

PATIENT JOURNEY FOR BULLOUS PEMPHIGOID

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EUROPEAN REFERENCE NETWORKS
FOR RARE, LOW PREVALENCE AND COMPLEX DISEASES

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1. BULLOUS PEMPHIGOID

1.1. OVERVIEW OF CONDITION

Orphanet:

- 1) Bullous Pemphigoid is an autoimmune blistering disease characterized clinically by highly pruritic tight, often large, blisters with a clear content.
- 2) BP is immunologically characterized by the production of autoantibodies directed against two structural proteins found in the dermal-epidermal junction and ensuring dermal-epidermal cohesion: BP antigen 1 (BPAG1 or AgBP230), and BP antigen 2 (BPAG2, AgBP180 or collagen XVII). The binding between the autoantibodies and these proteins leads to the separation between the dermis and the epidermis and to the formation of blisters. Some drugs are associated with the onset of BP (diuretics, antiarrhythmics, neuroleptics, gliptins, immunotherapies).

1.2. PREVALENCE

Orphanet:

Bullous pemphigoid (BP) is the most common autoimmune subepidermal blistering disease of the skin and mucous membranes. It has an estimated prevalence of 1/4,000 in Europe. Its incidence has tripled during these last 20 years in Europe and it is currently estimated at 20 new cases /1,000,000 inhabitants per year.

1.3. (OTHER...)

It affects people worldwide primarily in their 70's & 80's – with rare exceptions of younger people from their 50's. The mean age of patients is around 80 years old.

It has been observed that people with neurological diseases (Alzheimer's, Parkinson's, demyelinating diseases) develop BP more frequently.

This work concerns mostly BP in the elderly. The consequences of the disease, of treatments, of daily life with the disease will be different for rarer PB, i.e, the one affecting younger people, pemphigoid in children or pregnant women (pemphigoid gestationis).

2. METHODOLOGY

2.1. PATIENT ORGANISATION INVOLVED

France: A few patient representatives and listeners from the *Association Pemphigus Pemphigöide France* report on the Bullous Pemphigoid condition in the elderly.

United Kingdom: A few patient representatives and patients from *PEM Friends* report on the disease.

2.2. METHODOLOGY

These 2 groups got together on zoom and followed the original template process suggested for all patient journeys.

The discussion was conducted as a chat where experiences were shared.

The AIBD ePAG SKIN representative, Laurence Gallu, took the minutes, wrote down all the information gathered and sent it back to all the participants for corrections and clarification. She had to transfer and update it to the new proposed patient journey model.

It was then sent to the health care professional team of the AIBD ERN SKIN team and to the Italian and German Patient Organizations so they could add their input as well.

3. OVERVIEW OF STAGES TO THE JOURNEY

Timeline	Stage of Journey*	Comment
	First Presentation	Severe rash, intolerable itching
	Diagnosis	Needs to be quicker, especially in atypical forms
	Treatments	Need to come up with an overall best treatment plan
	Relapses	
	Follow Up & Burden	Throughout the illness; day to day issues

**NB: Stages of the Journey are condition specific and should be defined at the beginning of the process to develop a Patient Journey.*

4. STAGES OF THE PATIENT JOURNEY

4.1. FIRST SYMPTOMS

4.1.1 CLINICAL PRESENTATION / SYMPTOMS

- 1) Very severe rash, itching, patches of redness, pimples
- 2) Skin & scalp affected – More rarely affects the mouth but can do so
- 3) Blisters appear and burst; this leads to painful erosions and leave the skin raw
- 4) A crust forms after the blisters have burst – redness and a sensation of heat may be felt on the skin

4.1.2 PATIENT NEEDS

- 1) Need for a quick diagnosis
- 2) Tele-dermatology is now being used in some areas – a nurse sends pictures to a dermatologist for a diagnosis, which further delays the process as it adds another step
- 3) Accessibility to appropriate care – it depends on where you live. In France, many dermatology departments now have an emergency drop-in clinic

