"The Cancer that Carried the Chalk"—NXP2+ Paraneoplastic Dermatomyositis Unleashing Calcinosis Cutis and Peripheral Neuropathy

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Paraneoplastic dermatomyositis (DM) is a rare but significant manifestation of underlying malignancies, often presenting with unique clinical challenges. Idiopathic inflammatory myopathies are a heterogeneous group of disorders that cause muscle weakness and multiorgan involvement, affecting the skin, heart, lungs, and joints.[1] Dystrophic calcification causing calcinosis cutis occurs in 20–40% of juvenile DM cases.[2]

A 36-year-old female diagnosed with mucinous cystadenocarcinoma of the ovary and treated with surgery and chemotherapy 1 year prior presented with a 3-month history of dysphagia, generalized weakness, and inability to walk. She had proximal muscle (shoulder and hip girdle) weakness with Medical Research Council (MRC) grade 2/5 power and bulbar weakness. On examination, she exhibited neck flexor and proximal muscle weakness, heliotrope rash (Fig. 1A), and a holster sign (Fig. 1B) on the bilateral proximal thighs, leading to a clinical suspicion of DM. Baseline hemogram, serum electrolytes, and CA-125 levels were normal, but erythrocyte sedimentation rate (ESR), C-reactive protein, and creatine kinase levels were elevated (1046 IU/L; reference range <145 IU/L). A multiplex line blot immunoassay tested positive for anti-NXP2 and anti-Ro52 antibodies, suggesting paraneoplastic DM. The patient was treated with immunosuppression and showed improvement.

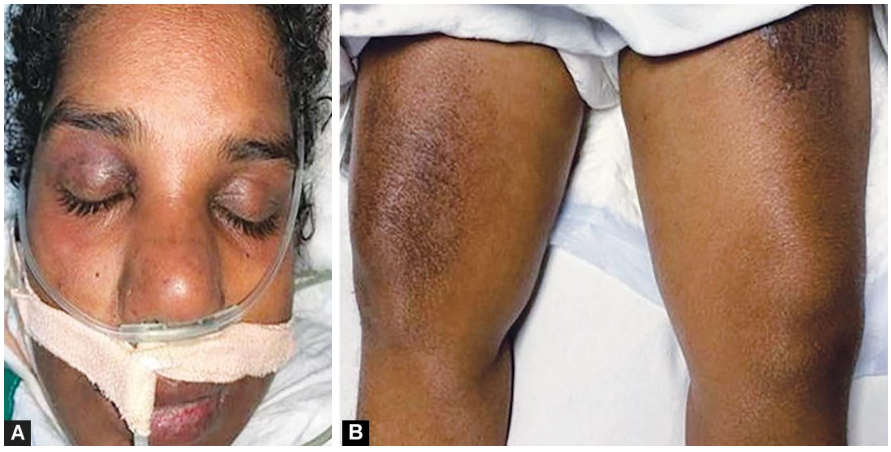
Ten months later, she presented with new-onset swellings in both arms, numbness in the medial two fingers of both hands, and anasarca of 3 months' duration. Local examination revealed 4 × 4 cm hard, painless subcutaneous swellings on both arms, mobile in all directions, with similar lesions on the abdomen and bilateral thighs. Bilateral Froment's sign and the card test were positive, but the median nerve was intact. Nerve conduction study revealed bilateral ulnar sensorimotor axonal peripheral neuropathy. The coexistence of DM and axonal peripheral neuropathy may be termed Neuromyositis. Chest X-ray PA view showed calcification in the right axilla (Fig. 2A). X-rays of the lower abdomen and thigh showed calcifications, and noncontrast computed tomography (CT) of the abdomen confirmed diffuse subcutaneous calcifications (Figs 2B and C). Fine needle aspiration cytology (FNAC) from the lesion showed the presence of calcium deposits consistent with calcinosis cutis, which was confirmed by Giemsa and von Kossa staining (Figs 2D and E). Myoblot testing was positive for anti-NXP2 and anti-Ro52.

The patient was treated with intravenous (IV) methylprednisolone pulse therapy (15 mg/kg/day × 5 days) followed by oral steroids and IV immunoglobulin 2 gm/kg given over 5 days. Her muscle power improved to MRC grade 4/5, and she was able to walk with support. During follow-up, a steroid-sparing agent (azathioprine) was added, and steroid dosage was gradually tapered.

