

AL amyloidosis Matters

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New rapid test for AL amyloidosis

In AL amyloidosis, abnormal plasma cells in the bone marrow produce proteins called light chains which are released into the bloodstream and go on to form amyloid deposits in the tissues and organs.



At the moment a test called the Serum Free Light Chain Assay (SFLCA) or Freelite™ test is used to measure the levels of light chains, which helps to determine AL amyloidosis activity and response to treatment. The test involves taking a sample of blood from a vein in an arm or hand which is sent away to a laboratory for analysis.

The new Seralite® test measures free light chains in serum samples. If free light chains are detected the device shows a pink line within minutes, similar to the way a pregnancy test works. As samples used for the test do not need to be sent to a lab for analysis, the test can take as little as 10 minutes and may allow easier and more rapid diagnosis and monitoring of AL amyloidosis.

Serascience Limited is a specialist diagnostics company established jointly by Abingdon Health and the University of Birmingham. Serascience received a CE mark for Seralite® in March 2015. The CE mark shows that the test complies with all the necessary EU legislation and means that the test, which so far has been available for research purposes only, can be made available for use in the NHS. Although obtaining the CE mark means this test is closer to being available in the clinic, it is likely to take some time before it is widely in use.

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Welcome

Welcome to the latest issue of *AL amyloidosis Matters*.

In this issue we focus on AL amyloidosis in soft tissue, provide a short report from the UK Amyloidosis Network meeting and highlight new developments in treatment.

We hope that you like our new look for the newsletter and welcome any feedback you have about the content.

If you have any suggestions for future articles or would like to provide a patient experience please contact me on 0131 557 3332 or email sue.perkins@myeloma.org.uk.

We hope you find this issue interesting and informative.



Sue Perkins
Service Development Manager

AL amyloidosis Matters

For feedback, comments and questions about **AL amyloidosis Matters** contact Sue Perkins on 0131 557 3332 or email sue.perkins@myeloma.org.uk

News & Notes

Genetic abnormality in AL amyloidosis affects response to Velcade®

Velcade (bortezomib)-based combinations are less effective in patients with AL amyloidosis who have a genetic abnormality called the t(11;14) translocation, according to a new study published in the *Journal of Clinical Oncology*. Researchers in Germany analysed over 100 AL amyloidosis patients who received Velcade as part of their initial treatment combination. The average length of time following treatment with Velcade that patients remained

symptom-free, or before the AL amyloidosis started to return, was significantly shorter in patients with the t(11;14) translocation. Patients with t(11;14) tend to have a form of AL amyloidosis which progresses at a slow rate; therefore it appears that the translocation is not itself a risk factor, but predicts poor response to Velcade. However, these findings should be considered preliminary and need validation before they will affect clinical practice.



Potential new drug for AL amyloidosis granted orphan designation

The US Food and Drug Administration (FDA) has granted orphan drug designation to Systebryl™ (PTI-110), a novel drug developed by the company ProteoTech, Inc., as a treatment for AL amyloidosis. Systebryl targets amyloid deposits that accumulate in organs such as the heart and kidneys, allowing them to be cleared from the body. FDA Orphan Drug Designation is designed to promote the development of drugs that may provide significant benefit to patients with rare diseases.

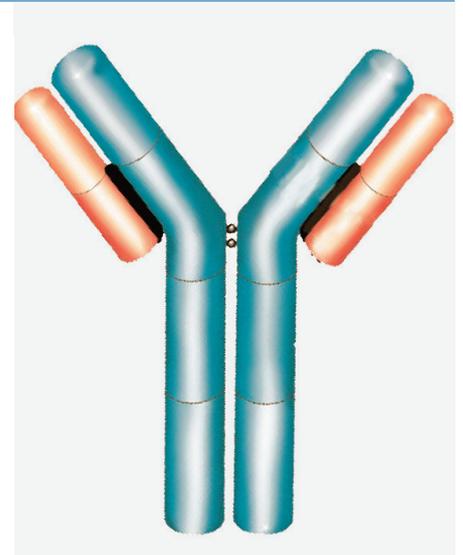
To encourage innovation in this area, pharmaceutical companies receive important development incentives including seven years of market exclusivity (the sole right to make the product), if it is licensed for use. If proven safe and effective in 'proof of concept' clinical trials - planned for later this year - Systebryl has the potential to be a 'first-in-class' drug for AL amyloidosis. Currently, there are no approved treatments for AL amyloidosis that directly act upon the amyloid deposits.



