



**CRS plus HIPEC in Mesothelioma Patient with Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS)**

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## Introduction

Peritoneal mesothelioma is an uncommon primary tumor of peritoneal lining. Approximately 20-30% of all mesotheliomas arise from the peritoneal serosal, as with pleural mesothelioma there is also a strong association with asbestos exposure. [1,2]

The main treatment procedure is cytoreductive surgery plus Hipec in association with neo-adjuvant and postoperative systemic chemotherapy. [3] We present herein a woman with mesothelioma with major comorbidity the Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS), which is a disorder characterized by significant impairment in function with severe debilitating fatigue post-exertional malaise, unrefreshing sleep, orthostatic intolerance, muscle-pain, and neurocognitive dysfunction such as difficulties with memory, concentration, comprehension, recall, calculation, and expression. All these symptoms are aggravated for hours, days, or longer following even minimal physical or mental exertion or emotional stress. Relapses may occur spontaneously. ME/CFS patients can also experience light, sound, chemical, and food sensitivities, which can trigger e worsening of their symptoms. Although mild immunological abnormalities (T-cell activation, low natural killer cell function, dysglobulinemias, and autoantibodies) are common in ME/CFS, subjects are not immunocompromised and are no more susceptible to opportunistic infections than the general population. The disorder is not thought to be an infection, but it is not recommended that the blood or harvested tissues of patients be used in others. [4]

This case is the first reported in the literature and we discuss the intra-operative and post-operative considerations.

## Case Report

ME/CFS since 2014, diagnosed 2020 according to the Canadian Consensus Criteria [4] with moderate to severity, Bell-Score 40 in stable condition under consequent pacing.

Analysis of functional G-protein-coupled-receptor autoantibodies (GPCR-AAb) using the bioassay of BerlinCures, a bioassay of spontaneously beating rat cardiomyocytes, confirmed positive GPCR-AAb

against  $\beta$ 2-adrenoceptor muscarinic M2 receptor. [2] Autoantibodies to vasoregulative G-protein-coupled receptors correlate with symptom severity, autonomic dysfunction, and disability in Myalgic Encephalomyelitis/Chronic Fatigue Syndrome. [5]

Diagnosis of peritoneal mesothelioma in February 2023. Neoadjuvant chemotherapy with cis-Platin/Permetrexed (4 cycles) provoked consequently new CT scan demonstrates a 60% down-staging of the disease and a complete cytoreductive surgery with 60 min HIPEC with paclitaxel 175 mg/m<sup>2</sup> and doxorubicin 30 mg/m<sup>2</sup> we performed.

During the operation there are blood potassium changes from 2,5 to 4,0 and then to 3,2 and finally 3,7 without evidence of cardiac arrhythmias or blood pressure changes.

In the first postoperative day an episode of cardiac pause of 6 sec was observed without evidence of arrest and a same episode of cardiac pause without arrest was observed for 8 sec in the third postoperative day.

ME/CFS deterioration constant on day 5 after receipts, with Bell-score 0-10, extreme sensitive to lights, sounds and touching, neurocognitive deterioration and very severe fatigue and bed bounding.

Under consequent pacing, maximal reduction of stimuli (lights, sounds, touching, conversation), feeding of pulpy or liquid nourishment in bed with straw and supportive Bromazepam 1,5 mg p.o. once a day on demand to reduce stimulus sensitivity in the first days, gradually amelioration within 1-2 weeks to Bell Score 30-40. The patient remains 9 days and discharged from the hospital without any problem.

Computerized tomography (CT) scan showed ascites and a large omental cake occupying the abdominal cavity. A biopsy under laparoscopic procedure showed a mucinous peritoneal mesothelioma. The tumor conference decided to start neo-adjuvant chemotherapy with pemetrexed and cis platinum.

Most important factor is the daily observation of electrolyte balance K<sup>+</sup>, Na<sup>+</sup>, Mg and He meticulous hydration of patient.

## Discussion

Many difficult problems arise in patients with ME/CFS who are anticipating surgery or anesthesia. General considerations for surgery or anesthesia in people with ME/CFS

Intracellular magnesium and potassium depletion has been reported in ME/CFS. For this reason, serum magnesium and potassium levels should be checked pre-operatively and these minerals replenished if

borderline or low. Intracellular magnesium or potassium depletion could potentially lead to cardiac arrhythmias under anesthesia. [6]

In our case, early in the first day in ICL we observed an arrhythmia and ECG pause for 10 sec and in the second postoperative day for 8 sec.

ME/CFS demonstrate vasovagal syncope (neurally mediated hypotension) on tilt table testing, and a majority of these can be shown to have low plasma volumes, low RBC mass, and venous pooling and vasodilators (nitric oxide, nitroglycerin,  $\alpha$ -blockers, and hypotensive agents). Taken to hydrate patients prior to and after surgery and to avoid drugs that stimulate neurogenic syncope or lower blood pressure. [7,8]

For this reason, histamine-releasing anesthetic agents (such as pentothal) and muscle relaxants (curare, Tracrium, and Mivacurium) are best avoided is possible. Propofol, midazolam, and fentanyl are generally well-tolerated. Most ME/CFS patients are also extremely sensitive to sedative medications-including benzodiazepines, antihistamines, and psychotropics-which should be used sparingly and in small doses until the patient's response can be assessed. [9]

On the other hand, the management of peritoneal mesothelioma remains in the era of systemic chemotherapy in combination with cytoreduction and HIPEC. [3]

This procedure is combined with morbidity of 30% and mortality 2% but the main fear in this patient with ME/CFS is the hypothalamic-Pituitary-Gonadal Axis suppression which rarely suppresses cortisol production enough to be problematic. In our case we were screened for the 24 h urine free cortisol level and twice in her hospitalization we provided cortisol supplementation. [10,11]

During the hospital stay the nurse staff know about the patient's sleep issues or sensitivities to light, sound, chemicals, food, or temperature so that nighttime disruption and exposure to sensory triggers can be minimized where possible.

Intravenous fluids consider in our case to total parenteral nutrition and intravenous saline to minimize the effects of low blood pressure and various volume and pooling.

People with ME/CFS often have comorbidities such as fibromyalgia, postural orthostatic tachycardia syndrome, mast cell activation syndrome, and joint hyperextensibility. If the patient has one or more of these comorbidities, surgery and anesthesia guidelines for those conditions should also be considered. [12]

Relapses are not uncommon following major operative procedures, and healing is said to be slow but there is no data to support this contention.

## Conclusion

In conclusion our case is the first reported in literature in which patients with MF/CFS are supported after cytoreductive surgery and Hipec with successful outcome.

- The insurance of magnesium and potassium levels are adequate,
- Hydrate the patients prior to and after surgery,
- Use catecholamines, sympathomimetics, vasodilators, and hypotensive agents with caution,
- Avoid histamine-releasing anesthetic and muscle-relaxing agents, if possible,
- Use sedating drugs sparingly,
- Ask about herbs and supplements, and advise patients to taper off such therapies at least one week before surgery,
- Consider cortisol supplementation in patients who are chronically on steroid medications or who are seriously ill.

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