4.1.3 NECESSARY ACTIONS

- 1) Quickly get an appointment with the GP to identify the disease and make sure it's not contagious.
 - a. Patients think they may have been bitten by an insect.
 - b. Most doctors suspect scabies or bedbug bites, and prescribe treatment accordingly, especially in atypical non-bullous forms of BP
- 2) Quickly get another appointment with the GP to get a letter to consult a dermatologist since multiple treatments have failed due to a previous mis-diagnosis and conditions are worsening – blisters are bursting.
 - a. Patients prefer that doctors say they don't know and refer them to someone who might know
- 3) Get an appointment with a dermatologist as soon as possible - delays are far too long especially since Covid (around 6 months) and in some areas, no appointment is possible because dermatologists are no longer seeing new patients.
 - a. The need of a referral to see a dermatologist is necessary in some countries
- 4) If the disease worsens and no appointment with a dermatologist is possible, we recommend going to the emergency room for advice or to an A&E, an emergency walk-in center (for dressings) and get a transfer to an AIBD competent center or a community dermatologist center.
 - a. Some GPs in the UK have extended their responsibilities to include dermatological interests and get more expertise

4.1.4 IDEAL OUTCOME & SUPPORT

- 1) Reducing the diagnostic delay
- 2) Needing of support, kindness and time to listen on the part of doctors
- 3) Taking into account the pain of the disease and the "torture" of itching - ferocious itching
- 4) Taking into account difficulties with movement and mobility
- 5) Taking into account difficulties with washing and dressing - difficulties of daily life
- 6) In nursing homes, having the option of consulting a specialist without waiting for the disease to worsen, and avoiding ill-adapted topical care due to the absence of a diagnosis.

- a. Better handling and management of topical care (few on-site nurses for the number of patients)
- 7) Taking into account the patient's other pathologies
- 8) Taking into account fatigue, sleep difficulties and anxiety and fear as patients don't know what is happening to them, all of which are linked to misdiagnosis. These uncertainties are difficult to manage.
 - a. Conversely, being aware of the "downplaying" of this disease in relation to the other diseases the person is suffering from

4.2. DIAGNOSIS

4.2.1 CLINICAL PRESENTATION & SYMPTOMS

- 1) Bullous Pemphigoid – evaluation of IgG4 tissue autoimmunity using DIF is valuable for diagnosing BP
- 2) Usually carried out within 3 to 6 months - because elderly people often only have skin lesions
- 3) 1st appointment:
 - a. In France, with a local dermatologist – rarely at the hospital
 - b. In the UK, the GP will refer patients to a dermatological clinic within the hospital where they will be seen and treatment will be decided and they may be assigned to a particular dermatologist. A biopsy will also be arranged to confirm diagnosis

4.2.2 PATIENT NEEDS

- 1) The longer it takes to diagnose the disease, the more severe it becomes: there are numerous, widespread blisters and the skin is raw on large parts of the body, feet and hands
- 2) Severe difficulty moving around, getting dressed, sitting up - getting out of bed, washing...
- 3) Need to understand the disease and whether it is contagious – the nature of the disease should be explained
- 4) Need to be aware of the diagnostic procedures - namely DIF and serum studies to detect targets for autoimmunity
- 5) Need for a GP who is aware of the disease and able to refer rapidly the patient to an office base dermatologist (and consequently able to get an early appointment) or to refer the patient to a dermatology department
- 6) Need to deal with psychological and social consequences

4.2.3 NECESSARY ACTIONS

- 1) Plan well the first appointment with the dermatologist: it's essential to go with someone and with a list of questions prepared in advance.
 - a. Take all medical records with you so that you can provide a list of the medications used on a daily basis.
 - b. Take pictures in advance of the lesions to show at the first appointment
- 2) At this appointment, patients must learn how to apply the treatment - what dose and how to apply it all over the body
- 3) At this appointment, given that patients are often elderly and in pain, they are likely to be panicked and lost, so it's essential that a caregiver be present to listen to the recommendations
- 4) Need for a nurse to apply the treatment; the spouse is not always inclined to do it (disgust) and doesn't know if it will be applied properly - inform nurse or spouse not to forget to wear gloves
- 5) Dealing with blisters is hard – need to avoid blisters from joining each other into one big one – there is ignorance on the part of GPs & nurses regarding the need to burst but never to derroof them
- 6) Dealing with aspirating the blisters is a challenge – many nurses or clinicians don't seem to know whether to or not and how to. Many nurses refuse to aspirate