Anti-amyloid monoclonal antibody to be tested in humans

Treatment for AL amyloidosis is limited to reducing production of the amyloid-producing plasma cells in the bone marrow - existing amyloid deposits in vital organs remain unaffected. A small clinical trial has begun in New York on an anti-amyloid monoclonal antibody (called 11-1F4) which targets the amyloid deposits in an experimental animal model of AL amyloidosis. Monoclonal antibodies are a class of drug that mimic antibodies that the immune system produces in

response to foreign organisms (such as bacteria) that enter the body. Each group of monoclonal antibody recognises and attaches to a specific protein on the surface of cells. The 11-1F4 trial will investigate different doses of the monoclonal antibody. The goal of the trial is to establish the safety and effectiveness of 11-1F4 in patients. If successful, treatment with this antibody would represent an important contribution to the care of AL amyloidosis patients.



Special feature

Symposium update

By SUE PERKINS
Service Development Manager

This article talks about tests in AL amyloidosis presented at a recent international symposium held in April.



In April 2015 Edinburgh hosted an important symposium organised by The Binding Site, a pharmaceutical company who manufacture the Freelite® test (also known as the Serum Free Light Chain Assay or sFLC assay) used for the diagnosis and monitoring of AL amyloidosis.

This conference was The Binding Site's 7th International Symposium and featured some of the world's leading experts, including Prof Merlini from Italy, Dr Dispenzieri from the US and Dr Wechalekar from the National Amyloidosis Centre.

Dr Wechalekar spoke about a new test called Hevylite® developed by The Binding Site. He explained that this test may be useful for diagnosing AL amyloidosis, monitoring response to treatment and also finding out prognostic information (i.e. knowing how someone's AL amyloidosis might progress over time). It is therefore likely to be used alongside existing tests for AL amyloidosis in the future.

Clinical trials have indicated that around 2% of AL amyloidosis patients do not have markers - substances in the body used as

indicators or measurements - that are picked up by current tests for diagnosing and monitoring AL amyloidosis. It is therefore very promising that an additional test has been developed which may be able to provide information for this group of patients about their AL amyloidosis.

In addition, the Hevylite test can also provide useful indicators for all AL amyloidosis patients, not just the 2% mentioned above. The test works by identifying the ratios of different types of heavy and light chains a patient has, to calculate any abnormal ratios. Measuring the ratio, as well as the absolute levels of different types of heavy and light chains, is important to determine how well an AL amyloidosis patient is responding to treatment. For example, a normal ratio can show that a patient's immune system is responding which means their AL amyloidosis might not progress (worsen) quickly.

Prof Merlini from the Amyloidosis Research and Treatment Center, University of Pavia, Italy talked about AL amyloidosis free light chains, measured by the Freelite test. Measuring the level of free light chains is important in diagnosing

AL amyloidosis but also to see changes over time, in terms of how well treatment is working and whether a patient's AL amyloidosis is remaining stable when they are not on treatment. For some patients, especially those with cardiac amyloidosis, it is important to change treatment as soon as possible if their free light chain levels do not reduce, as this indicates that patients are not responding. Treatment response is important as it helps to prevent further damage to the heart which can have an impact on a patient's prognosis.

Summary

The symposium shows that there are some exciting new developments in AL amyloidosis tests, which are expected to improve diagnosis in difficult cases, and help to ensure the best possible treatment for all patients. It is already known that it is important to change treatments as soon as possible for patients whose AL amyloidosis is not responding to their present treatment. The new tests offer better ways to assess response to treatment, which will allow patients to change their treatment earlier.

To find out more about developments in AL amyloidosis at www.myeloma.org.uk/amyloidosis

MEDICAL MATTERS

AL amyloidosis and soft tissue

BY JUDE LEITCH
Patient Information Specialist

This article covers AL amyloidosis and soft tissue, explaining how soft tissue is affected by amyloid deposits and how this can be treated.

Introduction

In AL amyloidosis, abnormal plasma cells in the bone marrow produce an abnormal protein called amyloid.

The amyloid protein is only broken down very slowly by the body and starts to build up in the tissues and organs. The build-up of amyloid protein is called an 'amyloid deposit' and this build-up can happen almost anywhere in the body. Each patient has a different pattern of amyloid deposition, with different organs affected.

