Presentation and Discussion of a case study of a female patient with longstanding "atypical disease"

Introduction

- Mrs M
- D.O.B. 1/4/1946
- Longstanding Disease
- First contact Physiotherapy AS Clinic 2002

History

- 1961; age 16 years; generally unwell, swollen knees and ankles
- Admitted to hospital for 8 weeks
- Diagnosed Rheumatic Fever
- Treated with IM steroids and high dose Aspirin
- Complete recovery

History

- 1965-6 LBP following childbirth
- Treated conservatively no improvement
- MUA x2
- Traction and 3 week plaster cast
- Physiotherapy
- Ongoing intermittent pain

- Relevant Investigations??

History

- 1970, birth 2nd child
- Developed chest pain and multiple joint pain
- Felt she was being ignored
- Requested to see Psychiatrist

History

- 1973 admitted to hospital
- Prescribed Indocid

"They were wonderful"

- Complete recovery mild episodic flares until 1978
- Domiciliary visit from Orthopaedic Surgeon
- Manipulation " Mortal Agony, never felt such severe pain"

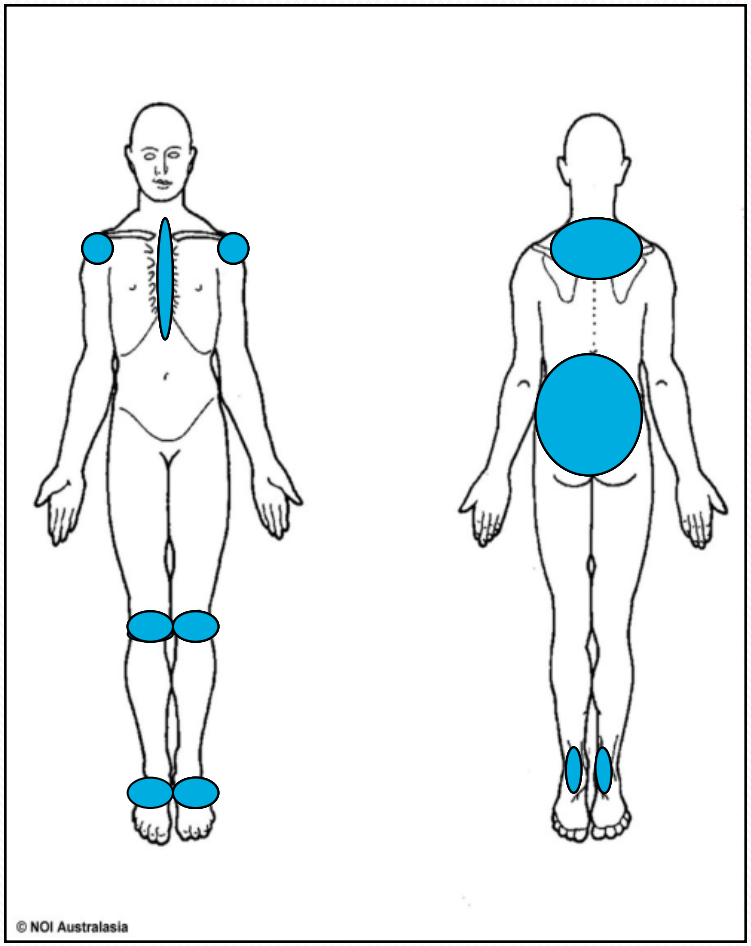
Reasoning

- With the benefit of hindsight, thoughts so far?
- Any medical concerns?
- Any further questions you would have asked?
- What is pattern of symptoms telling us?
- What would you do?

- Questions?

Pattern of Symptoms

- ✓ Insidious onset
- ✓ Age of onset
- ✓ Flares following childbirth
- ✓ Inflammatory Arthritis
- ✓ Intermittent worsening episodes
- ✓ Possible enthesitis
- ✓ Good response to NSAID's



Rheumatology History

- 1979 Referred to Rheumatologist
- Diagnosed Ankylosing Spondylitis
- Told “would probably end up in a wheelchair and become incontinent”
- “ My world fell apart- husband, 2 children and a job-------however secretly I was relieved to have a diagnosis; not all in the mind”

Reasoning

- What happened in 1973?
- What mechanisms are brought into play now?
- What do you think this Rheumatologist should have done?

Other stuff

- Around this time experiencing severe lateral trunk/back pain
- Dismissed by herself and medical team as part of her AS
- Tried various pain relieving methods
  - Acupuncture
  - TENS
  - Various NSAID's
- This pain actually turned out be a combination of ovarian cyst and endometriosis
- 1981 Hysterctomy

Summary so far

- Working Mum with 2 children
- Intermittent severe and debilitating pain and stiffness
- 18 years from first onset to diagnosis
- Poorly managed disease
- Bizarre treatments!!!

LESSONS

- Taking things at face value
- Never assume
- Education??
- Specialist Physio???
- Adequate management???
- Could we have yellow Flags already emerging through previous treatments impact and style of diagnosis?

