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Case Report

Arsenic Intoxication Causing Megaloblastic Anaemia- Lesson Learnt

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Abstract:

Megaloblastic anaemia is a common hematological abnormality encountered in clinical practice. We here report a case of 40-year-old male who presented to us with feature of anaemia and typical dermatological manifestation of arsenic intoxication. Complete blood count of patient showed pancytopenia with no circulating atypical cells. Bone marrow examination performed and showed megaloblastic change. Arsenic level in the hair was done and came out very high a. A very few case reports of arsenic causing megablastic anaemia were done in past. Aim of this case report is to create awareness among the physician.

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Introduction:

Arsenic is an element that raises much concern from the both environmental and human health standpoints. Humans may encounter arsenic in water from wells drilled into arsenic-rich ground strata or in water contaminated by industrial or agrochemical waste[1]. They may come in contact with arsenic in contaminated dusts, fumes, or mists. They may eat food contaminated with arsenical pesticides or grown with arsenic-contaminated water or in arsenic-rich soil[2].

WHO reported that at least 140 million people of 50 countries are exposed to arsenic through arsenic-contaminated groundwater at levels above 10 µg/L and a majority of them live in India and Bangladesh[3].

Chronic inorganic arsenic intoxication may lead to a severe multisystem illness characterized by a variety of signs and symptoms related to its effect on the skin and mucous membranes, as well as the gastrointestinal, cardiovascular, and peripheral nervous systems[4,5].Hematological abnormalities are also encountered with prolonged exposure to arsenic and are typically characterized by cytopenia including leukopenia, anemia, and thrombocytopenia in order of decreasing frequency[6,7]. In addition, rare reports in the literature have described megaloblastic maturation and dyserythropoietic changes[8,9]; thus, prolonged exposure to arsenic may result in a hematological picture resembling megaloblastic anemia. The following case report describes a patient who, at presentation, appeared to us with dermatological manifestation, gastrointestinal symptoms and anemia. During thorough investigation we have found, this anaemia is due to megablastic change due to arsenic which is very uncommon. A very few case reports have been found. That's why we want to create awareness through this case report.

Case Summary:

A-40-year-old man presented to us with generalized weakness, palpitation and fatigue for 3 months. He also gave history of numerous hyper and hypopigmented lesions on different parts of body for 6 months.

These first appeared on trunk and then gradually involved almost rest of the body which were painless, non-itchy and not associated with loss of sensation. For the last 6 months, he also noticed gradual thickening and pigmentation of palms and soles that were also painless and non-itchy.

He also complained of loss of appetite, constipation, progressive weakness and weight loss. The patient used to

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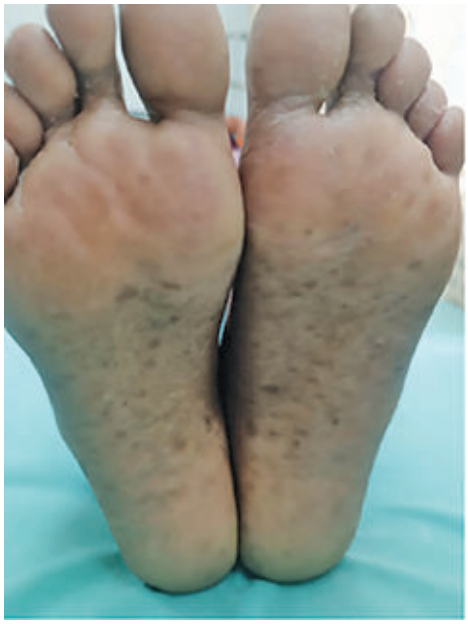

