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# PAX-5 NEGATIVE HODGKIN LYMPHOMA IN MESENTERIC LYMPH NODE IN A CHILD: A RARE CASE REPORT

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## ABSTRACT

Introduction: Classical Hodgkin lymphoma (CHL) as per WHO 2016 is a clonal lymphoid neoplasm. CHL contains Reed-Sternberg (RS) cells in a background of a non-neoplastic inflammatory infiltrate including lymphocytes, eosinophils, neutrophils, histiocytes, and plasma cells.The expression of PAX5 is reduced and in rare cases of CHL, PAX5 expression is absent in RS cell. This has been postulated to be caused by compromised B-cell specific transcription machinery and inactivity of immunoglobulin promoters, which results in low levels to absent expression of several B-cell-restricted transcription factors such as PAX5 and OCT2. Hence, the PAX5 negative cases of CHL are extremely rare and pose a major diagnostic challenge for pathologists. Case report: An 8 year old male child presented to the paediatric department with the complaints of prolong fever, loss of appetite, weakness and unexplained weight loss since 3 months. The general examination was non contributory but on CECT child was suspected for mesenteric gastro intestinal stromal tumour( Mesenteric GIST) with no other palpable lymph nodes. The mesenteric lymph node was excised and sent for histopath examination which revealed the findings of a rare case i.e. a PAX-5 negative hodgkin lymphoma presenting solely as mesenteric lymphadenopathy. Discussion: PAX-5 negative Hodgkin lymphoma is itself a rare case which is associated with bad overall prognosis but in our case important point was that, that it solely presented as mesenteric lymphadenitis which made a confusion to clinico-radiological team as a possibility of mesenteric GIST. Conclusion: PAX5-negative CHL may have worse clinical outcomes, when compared to typical PAX5-positive CHL.

**KEYWORDS:** Classical Hodgkin lymphoma, GIST, PAX-5, Mesenteric lymphadenopathy.

## INTRODUCTION

Classical Hodgkin lymphoma (CHL) as per WHO 2016 is a clonal lymphoid neoplasm. CHL contains Reed-Sternberg (RS) cells in a background of a non-neoplastic inflammatory infiltrate including lymphocytes, eosinophils, neutrophils, histiocytes, and plasma cells.[1]

Kanzler et al. microdisected and analyzed the RS cells from frozen tissue and showed nearly all RS cells carry immunoglobulin (Ig) heavy and light chain rearrangement, which supports the B-cell origin of these neoplasms.[2]

RS cells show somatic hypermutation in the IgHV gene and since these mutations occur in the proliferating B-cells in germinal centers (GC), they are recognized to arise from GC or post-GC B-cells.The RS cells therefore are expected to express B-cell specific markers.

According to WHO, the most specific B-cell marker is CD19 and since PAX5 is closely tied to this molecule, nearly all of the RS cells are reported to express PAX5 by immunohistochemistry. RS cells, however, are typically negative for CD19.[3] The PAX5 acts as a transcriptional factor that is expressed by B-cells and its binding sites serve as promotors for certain B-cell-specific genes such as those that promote CD19 expression.[4]

The expression of PAX5 is reduced and in rare cases of CHL, PAX5 expression is absent in RS cell. This has been postulated to be caused by compromised B-cell specific transcription machinery and inactivity of immunoglobulin promoters, which results in low levels to absent expression of several B-cell-restricted transcription factors such as PAX5 and OCT2. Hence, the PAX5 negative cases of CHL are extremely rare and pose a major diagnostic challenge for pathologists.[4]

Apart from being PAX-5 negative, the another uncommon feature of this case report is the unusual site of presentation of Hodgkin lymphoma i.e. mesenteric lymph node in a child as young as 8years.

Most patients with HL present with superficial adenopathy and are asymptomatic. The lymph node enlargement is usually painless, rubbery, matted, or discrete, and is most commonly located in the neck and supraclavicular areas. It is sometimes detected during a physical examination for other reasons and presentation of mediastinal enlargement is common during routine chest X-rays.

The commonest sites of disease are cervical, supraclavicular and mediastinal (over 50% of cases) nodes, while sub-diaphragmatic presentations are less common, and epitrochlear nodes, Waldeyer's ring, testicular, and gastrointestinal sites are uncommon.

Abdominal nodal involvement is more common in older patients or when fever or night sweats are present.[5]
In view of Indian literature, no known case of PAX5 negative CHL with primary mesenteric lymph node involvement in a male child of 8years was noted and it is extremely important to have a review of the literature on this extremely rare entity.

We here by present this rare case report to the best of our knowledge.

