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Review article

Considerations regarding sarcoidosis in the bariatric surgical patient

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Abstract The sarcoidosis patient who seeks surgical management for obesity presents many challenges. The interaction between sarcoidosis and obesity complicates both disorders and creates special issues to consider when contemplating surgery. This manuscript will review the approach to pre- and post-operative management of the sarcoidosis patient undergoing bariatric surgery. (Surg Obes Relat Dis 2017;▮:00–00.) © 2017 American Society for Metabolic and Bariatric Surgery. All rights reserved.

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Obesity is a national epidemic affecting over one third of U.S. adults, with a total annual cost of $147 billion. Besides these staggering costs, obesity has a major impact on morbidity and mortality [1]. This epidemic has resulted in a 24% increase in bariatric surgical procedures between 2011 and 2015 [2]. Management of the underlying medical problems in the bariatric surgery patient is paramount to minimize surgical complications and optimize outcomes.

Brief review of sarcoidosis

Sarcoidosis is defined as a noncaseating granulomatous disease that may manifest in any organ or tissue—most commonly the skin, lung, lymph nodes, liver, and eyes. The severity of the disease is variable, ranging from an asymptomatic state with no clinical consequences to a life-threatening disease. Although sarcoidosis is a ubiquitous disease that is found worldwide, it is more common in black females, but also occurs with a significant incidence in Caucasians and geographic regions far away from the equator (e.g., Northern Europeans). The disease is rare to present in persons <18 years [3].

The etiology of sarcoidosis remains elusive despite extensive investigations concerning the disease pathogenesis. Specifically, sarcoidosis is thought to result from immune mediated dysregulation of the Th1 CD4 antigen response directed by abnormal dendritic cell function, resulting in an inflammatory activation leading to granulomatous formation with epithelioid histiocytes, giant cells, and macrophages without substantial lymphocytic infiltrate [4]. Given the disease's preference for skin, lung, and eyes, it has been suspected that the causative antigens are airborne. Many infectious, occupational, and environmental exposures have been associated with sarcoidosis including mycobacteria, propionobacter acni (the common acne bacterium), firefighting, and the World Trade Center dust exposure [5,6]. There is also well-documented evidence suggesting a genetic predisposition to the disease through association studies with Human leukocyte antigen polymorphisms and sarcoidosis [6,7].

The diagnosis of sarcoidosis requires an appropriate clinical picture, histopathologic (noncaseating granulomas) investigation, and the definite exclusion of other granulomatous diseases. The lung is the most common organ

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involved with sarcoidosis and affects up to 95% of patients. Pulmonary sarcoidosis patients will often present with cough, dyspnea, chest pain, and constitutional symptoms such as fatigue, malaise, fever, and weight loss [8]. Abnormalities on chest imaging most often include mediastinal lymphadenopathy and may reveal micronodules in a perilymphatic distribution [9]. Additionally, fibrotic change in the lung may be seen. The physiologic evaluation also includes spirometry with lung volumes and diffusing capacity. Although sarcoidosis is thought to be an interstitial lung disease, and therefore would demonstrate restriction on spirometry, it may also affect the airways and cause an obstructive or mixed pattern on spirometry [8].

Due to the systemic nature of the disease, extrapulmonary organs may be most affected by sarcoidosis and can be biopsied to secure the diagnosis. Skin manifestations are the next most common site of involvement, with 25% of sarcoidosis patients presenting with specific (granulomatous) lesions such as papular sarcoidosis, largely found within the nasolabial folds and eyelids, nodular sarcoidosis, maculopapular sarcoidosis, lupus pernio, and sarcoid granulomas in tattoos [10]. "Nonspecific skin lesions" may also occur with sarcoidosis where sarcoidosis causes a skin reaction that is not granulomatous [10]. The prototypic nonspecific sarcoidosis skin lesion is erythema nodosum—an indurated, painful, erythematous to violaceous skin lesion on extensor surfaces, such as the shins. The third most common site of sarcoid involvement is the eye, with 25% to 80% of patients developing anterior or posterior uveitis. Although a sarcoid uveitis may cause no symptoms, it is potentially vision threatening, emphasizing the importance of thorough ophthalmologic examination in all sarcoidosis patients irrespective of the presence of eye symptoms [11].

