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Professional Issue.

Physiotherapy co-management of rheumatoid arthritis: Identification of red flags, significance to clinical practice and management pathways.

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ABSTRACT

Rheumatoid arthritis (RA) is a chronic, systemic, autoimmune disease. Physiotherapy interventions for people with RA are predominantly targeted at ameliorating disability resulting from articular and peri-articular manifestations of the disease and providing advice and education to improve functional capacity and quality of life. To ensure safe and effective care, it is critical that physiotherapists are able to identify potentially serious articular and peri-articular manifestations of RA, such as instability of the cervical spine. Additionally, as primary contact professionals, it is essential that physiotherapists are aware of the potentially serious extra-articular manifestations of RA. This paper provides an overview of the practice-relevant manifestations associated with RA that might warrant further investigation by a medical practitioner (red flags), their relevance to physiotherapy practice, and recommended management pathways.

Key words: rheumatoid arthritis; red flags; safety; physiotherapy.

Word count: 1,954

INTRODUCTION

Rheumatoid arthritis (RA) is a systemic, autoimmune, inflammatory condition that affects multiple tissues and organs in the body, in particular the synovial joints and peri-articular tissues. It is the most common of the inflammatory joint diseases. RA is associated with significant pain, functional impairments and co-morbid health conditions (Kvien, 2004). In recognition of the substantial health, psychosocial and community impacts imposed by RA, this condition is recognised as a National Health Priority Area in Australia and current health policies address the need to optimise health service delivery (Department of Health (Western Australia), 2009; National Health Priority Action Council, 2006). The systemic and progressive nature of the condition and associated co-morbidities (Briggs et al., 2009) also contribute to premature mortality (Myasoedova et al., 2010), particularly in individuals who experience extra-articular (EA) manifestations associated with the disease. In order to ensure safe and effective patient care, clinicians working in primary care need to be able to readily identify manifestations which may contribute to morbidity and mortality and influence prognosis.

Physiotherapy represents a critical component of the overall management for patients with RA, as substantiated by a strong evidence base, and reflected in clinical practice guidelines (Bell et al., 1998; Ottawa Panel, 2004a; Ottawa Panel, 2004b; Li et al., 2006a; Li et al., 2006b; Forestier et al., 2009; Royal Australian College of General Practitioners, 2009; Hurkmans et al., 2011). Recent data suggest that the physiotherapy workforce needs professional development in the safe and effective delivery of clinical physiotherapy services. In particular, the ability of physiotherapists to identify the presence of *red flags* in patients with RA and implement appropriate on-referral was highlighted as an essential skill required for safe and effective care (Briggs et al., 2012; Fary et al., 2012). Red flags have been defined as the “clinical indicators of possible serious underlying conditions requiring further medical intervention” (Hunter New

England NSW Health, 2005, p.1) and "…manifestations that suggest that physician referral may be warranted" (Leerar et al., 2007, p. 42). The broader definitions of red flags may equally be attributed to those serious physical findings whose management is outside the scope of physiotherapy practice, e.g. visual disturbances related to scleritis. This professional issue article is written within the context of this broader definition. The aim of this paper is to provide an overview of articular, peri-articular and EA red flags associated with RA and highlight specifically what clinicians need to *look* and *listen* for in practice, and the practice implications.

RHEUMATOID ARTHRITIS

Although there is no cure for RA, early identification and initiation of appropriate therapies are important to arrest the progression of symptoms and improve longer-term outcomes (Finckh et al., 2006; van der Linden et al., 2010). Physiotherapists need to be able to: (i) recognise signs and symptoms (musculoskeletal and other body systems) that at pre-diagnosis suggest RA, and (ii) identify any serious disease or medical condition associated with RA that may lead to irreversible damage or premature death (Beattie et al., 2011).

The following sections outline the articular, peri-articular and EA red flags associated with RA that are relevant to contemporary clinical practice.

Articular and peri-articular red flags in RA

Early recognition of the articular and peri-articular features of RA that may indicate disease-specific severity and that require on-referral is important for the primary care clinician, as these have implications for patient safety and best-practice care (Table 1).