## CASE REPORT

An 8 year old male child presented to the paediatric department with the complaints of prolong fever, loss of appetite, weakness and unexplained weight loss since 3 months.

General physical examination of the child was non contributory with no icterus, mild pallor, no lymphadenopathy (Fig.1), no hepatosplenomegaly. The child was admitted for further workup in our hospital. Fever was in the range of 99-100$^{c}$.

Laboratory investigations showed a normal complete blood count (Haemoglobin:11.6g/dl, WBC:6,000/mm$^{3,}$, platelet count: 3.4lakhs/mm$^{3}$ ), Liver function tests , Kidney function tests, Blood sugar levels and even the coagulation profile were all with in normal range. But, ultrasonography there was documentation of presence of heterogeneous lesion in peripancreatic lesion and patien was advised Contrast Enhanced CT (CE-CT).

On CECT, the radiologist gave a final impression as well defined lobulated enhancing mass lesion in left upper quadrant, likely to be a lymph nodal mass and they suggested a possibility of mesenteric gastro intestinal stromal tumour( Mesenteric GIST).

Further, patient underwent an exploratory laparotomy(Fig.2) and the radiologically suspected lymph nodal mass was excised and sent for histopathological examination. So, we received a grey brown globular soft tissue piece measuring in size 5x4x3.5cm which on serial sectioning showed grey white areas. Multiple sections of the tissue were examined and they showed presence of a lymph node with complete effacement of its architecture (Fig.3)by the mixed population of lymphoid origin cells alon with the presence of binucleate characteristic Reed-Sternberg's (RS)cells showing presence of eosinophilic macronucleoli(Fig.4).

The findings were confirmed by a panel of immunohistochemistry which showed CD3, CD20 positive lymphoid population and CD15, CD30 positive R-S cells but these R-S cells were negative for PAX-5(Fig.5 to Fig.9).

So, we referred the literature and correlated our findings and a final diagnosis of PAX-5 negative Hodgkin lymphoma of mesenteric lymph node was made.

The child was reexamined for any palpable cervical or any other lymph nodes, but found to be free of any visible lymphadenopathy.

