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PARA NEOPLASTIC RHEUMATOLOGIC SYNDROMES

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Various malignancies can cause symptoms of other organ systems in almost 15% of advanced cases and can be a presenting feature of malignancy. These paraneoplastic syndromes occur without direct invasion of affected tissues by malignant cells (tumor or metastases) and can be endocrine (one-third cases) followed by rheumatologic, hematological or neuromuscular. They are supposed to be caused by tumor-derived products such as antibodies, hormones, and peptides. Some of the musculoskeletal symptoms resolve after resection of malignant tumor and relapse on recurrence of the malignancy. Clinical remission of these symptoms can be used to assess response to anti-tumor therapy. Paraneoplastic syndromes, therefore, must be considered in the differential diagnosis of various rheumatic syndromes including arthritis, metabolic bone diseases, dermatomyositis, vasculitis, etc. Although the search for occult malignancy is not cost-effective in most rheumatology cases, it must be strongly suspected in cases of explosive onset and atypical presentation, especially at an older age. Usually, they do not respond to steroids and other conventional anti-rheumatic therapy. Treatment of these symptoms forms an essential part of palliative care in cancer patients. Early diagnosis of malignancy is possible with a correct diagnosis of paraneoplastic syndromes.

Some of these syndromes are described below:

1) ARTHRITIS: Symmetric or migratory polyarthritis due to leukemic synovial inflammation occurs in a significant number of cases. Knees, ankles, and wrists

are commonly involved joints. Pain is disproportionately severe though inflammation is usually mild. Carcinoma polyarthritis can also occur in solid tumors due to the deposition of circulating immune complexes in the synovium, especially carcinoma of the breast. Ovarian malignancies can be associated with palmer fasciitis, carpal tunnel syndrome, adhesive capsulitis, and shoulder-hand syndrome. Metastatic joint malignancies usually cause monoarthritis of the knee joint. Pyogenic arthritis is common in multiple myeloma and carcinoma of the colon.

Secondary hyperuricemia and gouty arthritis, though uncommon in solid tumors, occur in myeloproliferative disorders necessitating treatment with allopurinol. Jaccoud-type painless, non-erosive, deforming (reversible) arthropathy can occur in carcinoma of the lungs.

Multiple myeloma can present as amyloid arthropathy. This is symmetrical inflammatory arthritis affecting the hand, shoulder, and knee joints. 'Shoulder-pad sign' – prominent swelling around shoulders is a typical clinical finding. Synovial biopsy shows amyloid deposits.

2) HYPERTROPHIC OSTEOARTHROPATHY (HOA): This syndrome, a prototype of paraneoplastic arthropathy, includes digital clubbing, periostitis (severe deep aching or burning pain aggravated by dependency of limb) of long bones, and arthritis. It can be associated with intrathoracic (most common), hepatic, esophageal, colonic, or other malignancies. HOA can be primary or secondary (localized or generalized). Secondary generalized HOA can mimic rheumatoid hand in early stages. Control of primary disease leads to remission in secondary HOA.
3) BONE DISORDERS: Carcinoma of the lung or breast can lead to bony metastases. These painless lesions usually involve long bones, the spine, or the pelvis. An isotope bone scan is essential for the diagnosis of these lesions. Back pain is complained about by about 10% of patients with leukemia whereas nocturnal bone pain is a typical complaint in lymphoma.

4) MUSCLE DISORDERS: 7-10% of cases of dermatomyositis (DM) are associated with underlying malignancy. The period between onset of DM and diagnosis of malignancy may be considerable suggesting a shared predisposition. Secretion of myotoxic factors or specific antibodies by tumor cells leads to inflammatory muscle response. Polymyalgia rheumatica- a syndrome characterized by constitutional symptoms, pain, and stiffness of pelvic/shoulder girdle muscles, arthritis, and high ESR (> 100mm/hr usually)- can be a presenting feature of malignancy and may even respond to routine steroid therapy.
5) SYSTEMIC DISORDERS: Various other syndromes can be associated with malignancies. ANA positivity and lupus-like syndromes are described in malignancies. Other paraneoplastic syndromes include reflex sympathetic dystrophy (Ca ovaries), polychondritis (Hodgkin's disease), panniculitis (carcinoma of the pancreas), scleroderma, Raynaud's phenomena, digital gangrene, polyarteritis nodosa, and necrotizing vasculitis.
6) MALIGNANCIES ASSOCIATED WITH SYSTEMIC INFLAMMATORY DISORDERS: Lymphoproliferative malignancies are common in various autoimmune systemic disorders such as rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), Sjögren's syndrome (SjS), and DM. Patients of RA and SjS carry a 5- and 44-fold higher respective risk of developing lymphoproliferative disorders. Tumor-associated antigens may be produced by inflammatory cells in these diseases. Alveolar cell carcinoma is known to complicate scleroderma.
7) DRUG RELATED MALIGNANCIES: Immunosuppressive drugs used in the treatment of autoimmune diseases can lead to the development of malignancies- particularly non-Hodgkin's lymphoma. Cyclophosphamide, commonly used in lupus nephritis, can cause carcinoma of the urinary bladder especially in patients with a history of hemorrhagic cystitis due to metabolites excreted in the urine.

There is a growing concern about lymphoreticular malignancies following prolonged use of recently introduced biologic agents (etanercept, infliximab, etc). Prolonged use is, however, rare in India due to economic reasons.