Moving on

- 1981-1994
- Increasing fatigue and pain
- Treated with IM steroid injections when desperate
- Sold house and moved to a smaller one to help her to cope
- Struggling to keep working (her GP was also her employer
- 1994 “One morning the car would not start– decided to retire (48years)

Bath

- Referred to bath 1995
- Several scans Isotope bone scan followed by MRI
- Δ Metastasis Spine " I was told that I had cancer and had a short time to live"
- Multiple scans; no primary tumour found
- Assumption made that this was Atypical AS

Evidence

Destructive diskovertebral lesions in ankylosing spondylitis: appearance on magnetic resonance imaging.

Kurugoglu S, Mihmanli I, Kanberoglu K, Kanberoglu A.

Neuroradiology. **2001 Dec;43(12):1098-101.PMID: 11792053 [PubMed - indexed for MEDLINE]**

"We report magnetic resonance imaging findings of diskovertebral lesions in a case of ankylosing spondylitis mimicking metastatic and/or infectious disease. Multiple hypointense areas were seen on T1-weighted images corresponding to hyperintense areas on T2-weighted images in dorsal, lumbar, and sacral vertebral bodies and the manubriosternal joint, with accompanying soft tissue masses. Diagnosis was achieved through biopsy, regression of the paravertebral soft tissue masses, later detection of bilateral sacroiliitis on computed tomography, and presence of histocompatibility antigen HLA-B27."

Moving on again!

- Services Change 1999
- Consultant input from Bath
- Gwent Rheumatology Service

" Felt that everything I told him he listened pain did not change but I felt better"

- Referred to Orthopaedics (L.THR1999 R. THR 2000)*

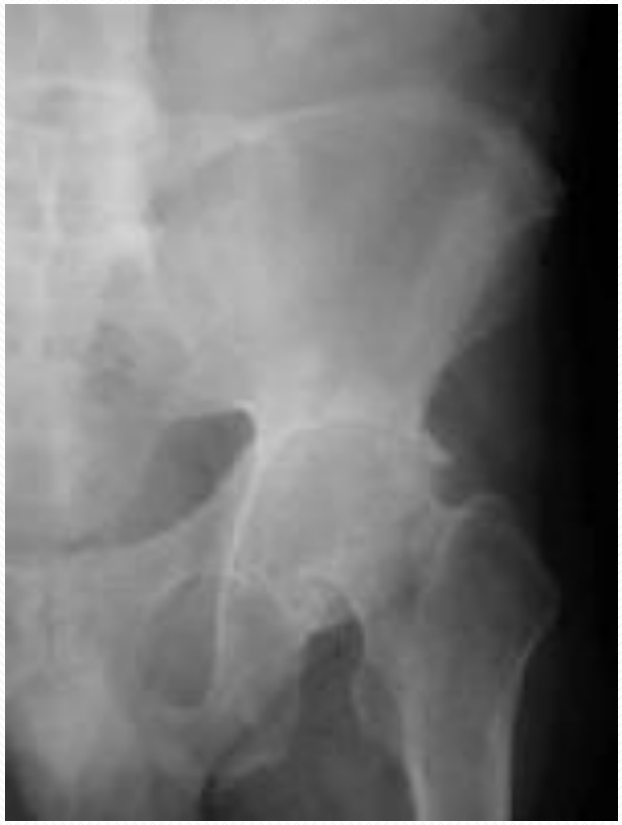
- Joined local newly formed NASS group

Reasoning

- Women have a significantly earlier age of disease onset and worse functional outcomes despite more radiographic severity in men[1D]
- There is suggestion that women have more peripheral arthritis[1E]
- A greater proportion of first degree relatives have a history of the disease[1C]
- In women, the symptoms of ankylosing spondylitis often first present during or post PREGNANCY

Lee, K *et al*. Are there gender differences in severity of ankylosing spondylitis? Results from the PSOAS cohort. *Ann Rheum Dis* 2007;66(5):633-638

Hip Joint involvement



- The hip joint space is narrowed uniformly.[2a]
- Axial migration of the femoral head occurs, and a collar of osteophytes may be seen at the femoral head-neck junction [2b]

2. Imaging In Ankylosing Spondylitis; Wilfred C.G. et al. Medscape Reference (2011) (last accessed July 2012)

Hip Joint involvement

- Typically is bilateral and symmetrical.[2c]
- Non destructive ankylosing form in young patients.[3a]
- Secondly, a slower unilaterally destructive process in older individuals.[3b]
- Hip disease suggests a more aggressive disease.[3c]

3. Hip involvement in ankylosing spondylitis: epidemiology and risk factors associated with hip replacement surgery; Bert Vander Cruyssen **et al.** *Rheumatology Volume 49, Issue 1* Pp. 73-81 (2010)

Physiotherapy Service (2001-2003)

- Increasingly reduced function
- Increasing pain particularly Thoracic spine
- Chronic Migraine
- Fatigue
- Poor sleep pattern
- Not responsive to physical treatment
- Increasing disease activity, marked functional deterioration
- Referred to Rheumatology Consultant
- BASDAI 9.0