The typical disease course of RA involves chronic low-grade inflammation with periodic flares which may present as articular or peri-articular manifestations (Prete et al., 2011). Inflammatory mediators contribute to the progressive destruction of joint tissue in the absence of disease-modifying treatment (Tarner et al., 2005). Chronic synovial inflammation, bone erosion, and cartilage destruction within the joint may lead to joint instability in both appendicular and axial skeletons.

Up to 86% of people with RA have involvement of the cervical spine (Mukerji and Todd, 2011), of whom 17-85% will progress to cervical spine instability (Wolfs et al., 2009). Furthermore, neurological deterioration is almost inevitable in patients with RA treated conservatively for cervical spine instability associated with myelopathy (Wolfs et al., 2009). The presence of cervical spine instability in RA also leads to a higher mortality rate (Paus et al., 2008; Wasserman et al., 2011). Recognising the potential association between RA and joint instability and identifying risk is particularly critical in the cervical spine, where instability and subluxation (particularly in the upper cervical spine) can have catastrophic consequences leading to sudden, unexpected death (Neva et al., 2006; Paus et al., 2008; Wasserman et al., 2011) or quadriplegia (Neva et al., 2006) due to compromise of the spinal cord and/or brain stem. Significantly, while a range of signs and symptoms are indicative of cervical spine involvement (Table 1), a large proportion of cervical instabilities are asymptomatic (Collins et al., 1991; Neva et al., 2006) highlighting the need for clinical vigilance in patients with RA. Moreover, the severity of cervical instability has been associated with the severity of RA activity in peripheral joints (Hirano et al., 2012) and a long duration of disease (Neva et al., 2006), further highlighting the need for clinical vigilance in this context. A recent survey of Australian physiotherapists indicated that only 64.4% of respondents would test for cranio-cervical instability when treating the upper cervical spine of patients with RA (Osmotherly and

Rivett, 2011). A clinical case on upper cervical spine instability in RA is published in this issue of Manual Therapy (Slater et al. 2013).

Instability also occurs in peripheral joints and may require splinting or surgical stabilisation to reduce symptoms and improve function.

Commonly occurring peri-articular conditions associated with RA include: tenosynovitis (often the first sign of inflammatory joint disease (Hmamouchi et al., 2011)) and tendon rupture; boutonnière deformity, swan neck deformity and carpal tunnel syndrome in the hand, and hallux valgus, medial longitudinal arch flattening and claw toe in the foot (Table 1). Notably, early evidence of hand deformities is a reliable indicator of more severe disease (Johnsson and Eberhardt, 2009), highlighting the importance of early recognition and appropriate intervention or on-referral.

Practice points

Assessing and monitoring disease severity is an important clinical skill. Tools to assist clinicians have recently been identified and could readily form part of best evidence practice including communication with the RA team or GP (Anderson et al., 2012).

Risk/benefit analysis: recommend screening for signs and symptoms of RA prior to implementing management, especially in the upper cervical spine: on-refer if in doubt.

Increased vigilance in using manual techniques in the cervical spine if suspicion of instability especially C1/C2.

INSERT TABLE 1 HERE

Extra-articular red flags in RA

As RA is a systemic, autoimmune disease, multiple organs and systems may also be affected. Understanding the implications of systemic disease involvement means that physiotherapy management can be better informed and contraindications to management are identified at an early stage, ensuring safe and effective patient care (Table 2).

Extra-articular features are largely influenced by inflammatory mediators associated with the disease process (Hochberg et al., 2008) and have a significant influence on prognosis (Turesson et al., 2002; Prete et al., 2011). For example, in a recent review on the epidemiology of EA features in patients with RA, based on studies with RA cohorts of greater than 100 patients, Prete et al. 2011 reported an overall incidence of 28% (19.8% non-severe form and 8.3% severe forms). The authors reported a greater incidence in northern European countries and among smokers, highlighting the role of environmental and genetic factors in their aetiology. Severe EA features may occur in individuals with recently diagnosed RA (Turesson et al., 1999).