Hepatic involvement is usually asymptomatic, but granulomas can be found on biopsy in approximately 60% of patients with less than one third exhibiting abnormal liver function tests [12]. Fig. 1 shows hepatic sarcoid granulomas seen intraoperatively. Granulomatous hepatitis or cirrhosis, resulting in portal hypertension, can occur in 18% of patients. Gastrointestinal sarcoid may involve any part of the alimentary tract and as such, may present clinically with a wide and quite variable symptomatology. Esophageal involvement may result in dysmotility, ulceration, or esophagitits. While often asymptomatic, .1% to .9% of patients with gastric sarcoid develop symptoms, from upper gastrointestinal bleeding secondary to ulcerations in the antrum, pylorus, and lesser curvature, to gastric outlet obstruction secondary to infiltrative pathology. Involvement of the small bowel may result in nutritional deficiencies (B12 and folate), protein losing enteropathy, and significant unintentional weight loss. Less commonly reported, colonic involvement can result in obstruction, strictures, bleeding, and may mimic inflammatory bowel disease [13].

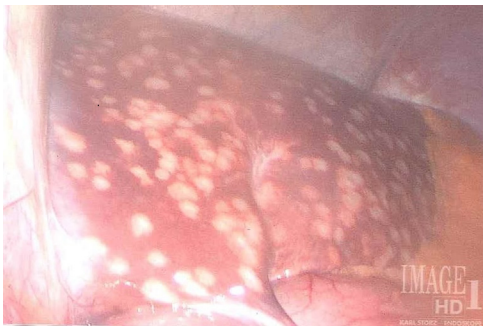

Fig. 1. Intraoperative photograph, sarcoid granulomas in liver.

Although cardiac sarcoidosis causes clinically significant disease in approximately 5% of sarcoidosis patients, it may cause life-threatening complications, such as cardiomyopathy or fatal arrhythmias. Therefore, all sarcoidosis patients should be screened for cardiac sarcoidosis, which should include at a minimum a medical history eliciting symptoms suggestive of an arrhythmia or heart failure as well as an electrocardiogram [8]. Vitamin D dysregulation due to upregulation of the 1 α-hydroxylase enzyme in activated sarcoidal macrophages and the subsequent overproduction of 1,25-dihydroxy vitamin D, the active metabolite, is fairly common in sarcoidosis and may cause hypercalciuria, hypercalcemia, nephrocalcinosis, nephrolithiasis, and renal insufficiency [11]. Sarcoidosis can also cause constitutional symptoms that are not attributable to granulomatous involvement of a specific organ but probably reflect a systemic response from release of inflammatory mediators. Such constitutional symptoms include fatigue, small fiber neuropathy, and pain syndromes [8,14].

Certain clinical presentations of sarcoidosis are so specific that a biopsy is not required for diagnosis [15]; these include Lofgren's syndrome and Heerfordt's syndrome. Lofgren's syndrome is characterized by acute symmetric polyarthralgia, erythema nodosum, bilateral hilar lymphadenopathy, and fever, and these patients tend to have a good prognosis [16]. Heerfordt's syndrome, also known as uveoparotid fever, is relatively uncommon and presents with fever, uveitis, and parotid swelling [17]. Unless one of these highly specific sarcoidosis presentations is present, the diagnosis of sarcoidosis requires that histopathology be obtained from an organ involved with sarcoidosis. Biopsies typically reveal compact, well-formed noncaseating granulomas containing macrophages, giant cells, and epithelioid cells encircled by lymphocytes [11]. Other causes of granulomatous inflammation, such as mycobacterial and fungal infections need to be excluded. Therefore, sarcoidosis is considered a diagnosis of exclusion, as other granulomatous disorders may also present with similar symptoms and clinical findings [4,18,19].

Once a diagnosis of sarcoidosis has been confirmed, an in-depth investigation of the extent of multisystem involvement should be performed. This should include assessment