- 7) Make sure to be informed of the upcoming appointment schedule (blood tests and additional examinations)
- 8) Relief of patients at knowing what's wrong with them, being able to put a name to their illness, and knowing that they'll be taken care of
- 9) Need for a close collaboration between health care providers / nurses and hospital based physicians or nurses

4.2.4 IDEAL OUTCOME & SUPPORT

- 1) Feeling reassured, that you can trust your doctor and knowing that he/she is familiar with your pathology is essential
- 2) To be able to consult a dental specialist (stomatologist in France) if there's something in the mouth – this case remains rare
- 3) Having access to home care nurse – especially in the case of some elder patients who live alone and have no one to put the topical CS, or cream on them – as some places on the body are impossible to reach... so getting nurse care is essential
- 4) Being able to get psychological support especially since Covid – the cause/consequence of the Covid vaccine is feared to be a trigger of the disease
- 5) Being able to contact someone in case of need - to have a doctor's contact details in case of difficulties, worsening of symptoms or occurrence of side effects
- 6) Being able to share with others who have been through the same thing – support and listening from peers and patient organizations

4.3. TREATMENTS

4.3.1 CLINICAL PRESENTATION/ SYMPTOMS

BEFORE diagnosis and while waiting for biopsy results, it is difficult to cope with the disease

- 1) Blisters continue to appear on a regular basis while waiting for treatment to control the disease. Blisters rupture, leaving the skin raw
- 2) Fierce itching persists

Treatment set-up in France:

- 1) Long-term topical steroids
- 2) Combined with other treatments if necessary:
 - a) Methotrexate
 - b) Immunosuppressants
 - c) Doxycycline
 - d) Biologics – Xolair (Omalizumab) & Dupilumab (Dupixent)

Treatment set-up in the UK:

- 1) Oral steroids (high dose) with topical steroids
- 2) Steroid sparing treatment: depending on patients' toleration:
 - a) Methotrexate
 - b) Immunosuppressants
 - c) Doxycycline
 - d) Dapsone etc

During the treatment set-up (France & UK):

- 1) Blisters, pain and itching are still on-going – but, most patients achieve control of disease activity and a disappearance of their itch after a mean delay of 10 days
- 2) Weakening and thinning of the skin
- 3) Appearance of purpura (purple spots)

- 4) Anemia, intense fatigue, shortness of breath, digestive disorders (methotrexate)
- 5) Fatigue, risk of infection, nausea (immunosuppressants)
- 6) Headaches, abdominal pain (Xolair – omalizumab)

4.3.2 PATIENT NEEDS

- 1) Having the possibility to be followed by a specialist who knows the disease and takes the time to care for the patient
- 2) Understanding the disease to become a player – since mostly elderly people are affected by this disease, the need to be accompanied by someone (a family member, a carer) is essential
- 3) Understanding the purpose of treatments
- 4) Being informed of any side effects of treatment and know if they are cause for concern – and then, the need to be followed by other specialists in order to reduce the side effects caused by the treatments (eg. high doses of systemic steroids can lead to early osteoporosis)
- 5) Need to be aware that comorbidities require treatments along with the treatment of BP
- 6) Being able to have access to a homecare nurse who is familiar with the disease
- 7) Exchanging experiences with other patients
- 8) Enabling patients to relieve pain, itching and lack of sleep
- 9) Being able to receive psychological support
- 10) Knowing which washing products to use in the shower and whether baths are recommended
- 11) Knowing how to pierce blisters, apply cream and non-adhesive and tubular dressings