Amyloid deposits can build up in the kidneys, heart, liver, spleen, digestive system or soft tissue, and may affect two or more organs at the same time. The build-up of amyloid in these tissues and organs gradually damages their function and, if the function of an organ is significantly damaged, it causes symptoms. AL amyloidosis does not affect the brain.

Soft tissue AL amyloidosis

Soft tissue refers to tissue that support, connect or surround organs and bone. This includes tendons, ligaments, muscle (e.g. the tongue), fat, skin, fibrous tissue, nerves and blood vessels.



Skin lesions in AL amyloidosis

When amyloid deposits build up in the blood vessels of the skin, for example, they can cause easy bruising, or lesions on the face or upper torso. The bruising may occur around the eyes giving a characteristic 'panda eyes' sign. Much more rarely, amyloid may directly deposit in the skin forming lumps or nodules on the arms and legs.

The other major sites of amyloid deposition in the soft tissue are the nervous system and in and around the mouth and tongue. This causes enlargement of the tongue (macroglossia) which can lead to difficulties in eating or swallowing. Amyloid may also deposit in the shoulder (the 'shoulder pad' sign).

These soft tissue manifestations of AL amyloidosis are now described in a bit more detail.

Nervous system

Amyloid deposits can affect the nerves of the hands, feet and lower

legs and may cause pain, numbness and tingling. This is called peripheral neuropathy and occurs in around 10 – 20% of patients. Treatments used in AL amyloidosis such as thalidomide and Velcade can also damage nerve cells, so these can exacerbate any existing peripheral neuropathy.

AL amyloidosis can also affect nerves controlling blood pressure, heart rate, gut movement and other body functions. This can cause a variety of symptoms including dizziness when standing up too quickly, nausea and diarrhoea and/or constipation. This is called autonomic neuropathy.

Around 20% of AL amyloidosis patients may develop a condition called carpal tunnel syndrome. This happens when amyloid deposits in the wrist press on nerves, causing tingling and pain in the wrists and pins and needles in the hands and fingers.

Macroglossia



Macroglossia is a marked enlargement of the tongue because of amyloid deposits often causing difficulty in eating or in speaking. Macroglossia is not very common in AL amyloidosis but it is very rarely seen in any other disease. If a patient has marked macroglossia it is very likely that this is caused by AL amyloidosis.

Shoulder pad sign



Sometimes amyloid is deposited in the soft tissues around the shoulders; this leads to characteristic swelling of both shoulders. This can be the first sign of AL amyloidosis.

Panda eyes



Periorbital purpura (panda or raccoon eyes) is a result of fragile capillaries around the eyes that are bruised easily, and is specifically characteristic of AL amyloidosis. It may appear after coughing, sneezing, or straining during a bowel movement. Not infrequently, panda eyes may arise after a simple action such as rubbing the eyelids.

Treatment and monitoring of AL amyloidosis in the soft tissue

At present, soft tissue AL amyloidosis is monitored clinically by regular examination and in selected cases by scanning using CT or MRI scans. The SAP scan – effective at monitoring the amount and location of amyloid deposits in the internal organs in AL amyloidosis patients – is not so useful for soft tissue monitoring.

The treatment of amyloid deposits in soft tissue follows the same approach as treatment for AL amyloidosis. Generally, the best treatment will take account of general health, age, which organs are affected by amyloid deposits and any previous treatment had.

Research and future directions

Much research is taking place to find more effective treatments for AL amyloidosis and finding the best ways of using them. Many of these are currently being tested in clinical trials taking place around the world.

Summary

AL amyloidosis can affect the soft tissue including the nervous system, the skin, muscles and blood vessels, generating a number of clinical symptoms and consequences.

Soft tissue AL amyloidosis can be monitored through regular examination in the clinic and, in certain patients, by using CT or MRI scans. It is treated in the same way as other manifestations of AL amyloidosis.

You can find out more about developments in AL amyloidosis at www.myeloma.org.uk/amyloidosis

Bursary available to help with costs of attending AL amyloidosis Patient and Family Infoday



Funding is available from Myeloma UK to help AL amyloidosis patients, carers, family members and supporters to attend an Infoday.

We know that many patients have to travel to attend the AL amyloidosis Infoday; if costs associated with travel are preventing you from attending, please ask for further details about our bursary.

The AL amyloidosis Infoday will be on 20 November at Park Crescent Conference Centre, 229 Great Portland Street, London, W1W 5PN.

