Multicentric reticulohistiocytosis: a rare cause of erosive arthropathy of the distal interphalangeal finger joints

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Background: Multicentric reticulohistiocytosis (MRH) is a rare systemic disease, presenting with typical skin abnormalities and erosive polyarthritis, which is often associated with malignancy.

Case report: A case of MRH arthropathy, in which the typical nodular skin manifestation of the disease was absent, is described in a patient with a past history of breast cancer and no evidence of recurrent or new malignancy.

Results: Careful clinical and roentgenological evaluation disclosed important clues to differentiate this condition from other more common distal interphalangeal arthropathies—namely, osteoarthritis and its “erosive” variant, rheumatoid arthritis, psoriatic arthritis, tophaceous gout, dialysis related hand arthropathy, and from the rarer fibroblastic rheumatism, all of which can be mimicked by MRH. Histopathology showed the characteristic histiocytic and multinucleated giant cell infiltrate with ground glass cytoplasm, and immunohistochemical analysis showed markers evocative of a monocyte/macrophage origin of MRH.

CASE REPORT
A 70 year old non-insulin dependent diabetic white woman was referred to us for a progressive deformity, only slightly painful, affecting the 2nd and 3rd distal interphalangeal (DIP) joints of both hands, which she had complained about for one year. In 1986 the patient underwent left mastectomy for breast cancer. In 1988 and in 1991, respectively, axillary nodes clearance and irradiation of superclavicular lymph nodes were further required owing to metastatic disease. No evidence of disease recurrence was subsequently shown during clinical, laboratory, and instrumental follow up.

Physical examination showed a bilateral mild swelling (fig 1A) of the 2nd and 3rd finger DIP joints resembling Heberden’s nodes, usually found in osteoarthritis (OA), together with joint instability and decreased range of motion. Accurate skin examination and palpation for breast masses and lymphadenopathy were negative. Laboratory findings showed a raised erythrocyte sedimentation rate (52 mm/1st h; normal <38) and C reactive protein (8 mg/l; normal <6 mg/l), mild normochromic-normocytic anaemia (haemoglobin 114 g/l), and leucopenia (white blood cells 3.7 × 10⁶/l). C3 and C4 complement levels were within normal limits and routine biochemistry was otherwise normal. An x ray examination of the hands showed a destructive arthropathy with prominent subchondral bone osteolysis, leading to joint space widening and severe malalignment of the 2nd and the 3rd DIP joints of both hands (fig 1B). The unexpected radiographic pattern, quite unusual for nodal OA, prompted us to perform a synovial biopsy, which showed a histological picture consistent with a histiocytic granuloma: the synovial membrane showed a nodular infiltrate of plump histiocytes with abundant finely granular eosinophilic cytoplasm, multinucleated giant cells, and fibrosis (fig 2). The cytoplasm of histiocytes and giant cells showed a striking periodic acid-Schiff (PAS) diastase resistant positivity and CD68 immunoreactivity, which failed to stain with anti-S100 and anti-CD1a. A diagnosis of multicentric reticulohistiocytosis (MRH) was established and, when further diagnostic investigation had ruled out the presence of primary or metastatic cancer, treatment with

Abbreviations: DIP, distal interphalangeal; MRH, multicentric reticulohistiocytosis; OA, osteoarthritis; PAS, periodic acid-Schiff; PsA, psoriatic arthritis
1. Subchondral sclerosis, osteophytes, joint space narrowing and, moreover, a tendency to ankylosis are typically noted also in the “erosive” variant of OA, which is considered by some authors merely as a phase in the evolution of finger OA. It is distinguished for the superimposition of erosions, commonly beginning as sharply marginated defects in the central portion of the joint giving a so-called “gull wing” appearance. Moreover erosive OA is usually heralded by marked inflammatory complaints (pain, redness, and warmth), whereas MRH is a relatively painless arthritis.

2. In our patient the distribution of articular lesions ruled out a diagnosis of rheumatoid arthritis, in which severe erosions of finger DIP joints occur less commonly (in about 3% of patients) and are usually associated with changes at more proximal joints of the hands. The absence of periarticular osteopenia and of joint space reduction further distinguishes MRH from rheumatoid arthritis.