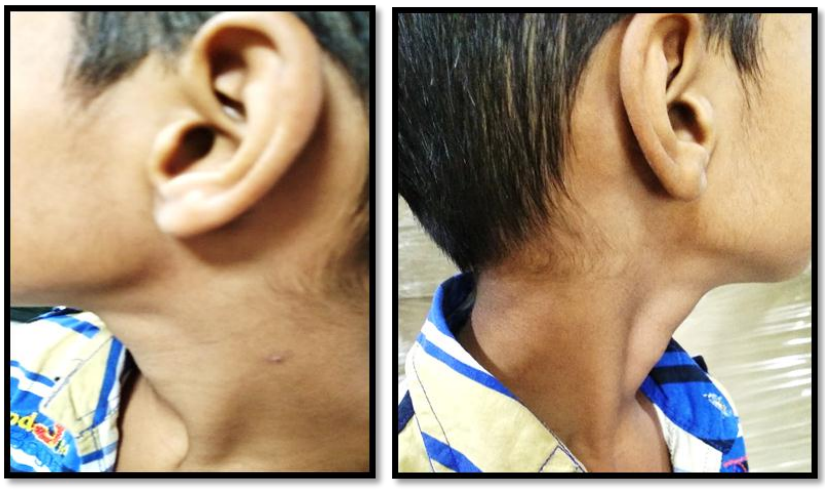

**Fig. 1: No Lymph nodes palpable in bilateral cervical region.**

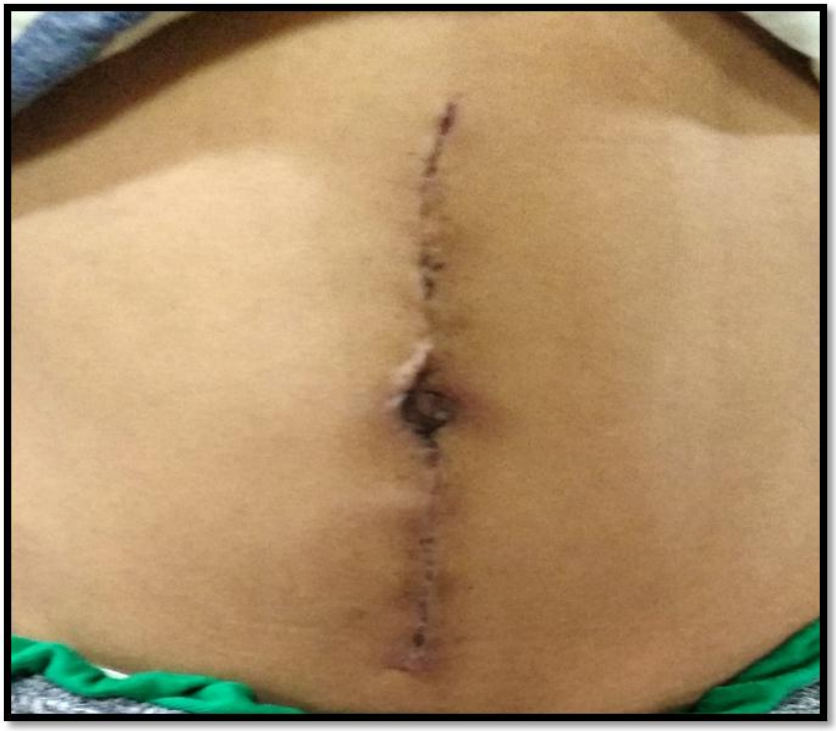

**Fig. 2: Exploratory Laparotomy incision mark on the patient.**

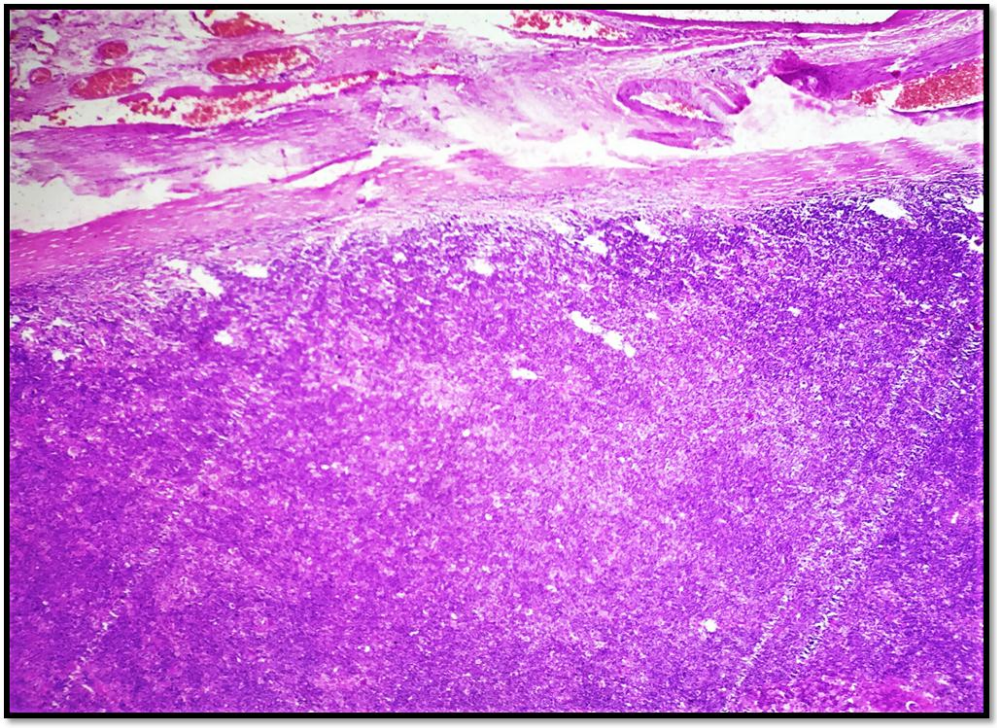

