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Short Communication

Disseminated Juvenile Xanthogranuloma

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Abstract

Review on Disseminated Juvenile Xanthogranuloma, with data on clinics, and the genes involved.

Keywords

Disseminated Juvenile Xanthogranuloma, Hystiocytes, skin lesions

Identity

Other names

JXG, Benign cephalic histiocytosis, Progressive nodular histiocytosis, Generalized (non-lipidemic) eruptive histiocytosis (skin), Xanthoma disseminatum (skin plus mucosa lesions), Erheim-Chester disease (adult form with bone and lung involvement).

Clinics and pathology

Disease

Phenotype/cell stem origin

Rudolf Virchow may have been the first to describe a child with "cutaneous xanthomas" in 1871 as noted in a 1954 report of this condition (Helwig and Hackney, 1954). JXG is a histiocytic condition (proliferation) in the spectrum of non-Langerhans histiocytosis that primarily affects children. The disease can be related with germline in neurofibromatosis type 1 (NF1) that implicate the potential role for MAPK hyperactivity in pathogenesis. Histiocytes are cells with specific histological and immunogenic properties, contributing to the immune response through antigen presentation and phagocytosis. JXG is defined by pathological infiltration by histiocytes within effected tissues.

Epidemiology

Preferentially affects children, usually occurs by 10 years of age, with one-half of reported cases occurring in the first year of life.

Twenty percent of the cases occur in adolescents and young adults. Male children are slightly more often affected than female children, with reported ratios ranging from1.1 to 1.4.

Clinics

Skin and soft-tissue presentation are the most common sites of involvement and can include the mucosal surface of the upper airway.

Cutaneous presentation consists of benign, usually asymptomatic, self-healing, red, yellow or brown maculopapular lesions primarily involving the head, neck, and trunk.

These lesions are usually believed to be benign and will regress spontaneously leaving a flat, atrophic scar or an area of altered pigmentation. Although systemic JXG without organ damage can have a benign course, CNS disease may be difficult to treat and is associated with severe morbidity (can cause diabetes insipidus, seizures, hydrocephalus and changes in the mental status) and mortality.

If cytopenias are noted in these patients then bone marrow involvement should be ruled out with a bone marrow biopsy and aspirate.

Liver infiltration may be noted in patients with elevated liver function testing, hypoalbuminemia, and an elevated erythrocyte sedimentation rate. Hypercalcemia can also be seen in patients with JXG.

Differential diagnosis Langerhan's cell histocytosis is the disease most often confused with JXG. Others disorders in the differential include fibrohistocytic lesion NOS, reticulohistiocytoma, hemangioendothelioma, Spitz nevus, malignant fibrous histiocytoma, and rhabdomyosarcoma or other solid tumor malignancies.

Pathology

JXG cells are small and oval with a bland, round to oval nucleus and pink cytoplasm. Touton cells are seen at dermal sites.
Immunohistochemistry reveals cells that express vimentin, lysozyme, CD14, CD68, CD163, stabilin 1 and factor XIIIa. CD1 is negative.

Treatment

Treatments include using treatments similar to Langerhans cell histiocytosis including agents such as vinblastine, prednisone, and methotrexate. Clinical trials and tertiary care center referrals are recommended for treatment and evaluation of JXG.

Prognosis

Patients with only skin or soft tissue involvement have a high survival rate, and lesions can spontaneously disappear over time in a majority of cases. Infants with large retroperitoneal masses, liver, bone marrow, or central nervous system involvement usually have good outcomes with chemotherapy. Outcomes in older children remain unclear due to the lack of published data on patients with JXG.

Genetics

High prevalence of BRAF V600E, LCH and other activating MAPK mutations

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