3. One year after the onset of symptoms, prednisone (5 mg daily), low dose methotrexate (10 mg intramuscularly weekly), and bisphosphonates (clodronate 100 mg intramuscularly weekly) was started. After a 12 month follow up no skin rash and no apparent neoplasia were noted, but hand x rays showed progression of the disease with further erosive involvement of both thumb interphalangeal joints, the left 5th proximal interphalangeal joint, and the right trapezio-metacarpal joint.

4. DISCUSSION

MRH is a rare systemic disease of unknown cause characterised by flesh coloured to reddish-brown papules and nodules over the skin (giving a so-called “coral beads” appearance around the nailfolds) and oropharyngeal and nasal mucosal surface, associated with a destructive and mutilating polyarthritus. Constitutional complaints such as fever, malaise, weight loss, and itching are commonly present. Data on its incidence and prevalence are unavailable. Fewer than 200 cases are described in literature and, except in the work by Barrow and Holubar, they are reported mostly as small sized series or isolated cases. This report is the second of two cases seen at our clinic over 30 years.

The arthropathy of MRH is a destroying, symmetrical, and relatively painless process usually localised but not confined to the interphalangeal finger joints. Cutaneous involvement occurs first in only 18% of patients, and in 21% it develops simultaneously with the arthritis, while in the remaining cases the typical skin lesions are missing at the onset, and follow arthritis after an average of three years. A diagnosis of MRH can easily be suspected when a patient is seen with the typical skin lesions associated with the erosive arthritis characteristic of the disease in its full presentation. On the other hand, the arthropathy of MRH, as the sole manifestation of the disease, can scarcely be differentiated from other more common arthritides by clinical and radiological methods alone.

Our patient presented with swelling limited to DIP finger joints, resembling Heberden’s nodes (fig 1A). Such a sign might have pointed to a diagnosis of nodal OA of the hands. However, the history, dating back only one year, and x rays of the hands, disclosing a bilateral symmetric involvement of the 2nd and 3rd finger DIP joints with a gross erosive process coupled with remarkable enlargement of the joint space (fig 1B), were against OA. The characteristic radiological changes of interphalangeal finger OA, such as subchondral bone sclerosis, joint space narrowing, and marginal osteophytic bone outgrowths, were absent.

5. Figure 2 Synovial membrane cellular infiltrate mainly composed of large histiocytes with eosinophilic ground glass cytoplasm, sparse multinucleated giant cells, and fibrosis (haematoxylin and eosin stain).
metastatic breast carcinoma and with a lymph node metastasis of an unknown primary carcinoma expressing the immunohistological phenotype of breast cancer cells. In our patient the diagnostic investigation showed no evidence of primary or recurrent neoplastic disease. On the other hand, MRH is associated with malignancy in about 30% of the cases reported, and it is considered by some authors to represent a paraneoplastic manifestation. Nevertheless, the wide spectrum of malignancies seen in association with MRH (breast, cervix, colon, stomach, lung, pleura, larynx, ovary, lymphoma, leukemia, sarcoma, melanoma, and metastasis of unknown primary cancer), together with the fact that the two diseases do not always run a parallel course, makes the paraneoplastic nature of this entity questionable.

Owing to the unfeasibility of controlled trials because of the rarity of the disease, there is no consensus about drug treatment of MRH. Hence, the treatment of this disease remains largely empirical. Nevertheless, remission or at least stabilisation of MRH has been achieved by treatment with corticosteroids, alkylating agents, methotrexate, and hydroxychloroquine, as single drugs or in combination regimens. In our patient the initial therapeutic attempt with low dose steroids, pulse methotrexate, and anti-bone resorptive agents did not improve the erosive changes, which rather extended to affect other finger joints.

In conclusion, although the definitive diagnosis of MRH rests upon histological examination of biopsy specimens, careful roentgenological reading and analysis of clinical features are the keys to the early diagnosis of this disease and enable differentiation of this rare disease from other more common erosive DIP finger arthropathies; the pathogenesis of this condition is unknown but, owing to the frequent association of MRH with cancer, it is mandatory to consider such a possibility during diagnostic investigation.

References