**Fig. 3(4x): Haematoxylin and eosin satined section from lymph node showing complete effacement of its architecture.**

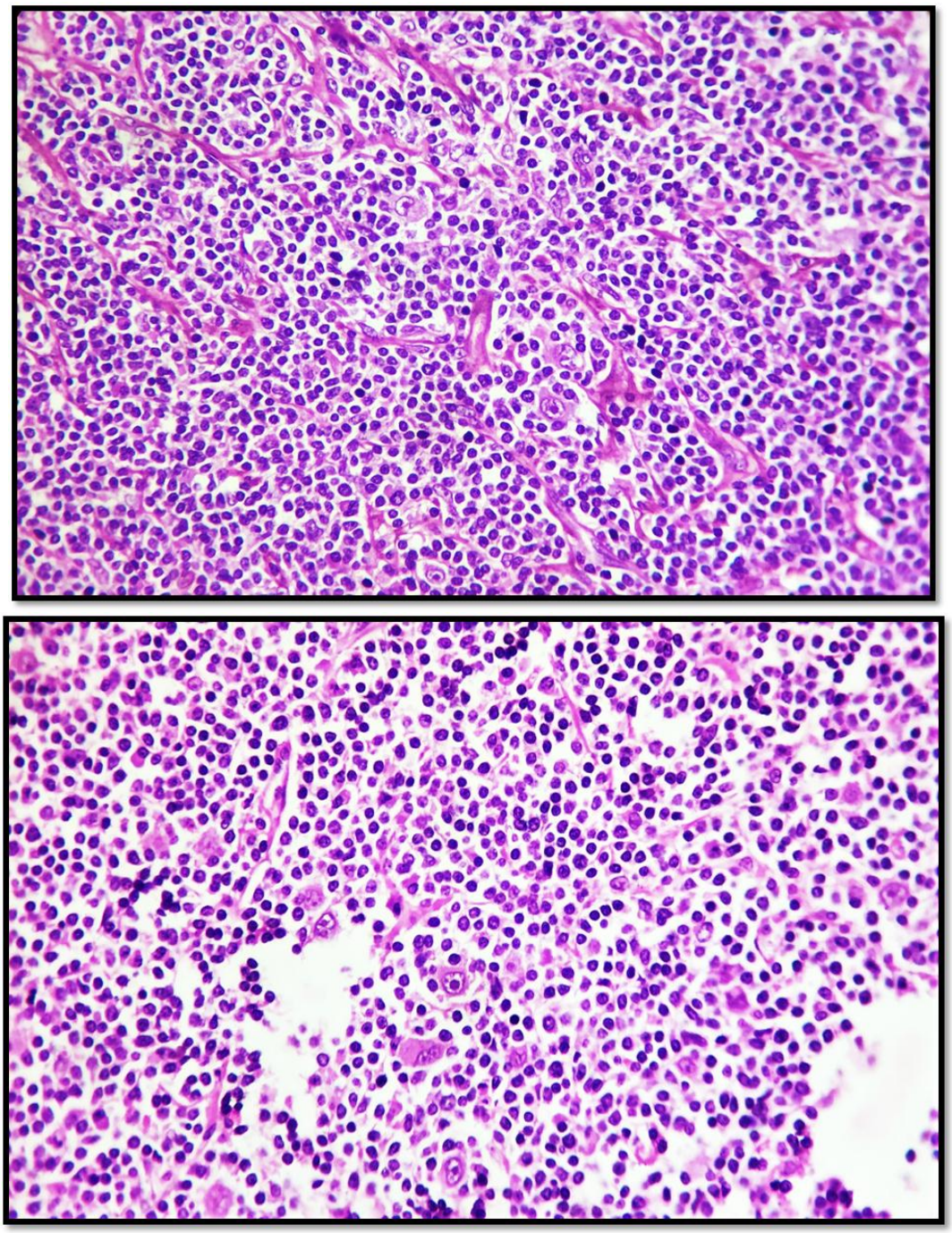

**Fig. 4(10x): Haematoxylin and Eosin satined section from lymph node showing mixed population of lymphoid origin cells along with Reed-Sternberg's cells.**