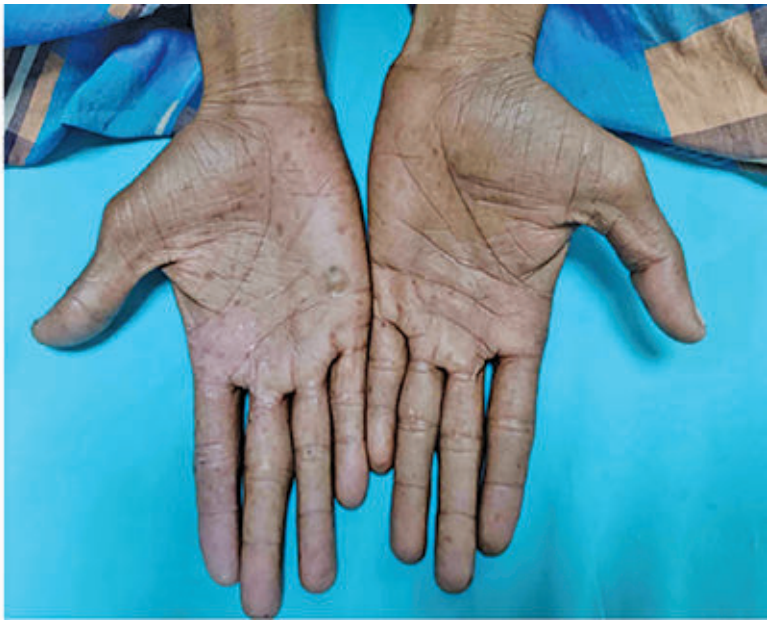

Figure 1: *Hyperkeratotic skin lesion of hand and feet*

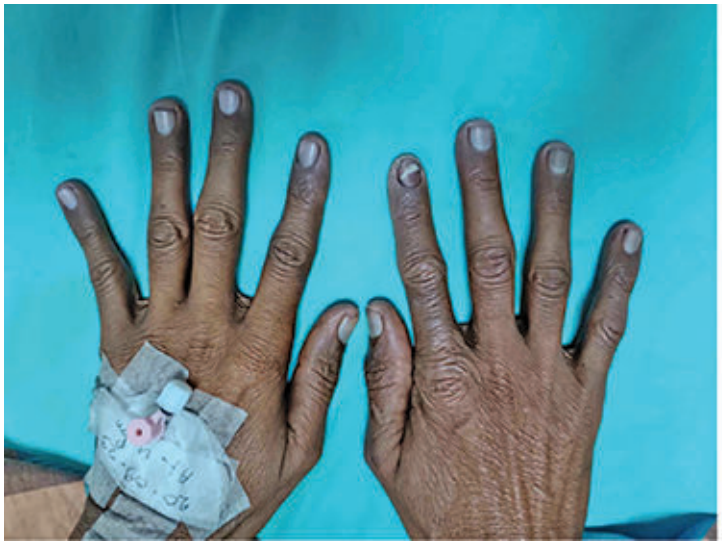

Figure 2: *Nail change*

Figure 3: *Conjunctivitis and sparse hair*

drink water from a tubewell for a long time that was marked red long ago due to high arsenic concentration.

On general examination, the patient looked emaciated, severely anemic and there were tachycardia. There were multiple hyperpigmented lesions involving both upper and lower limbs and trunk with scattered hypopigmented area giving rise to rain drop appearances. There were hyperkeratosis of palms and soles. Nails were brittle and one of it had transverse white striae (Mee's line). Hair was dry and spars.

On ophthalmic examination, visual acuity (without glass) of right eye was 6/24 and left eye 6/9 and conjunctiva was red, dry and inflamed. Other systemic examination revealed no abnormality. The complete blood counts showed pancytopeni b -5.2gm/dl,MCV-110 fl Wbc-3.2k/mL, Platelet-90k/μL.Livere enzymes were elevated and Renal function test was normal. PBF: showed pancytopenia. USG was unremarkable. Chest Xray was normal. Endoscopy of upper GIT showed erosive gastritis. Bone marrow showed hypercellular marrow. The erythroid and granulocytic

