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Hand surgery for Multicentric Reticulohistiocytosis: A new avenue of treatment and review of the literature

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ABSTRACT

INTRODUCTION: Multicentric Reticulohistiocytosis (MRH) is a rare non-Langerhans cell histiocytosis characterised by destructive polyarthritis and violaceous skin papules.
PRESENTATION OF CASE: In 2010, a 70-year-old woman with Palindromic Rheumatism was diagnosed with MRH. Within a few months, she developed ankylosis of the small joints of both hands which resulted in severe fixed flexion deformities of the fingers and thumbs. The joint disease failed to respond to medical therapies and the palmar skin of her left hand was becoming increasingly macerated. Therefore, she elected to undergo arthrodesis of the metacarpophalangeal joints to allow hand hygiene.
DISCUSSION: To-date, this is the first report of a surgical intervention for this rare condition and represents a novel avenue of potential therapy. Medical therapies for MRH are usually ineffective in preventing the debilitating small joint disease which often develops and there is on-going research into newer agents and alternative surgical techniques.
CONCLUSION: Once medical therapies are exhausted, clinicians should consider the input of Hand Surgeons in managing the inevitable and mutilating joint disease of this rare condition.

1. Case history

In January 2010, a 70-year-old woman presented to the Rheumatology clinic with flexion deformities affecting both hands. Her medical history included burnt-out Palindromic Rheumatism (1984) with consistently negative Rheumatoid serology (RhF < 10), raised ANA titres (2.5iU/mL) and no Extractable Nuclear Antigens. She had a left total shoulder replacement (1988) and bilateral total knee replacements (2002). Her medications were Sulphasalazine, Felodipine, Bisoprolol and Bendroflumethiazide. There was no family history or allergy of note.

On examination, there were mild flexion deformities of the proximal interphalangeal joints (PIPJ) and distal interphalangeal joints (DIPJ), affecting the ring and little fingers. Initially, the right hand was more greatly affected. Flexion to make a fist was achievable. There was no significant stiffness, pain or swelling within any joints of the distal upper limb. There were no palpable palmar fascial nodules or joint subluxations. The feet were not involved. There were no other symptoms or signs of connective tissue disease. Radiographs of the hands and feet were unremarkable. With an uncertain diagnosis, the opinion of a Hand Surgeon was sought.

Three months later, all digits of the right hand, and the left ring and little fingers were buried within the palm (Fig. 1); the MCPJs were 90° the PIPJs 60° and the DIPJs 100° flexed with minimal passive extension possible. The left index and middle fingers exhibited less significant flexion deformities in a similar pattern. The nails were well manicured and there was no palmar skin maceration. Moreover, multiple firm and irregular pink-coloured papules (1–4 mm) had developed on the dorsum of the hands (Fig. 2) which were not painful, itchy or apparent elsewhere. As before, no other abnormalities were detected during the clinical examination of other bodily systems.

A 4 mm marginal punch biopsy of a skin lesion showed poorly defined dermal aggregates of histiocytes and multinucleated giant cells, some with a wreath-like distribution of nuclei (Fig. 3). There was associated perivascular lymphocytic infiltration and dermal

Abbreviations: ANA, antinuclear antibodies; ENA, extractable nuclear antigens; PIPJ, proximal interphalangeal joint; DIPJ, distal interphalangeal joint; MCPJ, metacarphophalangeal joint.

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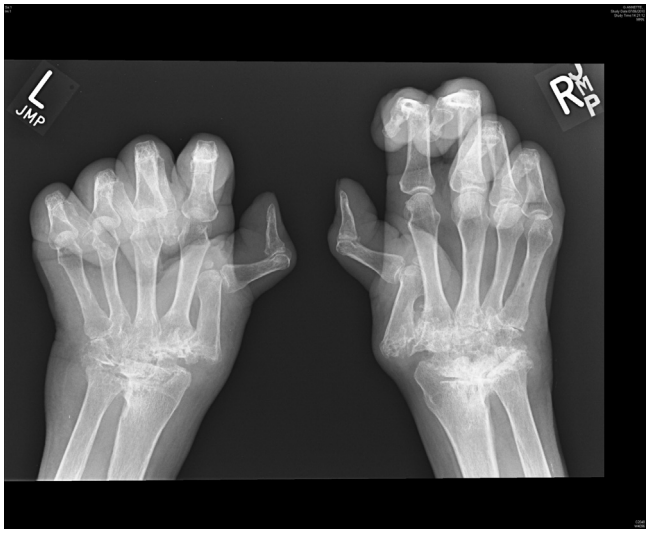

Fig. 1. An X-ray showing severe joint contractures of the left and right hands. No new erosions, peri-articular osteopenia, osteophytes or sclerotic change is clearly seen. There is old erosive carpal arthritis attributable to Palindromic Rheumatism.