Bursaries of up to £50 per person may be awarded to help towards costs for travel and accommodation. Limited complimentary places are also available.

Applications for a bursary to attend the AL amyloidosis Infoday need to be received by 31 July.

Please contact Hannah Bingham on 0131 557 3332 or email hannah.bingham@myeloma.org.uk to find out more about how to apply.

PATIENT EXPERIENCE

‘LESLEY, MAKE NO BONES ABOUT IT YOU HAVE A LONG ROAD TO TRAVEL’

Lesley Toft lives in Sale, Cheshire. Here she talks about her experience of AL amyloidosis, including how she was diagnosed, what treatment she received and the hard times she has had to cope with to get to where she is now.

Little did I know that early in 2013 when my Consultant Dr Payne looked me directly in the eye and said “Lesley, make no bones about it you have a long road to travel”, just how long and hard that road would be.

When weakness climbing the stairs led me to go and see my GP in October 2012, why would I, a healthy active person, have suspected that the following series of hospital tests would lead Dr Payne to suspect myeloma?

Following his suspicion, a bone marrow biopsy was performed under sedation at The Alexandra Hospital in Cheadle by Prof Yin. I was frightened and confused as I had never heard of myeloma.

When the call came with the result, my husband, John, took it and he was ecstatic... it was not myeloma but AL amyloidosis. Unsurprisingly, we had never heard of this condition either, but felt it must not be as bad as myeloma. However, our naivety was short-lived. We discovered that

in fact it was worse. We both felt in a state of shock, wondering when and what we would tell our two sons, who had recently lost their adoring auntie to cancer.

I was referred to the National Amyloidosis Centre (NAC) in London and my first visit was in January 2013 – just a month after I was diagnosed. I was extremely scared and apprehensive but everyone was so lovely, caring and über-efficient.

Their SAP scan confirmed that I had amyloid deposits in my kidneys, liver, spleen, bones, spine and a touch in my heart - the latter being the reason why Prof Yin wanted me to have chemotherapy prior to high-dose therapy and a stem cell transplant (HDT-SCT).

Prof Yin immediately started me on six months treatment of cyclophosphamide, Velcade and dexamethasone. A month later I returned to see him and reported feeling remarkably well. “Don’t speak too soon” was his reply. Frequent hospital appointments became a depressing way of life.

Knowing the HDT-SCT was ahead of me, I didn’t allow myself to take time off work. By the fourth cycle exhaustion had set in but somehow I dragged myself into work feeling quite unwell. Stubborn by nature I was determined to keep going in spite of John imploring me to take time off.

Then disaster struck our family and changed our lives forever.

On 24 April 2013, our son Craig, and John were chatting over a cup of tea

when John started rubbing his chest and collapsed on the floor. Craig knew instantly that his Dad was having a heart attack and promptly started CPR. Courageously he fought to save his Dad’s life, accompanying him into the crash room at the hospital. We were devastated when an hour later John died, with Craig by his side holding his hand.

I now had to hold my family together while living with a critical incurable condition.

Two and a half weeks later, battered by illness, the treatment and in a state of deep grief at losing John, who was my rock and the love of my life, I returned to work. By now I was struggling. Breathless just walking from the car park to my office, which I now had to reach by using the service lift, I was weakened having lost over a stone in weight.

By the time I was admitted to Manchester Royal Infirmary for my HDT-SCT on 18 November 2013, I had regained some weight but was suffering the side-effects of treatment: peripheral neuropathy, loss of taste, change in toilet habits and continued weakness in my legs.

I was under the care of the wonderful Dr Simon Gibbs, previously a Clinical Research Fellow at the NAC. He had recently opened a specialist AL amyloidosis clinic at Manchester Royal Infirmary.

I was given high-dose melphalan over the next two days and by the end of the week was still feeling fine. However, the very debilitating side-effects of the melphalan then

set in. I was being cared for in the High Dependency Unit and my hopes of being home for Christmas were fading as a series of infections followed. I ended up being allowed home for Christmas Day and between Christmas and New Year I was moved into an ordinary ward. However, weeks of diarrhoea and vomiting continued, reducing my weight to under six stones. Unbeknown to me, Dr Gibbs warned my sons that they should be prepared that I might not pull through. I was transferred back to the High Intensity Ward and rallied but continued to have more infections. Finally, three months later, I was allowed home on 14 February 2014. Dr Gibbs told me I had achieved complete remission (CR). Couldn't say better than that but I was gradually to realise it was only part of the story.

