

Diagnosing Patients with a PAD

Purpose

The purpose of this document is to give GPs the understanding they need to enable them to identify patients who may have an undiagnosed Primary Antibody Deficiency (PAD) and then to know what initial tests they can undertake and when to refer their patient to a Clinical Immunologist.

Background

Contrary to popular belief, most people who have a Primary Antibody Deficiency are adults and are diagnosed in their twenties and thirties. Many people believe that patients with an undiagnosed PAD will die very soon after the onset of disease, but for the majority, this is not the case at all. In fact PADs usually present as “revolving door” patients, with chronic infections of the upper respiratory tract that will not resolve despite their GP’s best efforts.

What are Primary Antibody Deficiencies?

Primary Antibody Deficiencies (PADs) are a group of Rare Diseases. These break down into separate groups, Common Variable Immune Deficiency (CVID) being named as such since it makes up the largest group in the disease sector. Diagnosing these conditions as soon as possible after onset of disease is crucial, since repeated infections lead to irreversible lung and other organ damage. The current average diagnostic delay is seven years, after which time most patients will have bronchiectasis.

How do PADs Present?

Most patients with an undiagnosed PAD will present with recurrent infections. The most common presentation is of upper and lower respiratory infection which sometimes resolve with treatment but keep returning despite appropriate antibiotic therapy. Patients with a Primary Antibody Deficiency often do not “look” unwell and this can be confusing. They do not look unwell because their immune system is not functioning appropriately. Anecdotally UKPIPS understands that many patients living with a PAD have a low normal temperature, many therefore being febrile at 37.0°C. However, other signs to look for are:

- Particularly severe, unusual and persistent infections, even if serum immunoglobulin concentrations are normal.
- Chronic infections such as sinusitis, tonsillitis, otitis media or recurrent boils.
- Enlargement of liver, spleen and /or other lymphoid tissue abnormalities.

- Failure to thrive in children.
- Requirement for frequent courses of oral antibiotics or intravenous antibiotics.

Why investigate for PADs?

Firstly, undiagnosed PAD patients will be experiencing unnecessary suffering. Many are diagnosed with chronic fatigue syndrome or mental health issues, which may or may not be present as secondary to the PAD. More worryingly, UKPIPS is frequently told that patients were diagnosed with hypochondria before finally gaining a correct diagnosis. Secondly, delayed diagnosis and instigation of appropriate treatment results all too frequently in irreversible organ damage.

Are PADs Difficult to Diagnose?

PADs are sometimes difficult to assess since much of the presentation is with “normal” infections. However, these diseases are relatively easy to diagnose, have good treatment options already approved and patients diagnosed early after the onset of disease will often be able to lead near to normal lives.

What Tests Should a GP order?

GPs who suspect that a patient may have a PAD should order the following:

1. Full blood count. Many PADs will be associated with low cell numbers which are often autoimmune including neutrophils, platelets etc.
2. IgG, IgA, IgM.
3. Lack of antibodies to childhood infections such as Chicken Pox.
4. Low or absent antibodies to vaccinations (childhood or otherwise e.g. Rubella, Hepatitis B)
5. Microbiology. This is a simple test which could provide much information to guide further investigations and management. This may be in the form of sputum, cough swabs, throat swabs etc.

When to refer to a Clinical Immunologist

If any of the tests are abnormal, the patient must be referred to a Consultant Clinical Immunologist without delay. However, even if these tests come back within normal limits and the patient continues to present with symptoms that imply PAD, they should be referred. This is because more subtle Primary Antibody Deficiencies which require more sophisticated testing can also cause serious illness but cannot be identified by tests available to GPs.

If unsure about the above investigations then please discuss your patient with a consultant immunologist, even prior to undertaking any investigations.

How to find a Clinical Immunologist

Consultant Clinical Immunologists work in specialist regional centres and patients have to be referred out of the immediate area in order to obtain appropriate diagnosis and treatment. A list of these specialist centres can be found on the UKPIPS, BSI and UKPIN Websites.

UKPIPS – www.ukpips.org.uk

BSI (British Society of Immunology) – www.immunology.org

UKPIN (UK Primary Immunodeficiency Network) – www.ukpin.org.uk

Funding concerns should never prevent a GP from either testing for a PAD or referring a patient for testing.

References:

Cunningham-Rundles, Charlotte and Maglione, Paul J. *Common variable immunology*. in Journal of Allergy & Clinical Immunology, Vol.129 No.5, May 2012

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