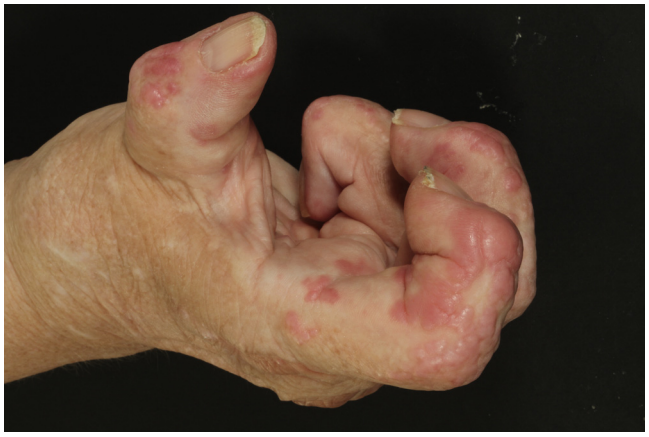

Fig. 2. A photograph of the right hand, showing the characteristic skin lesions of MRH.

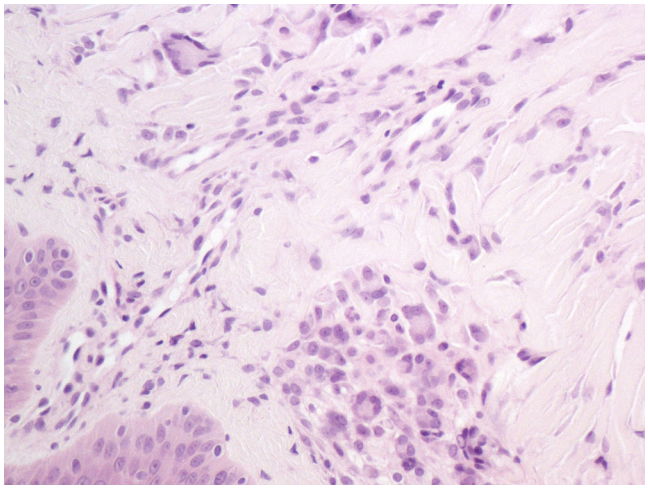

Fig. 3. A punch biopsy of a skin lesion on the left index finger showing histiocyte and multinucleated giant cell infiltration of the dermis (H&E stain, 200×).

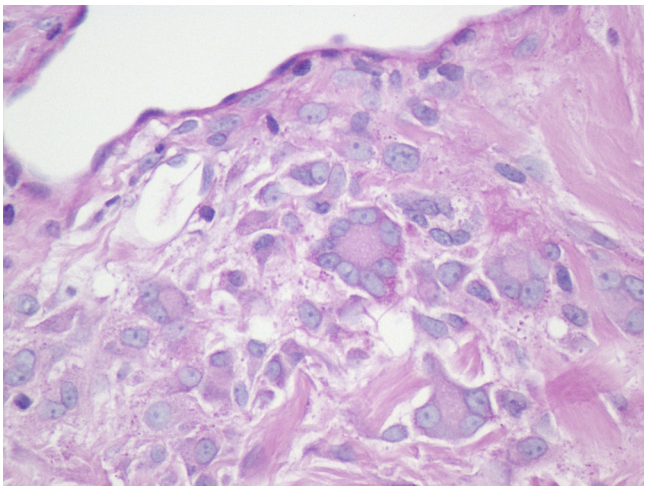

Fig. 4. A punch biopsy of a skin lesion on the index finger showing Periodic Acid-Schiff (PAS) staining positivity within the cytoplasm of some cells, with one giant cell exhibiting a wreath-like distribution of nuclei.

fibrosis. Periodic Acid Schiff (PAS) staining showed weak granular cytoplasmic positivity in the giant cells (Fig. 4). The histiocytic component was negative for S100 and CD1a. No microorganisms were present. These features alongside the clinical history indicated Multicentric Reticulohistiocytosis. In order to exclude malignancy, a full-body MRI was ordered which showed a right-sided, 4 cm spherical heterogeneous adrenal mass. The Endocrinologists later determined this to be a non-functioning adenoma.