I was left in no doubt as to the long, arduous road I was travelling. Buoyed up with a successful HDT-SCT, I returned to work full-time in March 2014. My appetite returned with a vengeance. My next appointment at the NAC for tests and SAP scan confirmed that complete remission had held but I realise I had pushed myself too hard too soon.

I have to confess that full-time work is physically demanding. Exhaustion consumes me, my legs are still weak, peripheral neuropathy is still present and my taste buds have not fully recovered. Copious amounts of balsamic vinegar gives flavour to food for the time being. Maintaining my weight can be quite fun as I eat whatever I want without gaining too much weight! I have tremendous support from my Manchester Royal Infirmary nurses Pippa and Amy and, of course, the outstanding doctors at the NAC.

The grieving process dominates my life. For 40 years John had always been there for me but was cruelly taken when I needed him most. Therapy with Macmillan is proving



Lesley Toft

very helpful. I have now reached the point where I know I need to make some adjustments in my life.

I cannot speak highly enough of the commitment of the NAC team. Their caring approach makes patients' visits as easy as possible. They hold the key for the future. Great advances have been made in developing new, less toxic, treatments and the first drug of its kind specifically for AL amyloidosis is about to enter Phase 2 of clinical trials. It is the result of many years of

outstanding work by Prof Sir Mark Pepys and the NAC team.

Thanks to the dedication of my doctors and nurses, the loving support of my family, friends and my new AL amyloidosis buddies, I am able to be here for my two sons who have endured far more in two years of their young lives than anyone should ever have to.

If you are interested in sharing your experience please contact **Sue Perkins** on **0131 557 3332** or **sue.perkins@myeloma.org.uk**

Fundraising news

Myeloma UK and AL amyloidosis

The work of Myeloma UK is diverse and far-reaching and the benefits of our work extend beyond the myeloma community. Despite being a charity for myeloma patients in name, our research and services are also tailored to meet the needs of AL amyloidosis patients.

How our work benefits AL amyloidosis patients

Clinical Trial Network

AL amyloidosis patients benefit from the development of the latest innovative treatments through our Clinical Trial Network which is speeding up access for patients to new and more effective drugs.

AL amyloidosis Matters Newsletter

Myeloma UK issues AL amyloidosis patients with this free AL amyloidosis newsletter three times a year which includes the latest treatment and research news and articles particularly relevant to those affected by AL amyloidosis.

Patient and Family

AL amyloidosis Infodays

Our annual event gives AL amyloidosis patients and family members the opportunity to hear about the latest treatments for AL amyloidosis direct from the experts. Attendees meet others affected by AL amyloidosis in a relaxed setting and can share experiences and get answers to any questions they may have about AL amyloidosis.

Myeloma UK Infoline

Our Information Specialists are available five days a week to answer your questions about AL amyloidosis. Contact us on freephone 0800 980 3332. We provide information, practical advice, emotional support and a listening ear to the AL amyloidosis community.



Sue Perkins and Ellen Watters ready to help at a previous AL amyloidosis Infoday

AL amyloidosis information

We provide information about AL amyloidosis, its treatment and management on our website and in print. We also offer information on a range of specific topics relating to living with AL amyloidosis, such as diet and nutrition, fatigue and travel insurance.

Ways you can support the work of Myeloma UK

Thank you so much to everyone who donates and fundraises to support the work of Myeloma UK. We are a registered charity and receive no government funding so rely on voluntary donations and fundraised income from supporters like you.

Here are a few ways you can get involved to support our work:

Fundraising

Get family and friends together and organise your own fundraiser: a coffee morning, bake sale or perhaps a sponsored charity head shave?

Just do it! Challenge yourself or your family and friends to take part in a run, trek or active event to raise money.

Donate: Set up a regular monthly Direct Debit.

Celebrate a special occasion or personal milestone with a donation in lieu of presents.

Leave a legacy: Donate to Myeloma UK in your will and invest in a future without AL amyloidosis.

Raise awareness

Share your story so people understand what it means to live with AL amyloidosis. You can do it through this newsletter, at an Infoday or online through the Myeloma UK Discussion Forum.

To raise money for **AL amyloidosis** research or the support and information services provided by **Myeloma UK**, call our Fundraising Team on **0131 557 3332** or email fundraising@myeloma.org.uk