lineages showed maturational shift to left with predominance of early precursors. The cells in erythroid lineage were predominantly normoblastic and megaloblastic. The cells of granulocytic lineage showed hyperactive and maturation arrest at myelocytic stage, giant metamyelocytes with dysprogranulopoisis. Megakaryocytes were hyperactive and >10% cells are dysmegakaryopoietic changes having multinucleated and polypoid megakaryocytes and bone marrow impression was Myelodysplastic change. Serum folate level was normal but S. Vit B12 level was <83pg/ml. We measured Arsenic concentration of his hair and it was high(5mg/kg) and we diagnosed the case as Chronic Arsenicosis with erosive gastritis with megaloblastic anemia with bilateral toxic conjunctivitis. He was treated with inj. Vit B12, anti-oxidant and symptomatic management.

Discussion:

In our case, from the clinical and laboratory data, we feel that our patient represents a case of chronic arsenic intoxication. The clinical features of chronic arsenic intoxication include Melano-keratosis: Melanosis i.e., dark pigmentation-diffuse and/or spotted keratosis, Melanosis: Diffuse darkening of skin starts in the palm and gradually spreads to the whole body, Spotted or rain drop pigmentation (spotted melanosis) is usually seen on chest, back or limbs, conjunctival congestion: Sometimes observed (4%) as reddish eye due to conjunctional congestion without any sign of inflammation like grating sensation, pain or sticky discharge[10]. Patients may come to medical attention with bleeding esophageal varices, ascites, jaundice, or simply an enlarged tender liver. Clinical examination often reveals that the liver is swollen and tender. liver enzymes may be elevated[11].

Our patient had similar dermatological manifestation and mild liver damage. Our patient had elevated levels of arsenic in hair consistent with the clinical picture of chronic intoxication.

Arsenic intoxication also has haematological complication which include varying degrees of marrow depression, even aplastic anemia. Among them Neutropenia and anemia are the most common manifestations of arsenic intoxication, and some patients may have pancytopenia. They may have a peripheral pancytopenia, indicating that arsenic may exert a direct toxic effect on cellular maturation. The anemia of arsenic intoxication is characteristically normochromic normocytic with no consistent morphologic abnormalities of bone marrow. Kyle and Pease do mention that megaloblastic erythroid precursors may be occasionally seen in the bone marrow[12]. Van Tongeren et al. have reported a case of chronic arsenic poisoning in a patient whose anemia was characterized by megaloblastic erythropoiesis in the bone marrow and serum folic acid was found to be low. These authors suggested that the megaloblastic anemia was due to folic acid deficiency and that perhaps the arsenic inhibited the enzymatic conversion of folic acid into its biologically active derivatives[14]. In contrast, our patient had evidence of megaloblastic erythropoiesis in the presence of vit B12 deficiency. Arsenic can cause vit B 12 deficiency[10]. Our patient had the typical laboratory manifestations of ineffective production of erythrocytes due to a megaloblastic process which included variation in size of erythrocytes with macrocytes on peripheral smear, low reticulocyte index, increased marrow cellularity with erythroid hyperplasia, abundant marrow iron, and morphologic evidence of megaloblastic maturation in the marrow. This laboratory data is characteristic of the megaloblastic anemias in which there is a nuclear maturation abnormality on the basis of defective DNA synthesis. Although adequate megakaryocytes were present in the bone marrow sections, the patient had a peripheral thrombocytopenia that improved without therapy as did the ineffective erythroid and myeloid production. Arsenic intoxication can produce megaloblastic erythropoiesis with secondary anemia is an interesting one. The typical megaloblastic cell is considered to have a defect in the synthesis of DNA and results in the nuclear maturation abnormalities. This impairment of DNA replication stems usually from a deficiency of purine and pyrimidine synthesis or incorporation as a result of a defect in established enzymatic pathways. These observations suggest that arsenic may directly interfere with the synthesis of DNA also evident in our patient[14,15].

Conclusion:

Diagnosing of chronic arsenic toxicity is challenging. An index of suspicion, proper history, multidisciplinary approach is needed for proper diagnosis. Further studies are needed to identify how arsenic cause Vit B12 deficiency in case of intoxication.

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