

Fibromyalgia symptoms and medication requirements respond to parathyroidectomy

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Background. *Fibromyalgia (FM), an ill-defined symptom complex, is characterized by musculoskeletal pain, headache, depression, fatigue, and cognitive decline, symptoms also seen commonly in primary hyperparathyroidism (PHP). Prevalence of concurrent PHP and FM and response to parathyroidectomy (PTX) of those with both conditions are unknown.*

Methods. *We reviewed prospective data of 4,000 patients with sporadic PHP who had PTX from 1995 to 2013 examining perioperative symptoms and medication usage for those with diagnosed FM. Cure was defined by normocalcemia at ≥ 6 months.*

Results. *Of 2,184 patients, 80 (4%) had a prior diagnosis of FM. Of evaluable FM patients, 97.3% had definitive cure of PHP. After PTX, 89% had improvement in ≥ 1 symptom attributed to FM, with improved cognition/memory most common (80%). Improvement in ≥ 2 , ≥ 3 , and ≥ 4 FM symptoms was appreciated by 71%, 43%, and 25%, respectively. Quality of life and wellness improved in $>50\%$. Postoperative use of drugs prescribed for FM often improved or resolved (narcotics, 77%; anti-inflammatories, 74%; "FM-specific medications," 33%; antidepressants, 30%); 21% discontinued all FM medications postoperatively.*

Conclusion. *FM is common in patients operated on for sporadic PHP. Of those with both conditions, after PTX 89% appreciate symptom response and 77% and 21% had a decrease in or discontinuation of medications, respectively. Before diagnosing FM, providers should exclude PHP, which is surgically correctable. (Surgery 2014;156:1614-21.)*

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SPORADIC PRIMARY HYPERPARATHYROIDISM (PHP) occurs in $\leq 0.5\%$ of the US population and is defined by persistent hypercalcemia in the presence of an inappropriately elevated parathyroid hormone level.¹ When the diagnosis is established, parathyroidectomy (PTX) often results in improvement of neuropsychiatric symptoms, including fatigue, mood swings, irritability, anxiety, depression, difficulty concentrating, memory loss, and sleep disturbance.² Definitive operative correction of PHP has been shown to improve quality of life,³ decrease the risk of long bone fracture,⁴ prevent the development of kidney stones,⁵ and slow the

progression of cardiovascular disease.⁶ When performed by experienced surgeons, cure after PTX is achieved in 95–99% of patients.⁷

Fibromyalgia (FM) is characterized by chronic widespread pain and arthralgias in addition to systemic manifestations that include mood alteration, fatigue, depression, cognitive dysfunction, and sleep disturbance.⁸ The prevalence of FM ranges from 0.7–6% depending on region, with women affected more often (75–90%).⁹ Age at diagnosis is usually between 20 and 50 years, with incidence increasing with age to affect $\leq 8\%$ of adults by age 80.¹⁰ Etiology relates to sensory sensitization by the central nervous system and augmentation of descending inhibitory pain pathways leading to increased response to painful stimuli, further exacerbated by deficiencies in the neurotransmitters norepinephrine and serotonin.^{11,12} Altered autonomic nervous system function contributes to fatigue, anxiety, and sleep disturbance with decreased production of growth hormone and insulin-like growth factor-1.¹² Dysfunction of serotonin reuptake pathways in the central nervous system may also lead to depression.¹¹

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The diagnosis of FM is clinical and is based typically on assessment of pain using the widespread pain index and symptom severity scale scores.¹³ Additional diagnostic criteria include the presence of symptoms at a similar level for ≥ 3 months, and the absence of a medical disorder that could otherwise explain the pain; hence, it is a diagnosis of exclusion.¹³ Although a number of inflammatory diseases are included in the differential diagnosis, including rheumatoid arthritis, systemic lupus erythematosus, polymyalgia rheumatica, myositis, ankylosing spondylitis, neuropathy, and even hypothyroidism, current diagnostic guidelines do not include routine evaluation of serum calcium to exclude PHP as a potential etiology.^{13,14} Treatment modalities involve cognitive-behavioral therapy and chronic use of pharmacologic agents, including anti-inflammatory medications, narcotics or other analgesics, antidepressants, calcium channel modulators, anticonvulsants, and muscle relaxants.¹¹

An economic burden, estimated at tens of thousands of dollars per patient with FM, further highlights the importance of accurate diagnosis and treatment of patients with chronic pain.¹⁵ Indirect costs include loss of productivity, unemployment, retirement, or disability, with an estimated 35% of patients with FM receiving social security disability at an annual incidence of 3.4%.^{15,16} FM health care expenditures correlate with severity of disease and presence of concomitant illness.¹⁵

Although FM and PHP have many overlapping symptoms (fatigue, musculoskeletal pain including myalgias, arthralgias and ostealgias, cognitive changes, short-term memory loss, depression, and headache), the prevalence of concomitant PHP and FM is unknown. The outcome of parathyroid surgery in patients with concomitant FM and PHP is also unknown. It was our hypothesis that patients with both diagnoses who undergo PTX for PHP would not have substantial symptom relief or decreases in specific preoperative medication use.

METHODS

We queried retrospectively a prospective PTX database, maintained with internal institutional review board approval (PRO08090450 and PRO11020368) and containing >4,000 patients, to identify all those who underwent PTX for sporadic PHP with a concomitant diagnosis of FM from January 1, 1995, to December 31, 2013, by 1 of 4 academic endocrine surgeons. All patients had preoperative confirmation of the PHP biochemical diagnosis and were offered

PTX according to symptoms and the current National Institutes of Health guidelines at the time of operation.

The charts of those PHP patients with a prior diagnosis of FM were reviewed to capture patient demographics, further perioperative clinical data, date of FM diagnosis, and specialty of the physician diagnosing FM, and preoperative and postoperative medication use (with dosage and frequency of administration) prescribed for symptoms attributed to FM. For the purposes of comparison, we identified calcium channel modulators, anticonvulsants, and muscle relaxants as "FM-specific medications" to differentiate them from antidepressants and from narcotic or anti-inflammatory medications, which are also taken frequently by PHP patients. Six patients were excluded for prior parathyroid exploration, histologic parathyroid carcinoma, follow-up of <6 months, or irretrievable operative, pathology, or laboratory records.

Symptoms were assessed during the initial clinic evaluation and again at the 6-month follow-up visit. Starting in 2011, subjective symptoms were also assessed using a modification of the standardized Parathyroid Assessment of Symptoms (PAS) score,¹⁷ specifically inquiring about the presence of fatigue, musculoskeletal pain (ostealgias, myalgias, and/or arthralgias), depression, cognitive decline or short-term memory loss, and headache, in addition to subjective quality of life and wellness; tender point assessment was not routinely performed by the treating physicians. Before 2011, these symptoms were routinely assessed at each visit and documented in the electronic medical record as well as our parathyroid database. Preoperative medication usage was compared with medication use ≥ 6 months after PTX.

Cure after PTX was defined as a normal serum calcium level at ≥ 6 months; failure or persistent disease was defined as redemonstration of hypercalcemia at <6 months. Long-term recurrence was defined as redemonstration of hypercalcemia after initial cure at ≥ 6 months after surgery.

Statistical analysis was performed using Statistics Online Computational Resource (SOCR; available from: <http://www.SOCR.ucla.edu>) with continuous variables expressed as a mean and analyzed using the Student *t* test. Categorical variables were expressed using the Chi-square test.

RESULTS

Of the 2,184 patients treated at our institution for sporadic PHP per the study period and conditions, a preceding diagnosis of FM was

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