Most EA features are an expression of rheumatoid vasculitis, occurring as a consequence of chronic inflammation, causing organ-specific manifestations, usually in the cutaneous (Figure 1) and neurological systems (Genta et al., 2006), but may also occur in other systems (Table 2), such as the visual system (Figure 2). Drug-induced conditions associated with RA are also significant, for example glucocorticoid-induced osteoporosis and diabetes mellitus, and the increased susceptibility to cancer and infections as a consequence of immunosuppressive agents. Table 2 provides an overview of practice-relevant EA features and co-morbidities, adapted from Young and Koduri (2007) and Prete et al. (2011).

While a large volume of studies have been undertaken to characterise the epidemiology of EA manifestations of RA, comparability between studies is limited due to substantial sampling

differences, the absence of a standard classification system for these manifestations (Turesson and Jacobsson, 2004; Young and Koduri, 2007; Prete et al., 2011) and the complexity in distinguishing these manifestations from co-morbid conditions associated with drug therapies and disease duration (Young and Koduri, 2007; Prete et al., 2011).

INSERT TABLE 2 HERE

INSERT FIGURE 1 AND FIGURE 2 HERE

Practice points

A thorough patient history and physical examination are critical in patients with RA (see Castrejón et al., 2012).

Identification of EA features requires a thorough clinical assessment, including screening for other systemic signs (e.g.; dyspnoea, skin lesions, itchy eyes), in conjunction with screening for articular and peri-articular features (e.g. Figures 1-2).

Cardiac, neurological and pulmonary manifestations have the potential to cause disability and may require modification of physiotherapy management. Reduced cardiac, pulmonary and neuromuscular performance may lead to fatigue, dyspnoea and reduced capacity to engage in aerobic and strengthening exercise and perform functional tasks.

EA features require a broad consideration of management and may indicate the need for on-referral. Referral communications should highlight key aspects of a patient's medical history that suggest RA (see Jack et al. 2012).

Assessing and monitoring disease activity

The use of screening tools in clinical practice may alert the clinician to the presence of an inflammatory joint condition and assist in identifying red flags and recognising the implications

for physiotherapy management. Current recommendations for clinically-appropriate tools to measure RA disease activity are available (Anderson et al., 2012). A self-administered early inflammatory arthritis detection tool has also been developed for use in primary care (Bell et al., 2010). Although the psychometric and scoring properties of the instrument are yet to be established, use of the 11-item instrument in physiotherapy practice may help alert the clinician to possible RA or other inflammatory joint disease. Further, use of the gait, arms, legs and spine (GALS) locomotor screening examination for RA (recently tested for use among physiotherapists) has high specificity, suggesting utility as a physical screening test in primary care settings (Beattie et al., 2011).

While this review is focussed on red flags, psychological co-morbidities (such as depression and anxiety) commonly associated with pain and impaired function as a consequence of chronic and progressive diseases such as RA (McKnight-Eily et al., 2009) should be screened for and on –referral is recommended when appropriate.

SUMMARY

RA is a chronic, progressive and serious systemic condition, potentially causing death. Timely identification of potentially serious articular, peri-articular and EA manifestations of RA is imperative to ensure safe and effective patient care and enhances the role of the physiotherapist as part of an interdisciplinary health professional team. Timely on-referral of patients to a general practitioner, rheumatologist or orthopaedic surgeon can minimise delays in accessing appropriate care and optimising patient outcomes.

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Table 1 Articular and peri-articular manifestations associated with rheumatoid arthritis, representing potential red flags