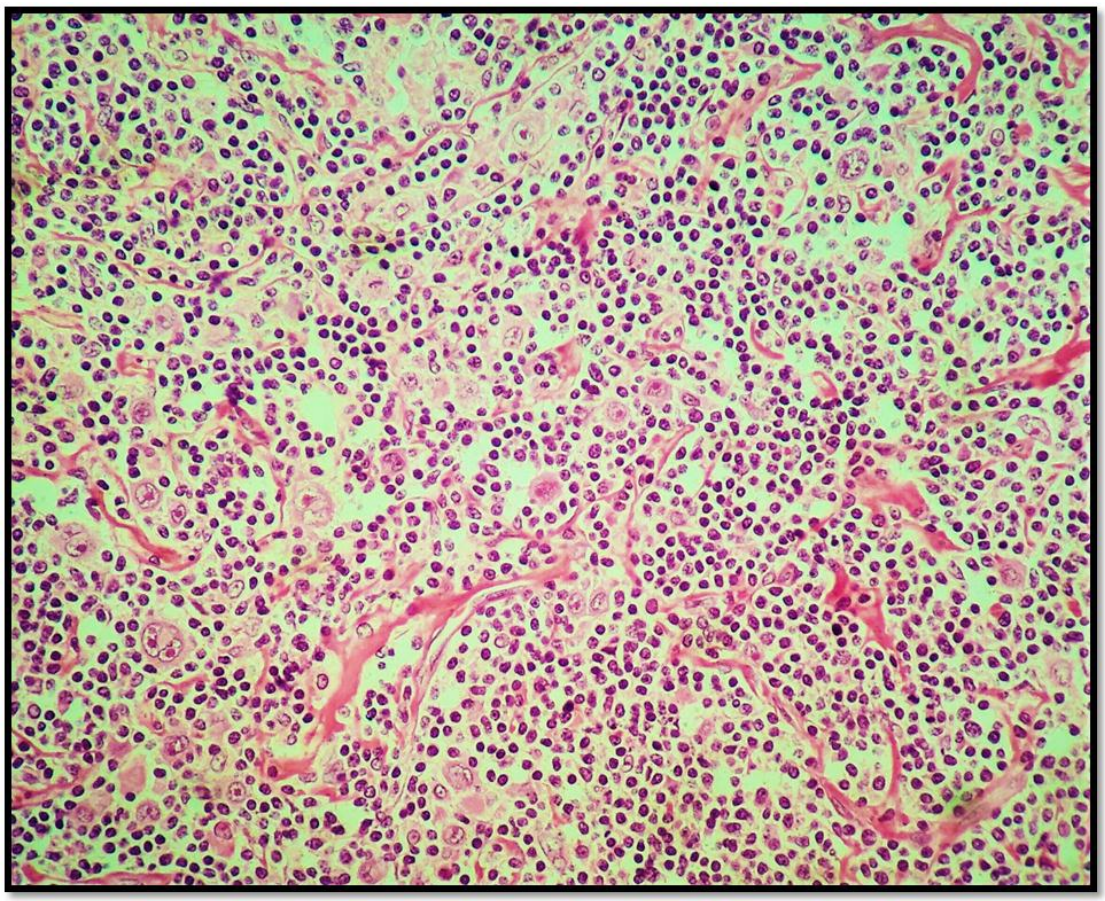

**Fig. 4(10x and 40x): Haematoxylin and Eosin satined section from lymph node showing mixed population of lymphoid origin cells along with Reed-Sternberg's cells.**