4.3.3 IDEAL OUTCOME & SUPPORT

- 1) Reducing the number of blisters
- 2) Relieving itching and pain
- 3) Providing high-quality local care and follow-up by a specialist who is familiar with these diseases
- 4) Understanding clearly the side effects because they can be frightening – side effects of steroids especially (diabetes, high blood pressure, osteoporosis...)
- 5) Relieving sleep deprivation by means other than additional allopathic treatments - giving priority to hypnosis, relaxation, etc.
- 6) Being also looked after by professionals who may have a general view: the GP or the geriatrician who will be able to act as a link between the various specialists who follow the patient, as some patients may suffer from several pathologies and have multiple treatments
- 7) The value of this general overview: updating prescriptions, sorting them out because some treatments are no longer necessary and are proving to be counter-productive
- 8) Checking mouth complications and advice on which foods to eat and which to avoid

4.4. RELAPSES

4.4.1 CLINICAL PRESENTATION / SYMPTOMS

- 1) Relapses can occur a few months after the start of treatment if the treatment is reduced too quickly
- 2) Relapses can also occur if topical treatment is not carried out correctly
- 3) Relapses also occur if treatment is inadequate, insufficient
- 4) Complementary treatments aim to reduce and prevent relapses – methotrexate/ Xolair (omalizumab); in the case of omalizumab, it is important to note that this is an off-label expensive treatment

SYMPTOMS:

- 1) New itching, which is a precursor of new blisters (on the skin)
- 2) New blisters on the skin and persistent itching
- 3) These relapses do not always affect the same part of the body
- 4) A few rare cases in the mouth

4.4.2 PATIENT NEEDS

- 1) Need to know how many new blisters it takes in a given period of time for patients to consider that they are having a relapse and inform their doctor
- 2) Need to understand the pain threshold because patients are different with the number of blisters they can tolerate
- 3) Need to understand the blister location
- 4) Need to understand the co-morbidities
- 5) Need to be able to contact the doctor's secretary or write a letter to the consultant

4.4.3 NECESSARY ACTIONS

- 1) Making sure the treatment is carried out correctly, sufficiently & adequately
- 2) Making sure complementary treatments (methotrexate/ xolair – omalizumab) are put in place and are well tolerated

4.4.4 IDEAL OUTCOME & SUPPORT

Being able to contact the specialist doctor or a referral person so that patients know whether their relapse is minor and requires only monitoring, or whether they need to see a doctor quickly

4.5. FOLLOW-UP CARE & BURDEN OF THE DISEASE

4.5.1 CLINICAL PRESENTATION / SYMPTOMS

Important signs to watch out for:

- 1) fever (infection)
- 2) fatigue (anemia)
- 3) digestive problems
- 4) sleeping disorders
- 5) osteoporosis
- 6) high blood pressure
- 7) diabetes
- 8) Throughout the illness:
 - a. Positive evolution or absence of blisters and wounds
 - b. Watch out for drug interactions
 - c. Frequent sensation of skin sensitivity, skin fragility and skin physical discomfort

4.5.2 NECESSARY ACTIONS

- 1) Blood monitoring/blood tests – these are very important since:
 - a. some medications can affect your liver function (every 3 months but may be more frequent) – they aren't to monitor the disease as such
 - b. some medications (eg. Dapsone) in the UK need a blood test before being given as some people can't tolerate it (the blood test will show this)
- 2) Frequent visits to the dermatologist at the start of the disease; more spaced out thereafter
- 3) Preparing a list of questions before each appointment with the GP or specialist doctor
- 4) Going to the doctor's appointment accompanied – this reassures patients and carers
- 5) Throughout the illness:
 - a. Watching out for drug interactions
 - b. Knowing that doses must be respected and not lowered even if there is a clear improvement
 - c. Careful monitoring in the event of superinfections (streptococci, staphylococci, herpes, fungi)
 - d. Careful monitoring of fever, thick scabs surrounded by a red, warm halo

4.5.3 PATIENT NEEDS

- 1) Need for psychological support – difficulty in talking to those around
- 2) Being informed about vaccines – knowing which ones are necessary
- 3) Throughout the illness:
 - a. Reduction of treatment
 - b. Getting advice on the application of comfort creams and prescription of creams that may be reimbursed by the health insurance system
 - c. Other people's gaze:
 - i. rejection/exclusion from social and/or family environments