Articular and peri-articular manifestations	***Listening* for: reports of**	***Looking* for: examination and findings**
Cervical spine instability	Pain at the back of the head and/or neck. Sensory and motor changes in the upper limbs. Vertebro-basilar artery insufficiency symptoms. Lips and tongue sensory disturbance. Symptoms of spinal cord compromise, including possible lower limb symptoms such as gait disturbances.	Thorough subjective and physical examination including comprehensive neurological examination; view computed tomography/magnetic resonance images to ascertain cervical cord compromise, especially C1/C2; Babinski/Hoffman sign, clonus, reflexes, sensation. (see Slater et al. 2013)
Tenosynovitis	Swollen, painful tendons. Pain on resisted movement/load.	Crepitus on movement; warmth; evidence of swelling.
Tendon rupture and/or joint dislocations of the hand/wrist or foot/ankle joints	Loss of function; deformity	Rupture: loss of tendon function, joint instability and tendon discontinuity. Discordance between active and passive joint movement. Dislocation: lack of synovial joint congruity in active and passive movement.
Boutonnière deformity	Mechanical dysfunction related to fine motor tasks using the digits and gross motor tasks using the hand and wrist.	Combination of flexion of proximal IP joint and hyperextension of distal IP joint.
Swan neck deformity	Mechanical dysfunction related to fine motor tasks using the digits and gross motor tasks using the hand and wrist.	Limitation of active flexion of the proximal IP joint. IP joint instability. Combination of flexion at MCP joint, hyperextension of the proximal IP joint and flexion of the distal IP joint.

Carpal tunnel syndrome	Pain and/or sensory disturbance in the hand in the median nerve distribution; wasting or weakness with gripping; dropping things; symptoms worse at night; shaking the hand helps.	Sensory and motor examination of relevant peripheral median nerve distribution (negate differential spinal root compression that may mimic carpal tunnel involvement). Positive Phalen's and Tinel's tests. Screen for diabetes, thyroidism, B12 deficiency. Weakness or wasting in abductor pollicis brevis.
Hallux valgus, medial longitudinal arch flattening and claw toe	Pain in the foot. Reports of increased disability with gait and weight-bearing.	Postural and alignment changes in the foot, including: medial deviation of the first metatarsal and lateral deviation of the hallux. Pattern of dorsiflexion at MTP joint combined with plantar flexion at PIP and DIP joints for claw toes.
Synovitis-driven rotator cuff and/or glenohumeral symptoms	Shoulder girdle pain (e.g.; impingement or lateral shoulder pain) not mechanically-patterned and not responding consistently to therapy (e.g. tendon unloading).	Pattern of movement dysfunction (control or impairment of range) consistent with subjective complaint; warmth; crepitus; check for rotator cuff rupture. Partial or no response to simple analgesia.
Secondary osteoarthritis	Pattern of symptoms mechanically-patterned (i.e.; stimulus-response coupled: hurts and pain eases when resting), non-inflammatory joint degeneration.	Age-dependent. Longer RA disease duration and/or chronic synovitis. Insidious onset. Responds to simple analgesia. Bony tenderness on palpation. Bony enlargement. Crepitus with movement. No palpable warmth (difficult if patient also has a flare). Loss of joint space, osteophytes, subchondral cysts on plain X-ray.

Abbreviations: MCP – metacarpophalangeal; IP – interphalangeal; MTP – metatarsophalangeal; PIP – proximal interphalangeal; DIP – distal interphalangeal

Table 2 **Practice-relevant extra-articular manifestations and co-morbidities associated with rheumatoid arthritis, by body system, representing potential red flags.**

Body system	Extra-articular manifestation	What to look for	Co-morbidities/complications	What to look for
Skin	Rheumatoid nodules	Single or multiple subcutaneous nodules, >5mm diameter. Usually painless and on extensor surfaces.		
	Major cutaneous vasculitis [a]	Petechiae/purpura (red or purple skin lesions which do not blanch on pressure). Leg ulcers and peripheral gangrene (Figure 1).		
Pulmonary	Bronchiolitis obliterans organizing pneumonia (BOOP)	Dry cough, dyspnoea, wheezing, crackles on auscultation.		
	Pleuritis [a]	Sharp chest pain with deep breathing, coughing, sneezing.		
	Interstitial lung disease [a]	Dyspnoea, cough.		
Cardiovascular	Pericarditis [a]	Chest pain, dyspnoea Palpitations.		
	Vasculitis [a]	Signs of ischaemia or necrosis in affected organs/tissues.		
Neurological	Mononeuritis multiplex [a] Peripheral neuropathy [a]	Acute sensory and/or motor neuropathy, occurring as a result of vasculitis,		

