

WM: MANAGING THE SIDE EFFECTS OF TREATMENT

by Dr. Jeff Matous



Dr. Jeff Matous answers a question from the podium at the recent IWMM Ed Forum in Tampa.

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In this article Dr. Matous shares much practical and effective advice for WM patients concerning the management of side effects from treatments for the symptoms of WM. The advice he offers is the result of more than twenty years of practicing the art of medicine to benefit his patients with indolent blood cancers.

A wise professor once told me in medical school that one could be the smartest doctor in the world but if his or her knowledge was not effective then its impact was dramatically reduced. In other words, physicians need to practice the art of medicine in order to optimally assist their patients. This article focuses on an important aspect of the art of medicine, namely managing the side effects, when treating patients with Waldenström's macroglobulinemia (WM).

The determination of side effects in WM patients can be quite challenging and tricky because many of the problems experienced by WM patients from the disease are similar to and overlap with some treatment side effects.

Let us begin by reviewing common symptoms of WM and then by asking how we define “side effects” of treatment. We then list the side effects commonly associated with WM (note that some of these side effects mimic symptoms of WM) and suggest ways that have been shown to be effective in our practice for the management of these side effects. In conclusion, we consider the side effects that may occur when a WM patient is treated with rituximab. Throughout this discussion, we repeatedly emphasize the need for the patient to take the initiative in communicating with the treating doctors and nurses.

WM Symptoms

There are certain recurring problems that physicians find in WM patients:

- Tiredness, often but not always the result of anemia
- Night sweats
- Headaches and dizziness (hyperviscosity or thickening of the blood from too much IgM)

- Various visual problems
- Pain, numbness, or tingling in the extremities (neuropathy)
- Abnormal bleeding from the nose and gums
- Enlarged lymph nodes, spleen, liver
- Problems related to amyloidosis (see the article by Dr. Giampaolo Merlini in the *Torch* 14.2 (April 2013) pp. 1-4)

What exactly is a “side effect”?

The Food and Drug Administration (FDA) has a very specific definition of a side effect. This definition is broad and encompassing and therefore places a lot of responsibility on both the patient and the treatment team (nurse, doctor) to be in open communication with each other. According to the FDA, a side effect is:

“... any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and **which does not necessarily have to have a causal relationship with this treatment.** An adverse event (AE) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.”

In my view the important point to note is that WM patients should report any bothersome problem to their doctor and nurse and let us sort it out. Communicate. Even though we doctors often have high opinions of our own talents (at times even inflated) we do not read minds well, and it is imperative for patients to educate themselves about their disease, their treatments, and to **track and report** to their treatment team any possible side effects.

My lymphoma mentor, Dr. Oliver Press, used to say to his patients on treatment (and he could retire if had I paid him for each time I have used this phrase over the years), “If you have a problem now and did not have it before, we probably did it to you.”

Thoughts about how to communicate effectively with your team

Once you know what your treatment will be, gather as much information as possible about that treatment. What are the drugs? How are they given? What is the schedule? What are possible side effects? When do you need to call? This information should be written wherever possible. Utilize good websites (www.iwmf.com, www.lymphomation.org/, www.lls.org, etc). If possible bring other people with you to the treatment education session. Keep a journal or notebook – do **not** trust your memory. When complicated information comes fast it can resemble drinking water from a fire hose. Ask your team how to anticipate and manage the most common side effects of treatment.

OK, so is all treatment “chemotherapy”?

I define chemotherapy, loosely, as any approved substance we put into our body to try and kill cancer cells. The types of chemotherapy are changing, and the side effects from treatments are quite different one from another. Chemotherapy has evolved dramatically over the decades. To be sure, we still use

some drugs that have been in use for as much as fifty years to treat WM and other lymphomas (prednisone, cyclophosphamide, vincristine, doxorubicin). Even just a few years ago a drug called fludarabine (approved in the early 1990s) was a mainstay of WM treatment. The standard chemotherapy drugs we use now such as rituximab (used widely since the late 1990s), Velcade/ bortezomib (in use since 2003), and bendamustine (in use since 2008) have very different side effect profiles from their predecessors. In 2014 we are also at the cusp of an era where increasingly chemotherapy will be in the form of a pill or capsule!

