression gains momentum. Mol Interv. 2003;3(8):441-444.
37. Jacobs BL. Adult brain neurogenesis and depression. Brain Behav Immun. 2002;16(5):602-609.