		compression, or diabetes.		
	Cervical myelopathy [b]	Neck pain, upper limb pain, sensory and motor changes in upper limbs, gait disturbances.		
Visual	Sjögren's syndrome	Dry eyes and mouth. Skin, nose and vaginal dryness also present.		
	Episcleritis, scleritis [a], retinal vasculitis [a]	'Red eye', eye pain, photophobia, decreased visual acuity, dry/itchy eye (Figure 2).		
Haematological	Felty's syndrome [a, c]	Frequent bacterial infections, fever, weight loss, fatigue, splenomegaly.		
Metabolic/Endocrine			Osteoporosis	Minimal trauma fracture, height loss.
			Steroid-induced diabetes mellitus	Skin thinning, painful peripheral neuropathy.

[a] Severe manifestations are classified according to the Malmö criteria (Turesson et al., 2000; Turesson & Jacobsson, 2004)

[b] occurs as a consequence of subluxation of cervical spine joints due to instability of the cervical spine, especially the upper cervical spine (refer to Table 1)

[c] defined as chronic polyarthritis, neutropenia and splenomegaly

CAPTIONS TO ILLUSTRATIONS

Figure 1: Example of cutaneous vasculitis of the lower extremities

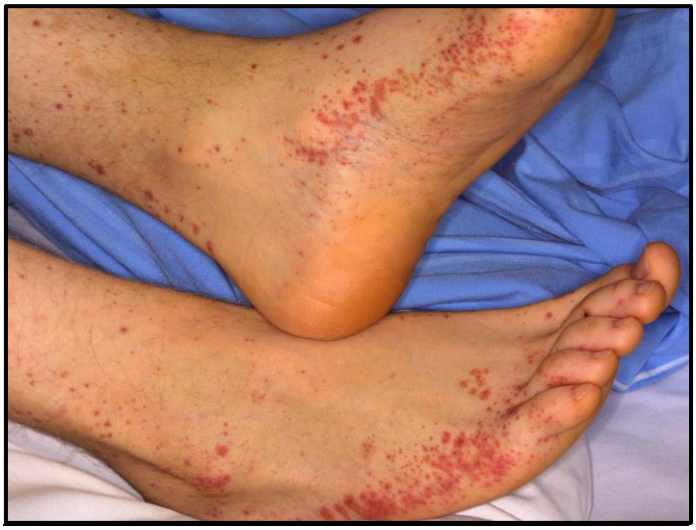

Figure 2: Example of RA-associated episcleritis of the right eye, termed 'red eye'

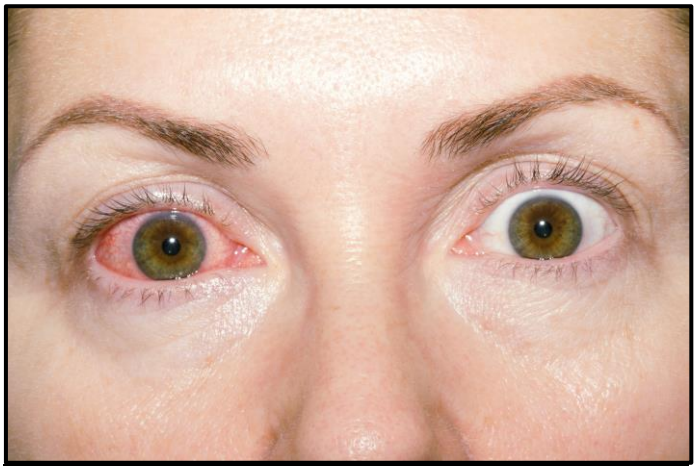

Figure 1: Example of cutaneous vasculitis of the lower extremities. The lesions do not blanch when pressure is applied. Reproduced through a licence agreement with DermNet NZ (http://dermnetnz.org/).

Figure 2: Example of RA-associated episcleritis of the right eye, termed 'red eye'. Reproduced through a licence agreement with Science Photo, UK (www.sciencephoto.com).