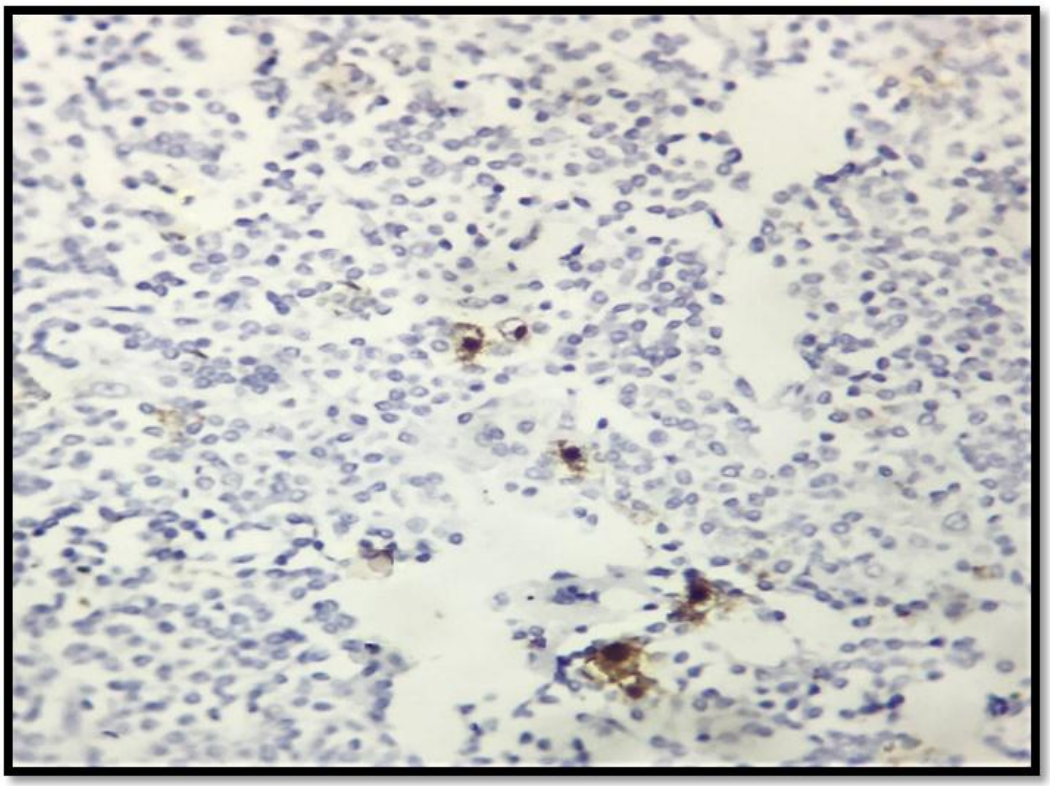

**Fig. 5(40x): CD 15 positive RS cells.**

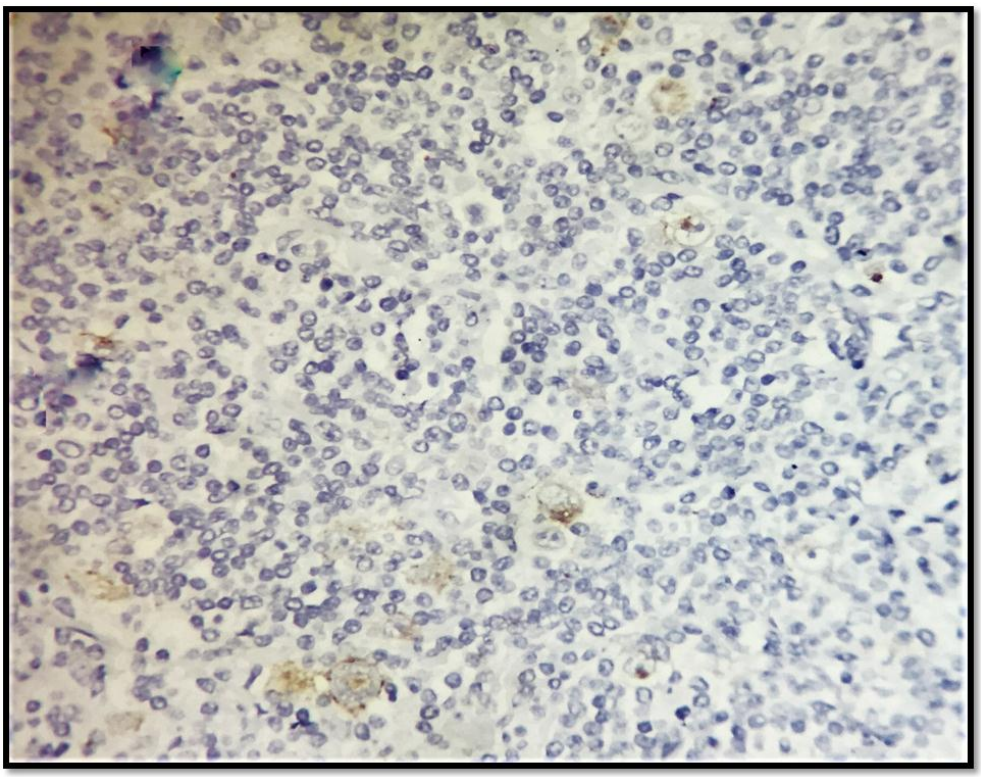

**Fig. 6(40x): CD30 positive RS cells.**

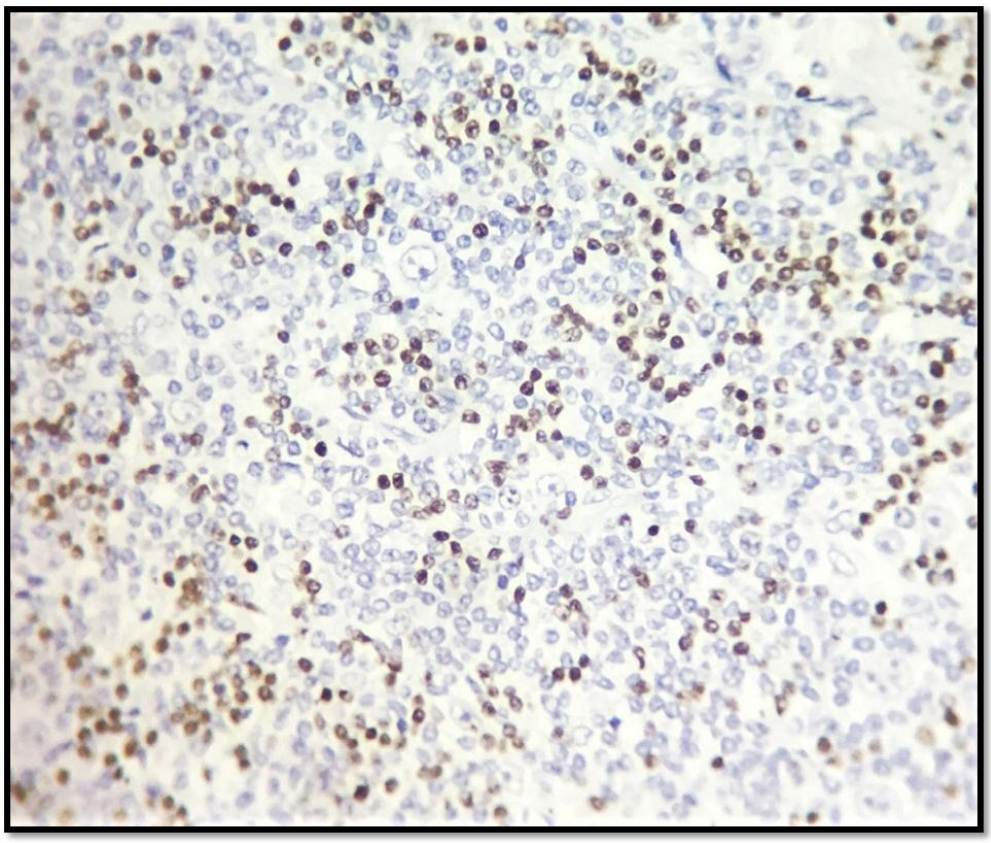

**Fig. 7(40x): PAX-5 negative RS cells.**

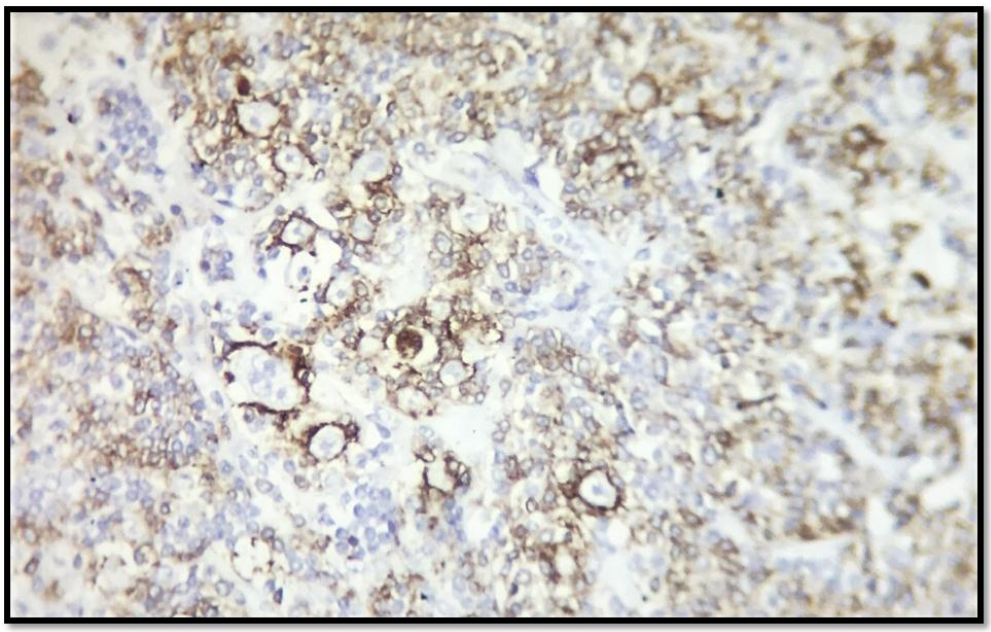

**Fig. 8(40x): CD3 positive lymphoid cell population.**

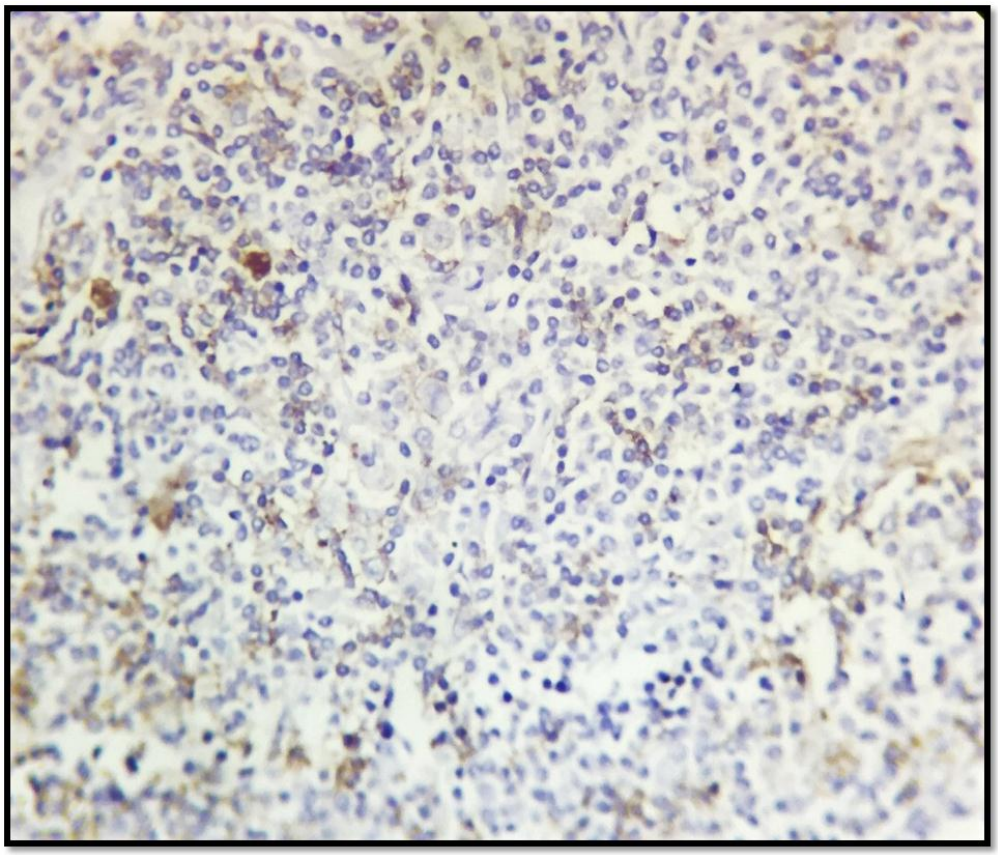

**Fig. 9(40x): CD20 positive lymphoid cell population.**

## DISCUSSION

The presentation of a young child with only mesenteric lymphadenitis i.e. an unusual site, which was suspected clinico-radiologically as mesenteric GIST and histopathologically turned out to be a rare case of PAX-5 negative Hodgkin lymphoma, makes one of the rare case reported by our institution and has limited literature in this context in India.

The incidence of lymphomas is increasing throughout the world as well as in India. Lymphomas show a definite male predominance throughout the world.[5] HL shows a peak incidence between 11-30 years and between 51-60 years. The first case of lymphoma was identified by

Thomas Hodgkin while working at the Guys hospital, London in the year 1832. It was in 1898 and 1902, when Carl Sternberg and Dorothy Reed gave the most important diagnostic entity for HD by defining the classical Reed-Sternberg cell (RS cell). Variants of RS cells were later identified.PAX5 negative CHLs are extremely rare since CHL is believed to be a B-cell neoplasm. PAX5 is a nuclear transcription factor and, among the hematopoietic malignancies, the expression of this marker is mostly restricted to B-cells.