Anti-NXP2 and anti-TIF1γ antibodies are linked to the presence of underlying malignancies. Dystrophic calcinosis typically occurs in collagen vascular diseases despite normal calcium and phosphate metabolism. Proposed mechanisms include tissue damage, inflammation, or necrosis, which trigger alkaline phosphatase release from damaged lysosomes. However, the exact etiology of dystrophic calcinosis remains unclear.[3]

Concomitant involvement of the peripheral nervous system in DM, termed "Neuromyositis", was first introduced by Senator in 1893.[4] Peripheral neuropathy may be one of the important extramuscular manifestations in patients with DM. The association between inflammatory myopathy and peripheral neuropathy is unclear. Matsui et al. reported two adult DM patients with polyneuropathy, showing vasculitis and vascular endothelial growth factor (VEGF) overexpression in muscle, skin, and nerve tissues. Other VEGF-associated factors related to vasculitis or capillary endothelial lesions may play a significant role in cutaneous and neurological manifestations of DM.[5]

In summary, DM can rarely lead to calcinosis cutis due to dystrophic calcification. The coexistence of DM and peripheral



Figs 1A and B: Heliotrope rash (A) and holster sign in the anterolateral aspect of the thigh (B)

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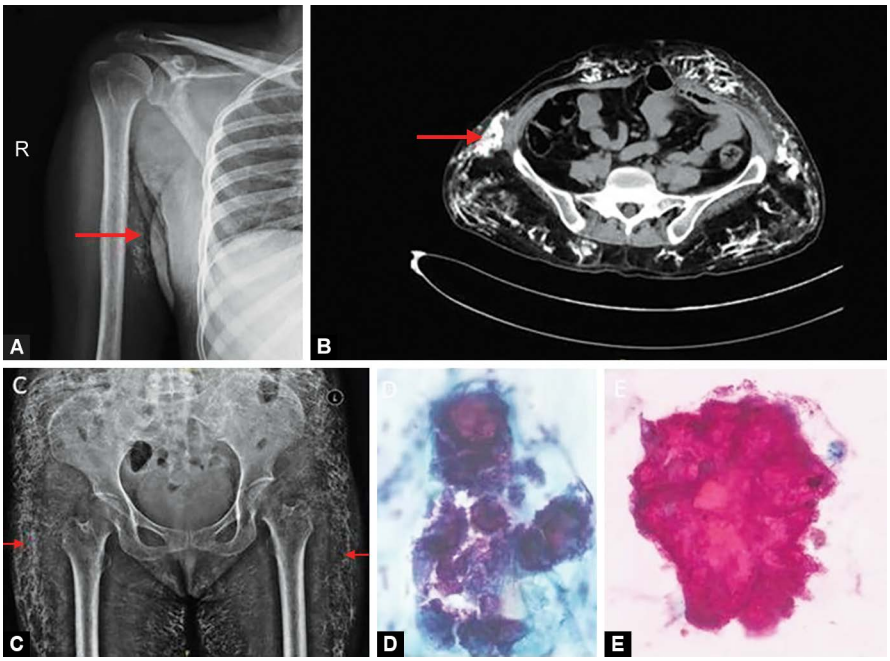

Figs 2A to E: Chest X-ray posteroanterior (PA) view showing calcification in the right axilla (A); contrast CT of the abdomen showing diffuse calcification in subcutaneous plane (B) (marked by arrow); X-ray of the pelvis and thigh showing calcinosis cutis (C) (marked by arrow); FNAC of the right axilla showing amorphous calcium deposition in Giemsa stain (D); and von Kossa stain (E)

neuropathy (neuromyositis) responded well to steroids, IV immunoglobulin, and immunosuppressive therapy. This case highlights that late and rare presentations of paraneoplastic DM can occur even after the successful treatment of primary ovarian cancer. A high level of clinical suspicion and prompt treatment are essential for the optimal management of these patients.

Authors' Contributions

Jayaram Saibaba, Nidhish Chandra, Deepak Amalnath, and DKS Subrahmanyam were involved in the conception, organization, and execution of the research project. All authors participated in writing the first draft of the manuscript as well as its review and critique.

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Conflict of Interest

None.

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