- ii. others being afraid of passing on something to you
 - iii. self-conscious of appearance – hair loss, body stretch marks, thin skin
 - d. Knowing how to explain your illness to those around you and explain it is neither contagious nor hereditary
- 4) Day to day issues:
- a. Administrative problems related to the illness:
 - i. In France: being able to obtain 100% reimbursement
 - ii. In the UK: prescriptions are free if one is over 60; under 60, prescriptions are free when the disease is listed as a chronic one – but, AIBDs are not on the chronic disease list!
 - b. Effects on daily life: getting help with house chores – cleaning, grooming and so on ...
 - c. Financial problems – low pensions, no health insurance:
 - i. Organizing financial support for home help
 - ii. Finding a solution to the very high cost of care – there is a lot left to pay for (specific shampoos, creams, maintenance and so on ...)
 - d. Work life – for BP patients who are still working:
 - i. Fear of losing their job, fear of a loss/reduction of salary
 - ii. Necessity of having to convince their employer that BP is a chronic and very serious condition
 - iii. Need to be able to take time off when ill (results of side-effects, relapsing & co-morbidities)
 - e. Organizing travel to doctor's consultations:
 - i. Being accompanied or arranging for someone to collect patients
 - ii. Organizing transport for medical or paramedical appointments
 - iii. Preparing and asking for prior reimbursement requests to the social services/ social security system
 - f. Traveling:
 - i. Organizing trips and holidays abroad
 - ii. In the UK, the cost of travel insurance can be an issue
 - iii. In France, when travelling in Europe, not forgetting to order a European health insurance card to avoid having to pay medical expenses on the spot
 - iv. Making sure patients have prescriptions and medical reports with them to deal with any emergencies

4.5.4 IDEAL OUTCOME & SUPPORT

- 1) Blood tests: understanding what information is important to monitor in order to notify the doctor without delay
- 2) Knowing the next stages of treatment and the disease
- 3) Staying in contact with the doctor treating the condition to deal with any side-effects resulting from treatment and those that persist or are the result of any drug interactions
- 4) Establishing a communication link between the GP and/or geriatrician and the specialist doctor
- 5) Knowing how to quickly recognize signs of superinfection
- 6) Improving nursing care: blister piercing and counting as well as dressings take time - which does not motivate nurses to care for these patients
- 7) Throughout the illness:
 - a. Pharmacist vigilance is advisable

- b. Being able to continue lowering doses without relapsing
- c. Knowing when to contact your doctor without delay
- d. Feeling better in your own skin
- e. Needing psychological support and group support – being able to contact people who are going through the same thing to ask practical questions and exchange tips and tricks that help in every day life

8) Day to day issues:

- a. Administrative problems related to the illness: in France, getting help if you are refused the 100% reimbursement by contacting the patient organization (the APPF) or a social worker
- b. Effects on daily life:
 - i. Needing domestic help and support from a social worker – inform them with a booklet so that they understand the disease and the difficulties involved
 - ii. Declaring a person of trust between the doctor and the patient
 - iii. In France, creating an MDPH (Handicap) file if necessary
- c. Financial problems: finding the necessary contacts in the appropriate organizations (social security + health insurance)
- d. Work life: need of employer's understanding and support
- e. Organizing travel to doctor's consultations: finding help for carers who have to take time off work to accompany patients

4.5.5 BEST PRACTICE

It is important to warn emergency services that the skin of these patients is extremely fragile, and in the event of hospitalization, it is necessary to point out that regular dressings are to be avoided for the maintaining of an IV drip. Tubular dressings are preferable.

Over all, BP is the same condition wherever it occurs but the subsequent journey is dictated by varying health systems or even regional differences within a health system.

An ideal outcome would be to compare the different treatment approaches with outcomes and come up with a definitive “best treatment plan” for BP.

5. ACKNOWLEDGEMENT

Association Pemphigus Pemphigoïde France (APPF)

PEM Friends (UK)

Associazione Nazionale Pemfigo/Pemfigoide Italy (ANPPI)

ERN SKIN AIBD Doctors

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