[4,5] The gene expression of PAX5 is increased during B-cell maturation and PAX5 expression has been shown to regulate B-cell proliferation and immunoglobulin secretion.[5] Hence, the absence of PAX5 in CHL is a very unusual finding and warrants further investigation.[6] PAX-5 negative Hodgkin lymphoma is itself a rare case which is associated with bad overall prognosis but in our case important point was that, that it solely presented as mesenteric lymphadenitis which made a confusion to clinico-radiological team as a possibility of mesenteric GIST. A study by Desouki et al showed five of 39 cases of CHL were negative for PAX5 by immunohistochemical staining; of the five CHL cases noted in this study, two were mixed cellularity, two were nodular sclerosis, and one CHL was not otherwise specified.[4] Hertel et al showed 4 cases of PAX5-negative classical Hodgkin lymphoma nodular sclerosis and one case of CHL, mixed cellularity type from 18 cases evaluated in the study.[7] In another study performed by Johri et al one case out of 24 cases of CHL lacked expression of PAX5.[8] A study by Foss et al showed 3 cases of CHL without expression of PAX5 by immunohistochemistry out of 31 cases that were evaluated.[9] In the differential diagnoses of PAX5 negative CHL, ALCL (a T-cell lymphoma) has to be considered and ruled out, typically by immunohistochemical staining and gene rearrangement studies. Unlike HRS cells in CHL, large cells in ALCL are commonly positive for CD45 and may express EMA.[10]In ALK positive ALCL, the tumor cells may have loss of many of the pan T-cell markers in addition to being positive for ALK1 staining. In the ALK negative ALCL cases, the tumor cells nearly always express CD2 and most are CD4 positive.[10] However, rare cases of ALCL with expression of PAX5 have been reported PAX5 expression in these cases has been reported to be due to extra copies of PAX5 and not PAX5 rearrangement. It is important to be aware of both of these entities, PAX5-negative CHL and PAX5-positive ALCL, and use extensive immunohistochemical stains along with gene rearrangement studies to define the origin of the neoplastic cells.

The strength of this study was the application of immunohistochemical panel which gave us the confirmatory evidence of PAX-5 negative hodgkin lymphoma in mesenteric lymph node in a child. The limitation of the study was that this was the single case reported with such a presentation so far.

## CONCLUSION

The clinical significance of the lack of PAX5 staining in CHL is unknown. A very small study of PAX5-negative CHL cases suggested that patients with PAX5-negative CHL may have worse clinical outcomes, when compared to typical PAX5-positive CHL. These patients are more prone to relapse or short-ended progression free survival.[10]

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