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Down's Syndrome with Hodgkin's Disease

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The frequency of acute leukemia, especially of the lymphoblastic type is higher in Down's syndrome as compared to the general population(1). Lymphoproliferative malignancies and other solid tumors have also been reported but an increased incidence has not been demonstrated(2,3).

The present report describes the occurence of Hodgkin's disease in a child with Down's syndrome. The association of Hodgkin's disease and Down's syndrome is not extensively documented in literature. In our review of literature we could collect two case reports of Hodgkin's disease occurring in Down's syndrome(2,3). There is also a report of a family where four members had trisomy 21 and a normal child developed Hodgkin's disease(4). The present report further emphasizes the association and discusses the treatment results.

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Case Report

A 6-year-old male child presented with intermittent fever and swelling of the right cervical lymph nodes of one year duration. There was no family history of consanguinity, cancer or chromosomal anomalies. The mother was 40 years old at the time of conception.

Physical examination revealed enlargement of the right cervical lymph nodes. Liver and spleen were not enlarged. The cardiovascular system was normal. Stigmata of Down's syndrome like mental retardation, hypotonia, mongloid slant of the eyes, epicanthic folds, flat occiput, microstomia, scrotal tongue, high arched palate, bilateral simian creases and incurved middle phalanges of both little fingers were present. In addition he had syndactyly and polydactyly of one hand (*Fig.*).

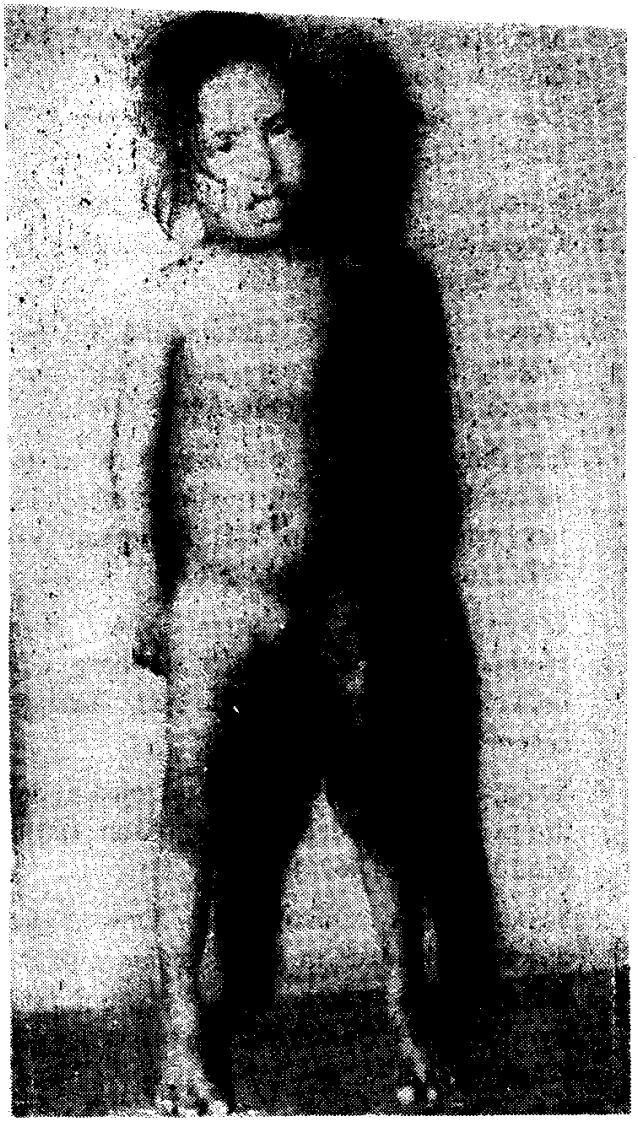

Fig. Clinical Photograph of the patient

Biopsy of an involved lymph node revealed Hodgkin's disease of mixed cellularity type. The initial laboratory values revealed a normal hemogram, normal liver and renal functions, and bone marrow. A chest radiograph revealed right paratracheal lymphadenopathy. The elecctrocardiogram and echocardiogram, were normal. Ultrasonography of the abdomen did not reveal enlargement of the liver, spleen or retroperitoneal lymph nodes. Cytogenetic study of the peripheral blood confirmed "regular" trisomy 21.

On the basis of clinical examination and investigations, he was diagnosed as a case of Hodgkin's disease stage IIB. The child received 6 cycles of COPP (cyclophosphamide, vincristine, prednisolone and procarbazine), followed by external radiotherapy to the involved areas. He tolerated both well and is in complete remission 2 years after therapy.

Discussion

Roughly, 4% of childhood cancers are directly attributable to genetic conditions(5). Down's syndrome is due to an excess of normal genetic material, a trisomy of chromosome 21. "Regular" trisomy 21 comprises more than 95% of all cases. less than one per cent of the cases consist of centric fusion between No. 21 and chr 13, 14 or 15(6). Our patient showed "regular" trisomy 21.

There is an increased incidence of leukemias and solid tumors in patients with Down's syndrome (15 to 20 fold and 2.6 fold, respectively)(2,3,7). An association

between Down's syndrome and lymphoreticular malignancies has also been reported though no incidence studies are available.

As mentioned earlier, the association between Down's syndrome and Hodgkin's disease is unusual and hence of interest in both clinical and research settings.

The mechanisms underlying the predilection to leukemias and other malignancies are unknown. It is believed that the extra genetic material present in these patients is responsible for the predisposition as well as the other features in the clinical picture. A probable working hypothesis could be that the excess of specific genetic material will alter particular biochemical pathways involved in the differentiation or function of various tissues(8). Other theories include impaired DNA mechanism in leukocytes, increased susceptibility to chromosomal breaks when cultured leukocytes are infected with viruses(9), increased activity of oncogenic proteins encoded on chromosome 21(8), increased mutation rate of stem cells(10), increased susceptibility to transformation by oncogenic viruses or mutagens(11) and various expressions of a single mutant gene(5).

The proto oncogene c-ets-2, which is localised to 21q-22.2-22.3, has been implicated in leukemogenesis(12,13). One of the 4 genes assigned to chromosome 21 cytosol superoxide dismutase (SODs), has been shown to be of importance in both aging and carcinogenesis and thus, has potential relevance to Down's syndrome(14).

Our patient received full doses of combination chemotherapy and local radiotherapy without any unusual toxicity. Hence reduction in the dosages of both types of therapy on the grounds of chromosomal anomaly would not have been justified. However, it is apparent that he is predisposed to acute leukemia both due to his inherent chromosomal anomaly(1), as well as due to the combined modality therapy given for Hodgkin's disease(15). A good clinical and molecular follow up will be interesting.

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