Intravenous zolendronate and methotrexate with steroids failed to improve her digital flexion deformities and consequently, the fingers were drawn into greater degrees of flexion and her left palmar skin became macerated. Physiotherapy did not improve her symptoms. We felt that given the degree of her deformities and the nature of this akylosing disease that splints were unlikely to confer any benefit. Since conservative and medical therapies had failed, we offered the patient palliative surgery. Given the degree of deformity and lack of supporting soft tissue, her joints were unsuitable for arthroplasty. Considering the absence of literature on this subject and the patient's preference for minimal surgery, she was counselled and consented for MCPJ arthrodesis. We felt that this approach was most sensible in order to allow for hand hygiene and if the outcome was satisfactory, then further fusion could be considered. Therefore, under general anaesthetic and tourniquet, the left MCPJs were approached with 4 longitudinal incisions. The joint surfaces were adequately prepared and held in appropriate degrees of flexion with temporary K-wires, allowing finger manipulation out of the palm and radial rotation of the index finger for opposition. AO compact 2 mm hand plates were placed dorsally to all 4 MCPJs.

Post-operative radiographs were satisfactory (Fig. 5). Following 6 weeks of firm nocturnal splint therapy, hand therapy was initiated. At one year follow up her MCPJs remained appropriately fused and she is able to hook grasp as well as achieve a weak key and fine pinch, which she believes is enough to improve her day-to-day life. The joint disease has stabilised and the papular rash regressed without adjuvant medical therapy. Orthopaedic and Rhuematological follow-up continues 6 monthly alongside radiological surveillance of her adrenal mass.

2. Discussion

First described by Goltz and Laymon in 1954,[1] MRH is a rare non-Langerhans histiocytosis characterised by destructive polyarthritis and multiple skin lesions. To-date, there are few published reports

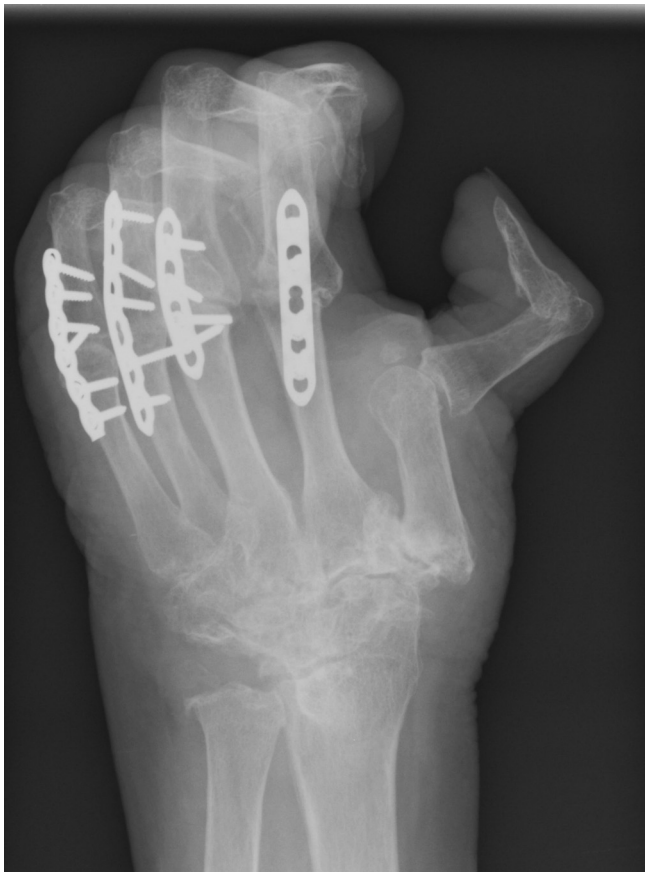

Fig. 5. A post-operative X-ray of the left hand and wrist showing adequate positioning of the dorsal AO compact plates.

on this rare condition and the pathogenesis remains unclear. Some authors suggest that MRH is a paraneoplastic phenomenon driven by tumour associated cytokine(s) or cytokine dysregulation[2–4] which is supported by its association with malignancy (28%)[5,6] and auto-immune disease (17%).[6]

MRH affects women more commonly than men (3:1), usually during the 4th decade of life and with no obvious ethnic predilection. The disease usually remits spontaneously within 5–10 years, but not before significantly deforming multiple joints and potentially infiltrating the skin, skeletal muscle, heart, lungs and gastrointestinal tract. Usually, the polyarthritis symmetrically affects the small joints of the hand, but may also involve the wrist and larger joints. MRH is documented to be the most destructive chronic inflammatory polyarthritis resulting in arthritis mutilans in over 45% of cases.[7]

MRH skin lesions are normally fast growing, non-tender and well-circumscribed violaceous papules of 1–10 mm. They most frequently arise over the dorsal aspects of the small joints of the hands, but may also appear on the elbows, neck, face and pinnae.[8] Occasionally, papules coalesce at the eponychium giving a cobble stone appearance, known as 'coral beading'. Sometimes, such lesions are mistaken for dermatomyositis[9] or Rheumatoid nodules, especially in the presence of deforming arthritis. Indeed, these conditions may co-exist so caution is required and histology is usually helpful.