Medical Interventions (2001-2003)

- Chronic Pain
  - Amitriptyline
  - Gabapentin
  - Botox Injections
  - Baclofen
  - IM Depomedrone
  - Clonazepam
  - Thoracic Epidural (steroid)

Ant-TNFά

- Prescribed Remicade & MTX (Feb 2004)
- Marked Improvement scores
- BASDAI 3.8 May 2004
- BASDAI 2.6 Sept. 2004

“ Wonderful! Felt the difference immediately”

Objective Markers / Goals

	BASMI	BASDAI	BASFI	BASGI
• 24.9.2004	3.8	2.6	2.2	1.9
• 30.9.2005	3.6	2.8	5.5	0.7
• 29.9.2006	4.8	6.4	4.8	6.2
• 28.9.2007	3.9	3.8	3.2	2.2
• 25.1.2008	4.2	6.1	6.0	6.4
• 30.1.2009	5.0	7.0	5.7	9.4
• 19.4.2010	5.8	6.78	7.4	7.0
• 4.7.2011	4.8	8.03	8.0	7.45

Reasoning

- Developed Abdominal pain and changes in bowel habits
- Remicade MTX combination discontinued
- Despite IM steroids functional deterioration +
- Subsequent scores are reflective of her medication changes
- 2006 Adalimumab
- 2007 ANA +ve Symptoms of Lupus Discontinued Adalimumab
- 2008 Chose to restart

Side effects of Infliximab

- Mild stomach pain or upset [4a]
- Bloody, black, or tarry stools[4a]
- Nausea, vomiting, or diarrhea[4a]

4. Inflximab side effects; http://www.drugs.com/sfx/infliximab-side-effects.html (Last Accesses July 2012)

2008

- ?Allergic Reaction to Adalimumab
- Swelling Hands face
- Ankle Oedema persistent despite discontinuation
- Gall stones ↑ Liver enzymes+
- Complex Cholecystectomy

Side Effects of Infliximab

- Severe allergic reactions (rash; hives; itching; difficulty breathing; tightness in the chest; swelling of the mouth, face, lips, or tongue) [4b]
- biliary pain, cholecystitis, cholelithiasis, and hepatitis have been reported.[4c]

2009-2010

- Adulinimab re-introduced May 2009
- General Health and Function improved
- Nov 2009 developed Pustular Psoriasis

(palmer and plantar)

** Has gradually decreased her involvement with NASS as feet are painful and unable to exercise in hydrotherapy pool

Side effects

- Psoriasiform eruption (erythematous, slightly scaling, well-shaped pruriginous plaques) has been reported.[4d]
- Development of antibodies to Ant-TNFά(up to 51%), development of antinuclear antibodies (about 50%), newly detected anti-dsDNA antibodies (about 20%), lupus and lupus-like syndromes (uncommon)[5]

Humira side effects; http://www.drugs.com/sfx/humira-side-effects.html; (Last accessed July2012)

What to do?

- Considering this ladies complicated history and her present deterioration how best can this be managed?

Problem List

- Reactions to meds
- Effect of discontinuation on AS
- Reduced function and ability to continue physical activities
- Pain management

Treatment Plan

- Referral to Dermatology effective management of Psoriasis
- Referral to specialist MDT clinic to monitor and manage medication, pain and functional issues of AS

Combined clinics

- March 2011; Off, Adulinimab due to orthopaedic Surgery
- Generally unwell; night sweats, back pain, fatigue and fainting; no local signs of infection
- Symptoms probably due to AS
- BASDAI 7.2

PLAN:

- Resume Adulinimab; Review 2/12

Outcome

- June 2011
- ANA +ve ↑ ds DNA anti-body
- Adulinimab discontinued
- MRI Imaging sequences requested
- Enterocoxib trial with BP monitoring
- July 2011 BASDAI 7.5
- Referred to Gastro-enerology
- Switch to Etanercept

Mode of action Ant-TNFά

- TNF-alpha; mediator of inflammation and tissue damage in inflammatory arthritis
- Selectively bind TNF-alpha in the cellular micro environment, thereby preventing interaction with membrane-bound TNF receptors on target cells.
- Etanercept is a recombinant fusion protein of the soluble type II TNF receptor on a human IgG1 backbone
- Adalimumab is a recombinant human monoclonal antibody specific to TNF
- Golimumab is a fully human anti-TNF IgG1 monoclonal antibody that targets and neutralises both the soluble and membrane-bound forms of TNF

Adverse Effects

- Tuberculosis; Bacterial infections, including sepsis and pneumonia, invasive fungal infections, and other opportunistic infections
- Demyelinating disease, seizures, aplastic anaemia, pancytopaenia, and drug-induced lupus
- Formation of antibodies ↓ efficacy "Etanercept does not appear to generate neutralising antibodies"

TREATMENT

- November 2011
- 3/12 trail Golimumab
- March 2012
- Continuing on Golimumab
- Reports 100% improvement
- No side effects

Questions?