For WM patients there are so many different treatment options that to review them is beyond the scope of this article. One can review them in IWWMF Ed Forum talks or by visiting the NCCN (National Comprehensive Cancer Network) website at www.nccn.org/professionals/physician_gls/PDF/waldenstroms.pdf.

Common, general side effects from chemotherapy

Even though certain treatment side effects are fairly common for different treatments, it is very important to know the most common side effects for your specific treatment. Before you start on any treatment, your doctor and nurse should discuss the potential risks and benefits of the treatment with you. This always happens when you are treated in a research study or clinical trial and should happen with every treatment. This is called “informed consent.”

Some common chemotherapy side recommendations for management are:

- Nausea or vomiting. We have great medicines to prevent or treat nausea these days.
- Constipation. Stay ahead of this with stool softeners, watching your diet, and exercise.
- Diarrhea. Certain over-the-counter remedies such as loperamide usually help.
- Low blood counts. Be aware of your white blood count due to increased infection risk.
- Certain treatments increase the risk of shingles. Ask your doctor about use of an antiviral. Get your flu vaccine. Some patients who are subject to severe infections and low levels of antibodies such as IgA and IgG may benefit from IV gamma globulin infusions.
- Hair loss (increasingly rare).
- Fatigue. Fatigue is the toughest symptom to sort out since fatigue can be due to WM and/or treatment. Exercise and get rest (but not too much – keep naps short) and your fatigue should diminish as your disease recedes.
- “Chemo brain.” Exercise your brain just like you would your muscles – use it! If this condition continues to be bothersome, most clinics have access to psychologists who can help.

- Peripheral neuropathy. PN can be caused by the disease itself (the effect of IgM on certain patients) or by certain chemo drugs (bortezomib, vincristine, thalidomide). For prevention of severe neuropathy, the best strategy is to report any symptoms quickly to your treatment team. There are prescription and nonprescription remedies, and every clinic has its own recommendations.
- Anxiety and depression. These are common problems, worsened by steroid medications such as prednisone or dexamethasone. There is a lot in the way of support and help out there, and many patients benefit from prescription medications.

We should talk in more detail about rituximab

In almost all treatment situations we utilize a drug known as rituximab (Rituxan), which is a monoclonal antibody, a type of “targeted” therapy. In some instances rituximab may be used alone, but increasingly it is combined with other chemotherapeutic agents.

Rituximab has certain side effects, which are more pronounced and indeed unique in WM patients.

Any patient treated with rituximab, administered over several hours in a day by vein, may have as a side effect an allergic reaction whereby patients experience fever, chills, shakes, hives or even more severe problems such as breathing trouble, low blood pressure, and anaphylaxis. For reasons just being worked out by researchers, these allergic reactions appear to occur more frequently in WM (up to one in six patients) and to be more severe. For the majority of patients who experience allergic reactions to the drug, rituximab can still be given by adjusting preventative medications for the infusion. Some patients, however, simply cannot tolerate the drug no matter which preventive measures are taken. For such cases we can use ofatumumab as a substitute antibody.

A second unusual reaction to rituximab is a “flare,” whereby the IgM level can **increase** during the first few weeks of rituximab therapy, sometimes to levels that cause the blood to thicken (hyperviscosity syndrome), making patients ill. This flare reaction is usually limited to patients with IgM levels above 4,000 or 5,000 prior to rituximab treatment and can be mitigated by combining the rituximab with other chemotherapy. In many instances plasmapheresis (using a machine similar to dialysis to temporarily remove IgM from the blood) done in the days preceding infusion of rituximab is recommended to prevent symptoms of the so-called rituximab IgM flare.

Summary

There is no substitute for becoming as well informed as you can be regarding your disease and the specific treatment proposed for you. Avail yourself of the great resources of the IWWMF and especially of the professionals taking care of you – your doctor and nurses.

I wish to thank Megan Andersen, NP, who has been such a valuable resource to our WM patients in the Rocky Mountain region and who contributed to this review. Thanks are due as well to the IWWMF, to WM researchers worldwide, and, most of all, to the great WM patients.

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