There is no diagnostic serological test for MRH. Recognised biochemical abnormalities include raised serum and tissue TFN-α,[10] hypercholesterolaemia (~50%)[11] and elevated inflammatory markers; however, there is still no consensus on the exact cytokine profile.[6] Histologically, the dermis is infiltrated with histiocytic and multinucleated giant cells (25–40 μm), usually exhibiting eosinophilic ground-glass cytoplasm. Their nuclei are vesicular, with distinct membranes and 1 or 2 prominent nucleoli. Such giant cells are agreed to be PAS positive and diastase-resistant but S100 protein, CD1a and alpha-1-antitrypsin negative. Tissue surrounding the typical skin lesions shows diffuse lymphocytic infiltration and appears fibrotic with subtle loss and fragmentation of the collagen matrix. A comprehensive description of the histological features is offered by Gorman et al.[6]

There is no consensus on the management of MRH. Case-based evidence to-date suggests that mild to moderate joint disease may be initially treated with glucocorticoids and immunosuppressive agents.[12] Anti-TNF therapies have been largely unsuccessful.[10,13–17] Similarly bisphosphonate infusions have shown no true benefit,[2–4,18] despite being known to accumulate in the reticuloendothelial system inducing macrophages/monocytes apoptosis and exerting anti-arthritic effects through the suppression of osteoclasts.[19] Commonly, medical therapies follow a long and protracted course with disappointing results. Also, due to publication bias and other factors, it may be assumed that the proportion of non-responders is under-represented in the literature. Of note, no reports to-date have suggested that physiotherapy or splinting has a role in managing this ankylosing disease.

There are no published reports of surgical interventions for MRH. Whilst inflammatory MCPJ arthritis may be amenable to joint replacement or resurfacing, the pre-requisites of good bone stock, minimal deformity and adequate supporting soft tissue[20] are almost always lacking in MRH. Also, in the absence of surgical literature on MRH alongside insufficient data on joint replacements for well recognised small joint arthritis of the hand, we felt that offering an athroplasty would not be ideal and a more predictable, definitive procedure (in the form of arthrodesis) was appropriate. Therefore, as with other mutilating arthritides, we suggest that MRH arthritis refractory to medical therapy may be addressed safely and satisfactorily with arthrodesis of the MCPJs, PIPJs or DIPJs in accordance with surgical options and patient preference. Once medical therapies have been exhausted, we advise that clinicians collaborate with Hand Surgeons in order to report on their experiences of managing MRH and elucidate the ideal treatment pathway.

3. Conclusion

This is the first report of hand surgery for MRH and represents a novel avenue of therapy. Although this report does not offer a definitive management algorithm, we advocate that clinicians seek the input of Hand Surgeons in managing the inevitable and mutilating joint disease of this rare condition.

Conflict of interest statement

None.

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Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request

Author contributions

RGW co-authored the present report, researched the background to the case, analysed the data, liaised with all parties at each hospital site and obtained consent from the patient described. He approved the final version. SD assisted in the care for the described patient during her inpatient orthopaedic care. He assisted in background research, analysis of the data and co-authored the report, as well as approving the final version. PC is the Orthopaedic surgeon caring for the patient prior to surgery and performed her arthrodesis. He co-authored the article and approved the final version. JGM was the Histopathologist confirming this rare diagnosis. He prepared the slides for this article and the related descriptions. He participated in the background research, data analysis, and co-authored the article as well as approving the final version. DM is the Rheumatologist caring for the patient. He participated in the background research to the article, data analysis, co-authored the report and approved the final version.

Disclaimer

All authors have seen and agreed to the submitted version of the paper and bear responsibility for it. The material is original and has neither been published elsewhere nor submitted for publication simultaneously. If accepted, all authors accept that that this paper will not be published elsewhere in the same or a similar from. All authors have had full and the right to publish all the data.

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