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RESEARCH ARTICLE

A 13 year-Old Female with Rosai-Dorfman Disease

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Abstract

Rosai-Dorfman or Sinus histiocytosis with massive lymphyadenopathy is a benign self limiting, rare condition of unclear etiology, RDD is of two types familial and other type is associated with infection where titres of Epstein Barr virus and measles virus were found elevated, disturbance in immune system occur in some patients. In some cases human herpes virus 6 DNA has been detected in biopsy samples[1]. It may present as massive bilateral cervical lymphadenopathy with systemic symptoms and characterized by histiocytosis and emperipolesis[2,3]. RDD is mostly seen in children and young adult population of Caucasians and African origin. In our case a 13 years old female presented in OPD with fever for six months and multiple neck lymph nodes with progressive increase in size over a period of 4 months, one located in the pre-auricular region which was 4 cm , another in the sub-mandibular region approx 3 cm in size and also in sub occipital region 4cm in size and bilaterally palpable lymph nodes along sternocleidomastoid muscle which was more than 6cm in diameter .Clinical examination showed discrete, non-tender, painless, mobile nodes and not attached to skin or underlying structures. There were no signs and symptoms of acute inflammation over the lymph nodes. Biopsy of the nodes was performed and cells expressing positive immunoreactivity for protein S-100 and negative for CD 3 staining which was in keeping with Rosai-Dorfman disease .RDD is a benign pathology, self-limited and various nonspecific therapies available ,the prognosis is excellent

Introduction

Rosai-Dorfman disease or sinus histiocytosis with massive lymphadenopathy (SHML) is a rare disease with unexplained etiology but various explanations like immune disturbance, Epstein Barr virus, measles virus have been postulated .Some authors relate it bone marrow stem cell origin[1]. In year 1969 Rosai-Dorfman described four cases of this disease and then in 1972 additional similar cases were diagnosed with clinicopathological diagnosis[4]. It is a benign histiocytic disorder with massive enlargement of lymph nodes, mainly observed in Caucasians and African children and young adults. It is probably associated to viral infections, like Epstein-Barr, and immunological disorders[5]. The common clinical presentation is massive bilateral cervical, painless, lymphadenopathy accompanied by systemic symptoms like fever. There is leucocytosis, polyclonal hypergammaglobulinemia and elevated sedimentation rate[5]. Other lymphatic sites like mediastinal, axillary and inguinal lymph nodes are rarely involved However, extra nodal sites like eyes, head and neck, skin, bone, skeletal muscle, CNS, GI tract, liver, breast, uterine cervix etc are also affected[6][7]. The diagnosis is made by biopsy and immunohistochemistry which shows histiocytosis, emperipolesis and immunoreactivity for protein S-100[8].

Case Report

13 years old female presented in OPD with fever for six months and multiple palpable neck lymph nodes for 4 months. She had continuous low grade to moderate grade fever without weight loss and night sweats. Neck lymphadenopathy appeared as multiple discrete, painless lymph nodes, not fixed to under lying tissue or skin, not matted and were mobile, which had gradually increased in size in anterior neck triangle on left side and right side of neck along the sternocleidomastoid muscle and posterior region of neck (Fig 1&2). Patient had no history of recent weight loss, no history of contact tuberculosis, no h/o photo sensitivity,and no h/o of rash or joint pains. Patient had been on ATT (four drug regime) for six months with no improvement .

On examination vitals were stable, she was afebrile, her weight for height and height for age appropriate for age and sex. Systemic examination was within normal limits and she had no organomegaly. Complete blood count Hb 11.8 grams %, total leukocyte count is 10,000. With Neutrophils 56%, Eosinophils 1% Basophils 3%, lymphocyte 37% and Monocytes 3%. Peripheral smear showed normocytic hypochromic anemia. ESR 28 mm ist hour. CRP 1.2 mg/l. Aerobic blood culture after five days was negative. Sputum for AFB sent for three consecutive days negative. ASO titres normal, VDRL test negative viral markers negative, Liver, renal and thyroid function tests were normal and serologic exams for Epstein-Barr virus, cytomegalovirus, HIV, HBV, TORCH screen and HVC were negative as well as the diagnostic study for tuberculosis including tuberculin skin test and Interferon gamma release assay. Serum protein electrophoresis and Immunoglobin levels were normal.

Ultrasound abdomen was within normal limits no aortic or Para aortic lympnodes found, chest x ray normal. MRI showed mediastinal widening with bilateral lymphadenopathy which did not involve major vessels. Ultrasonography study of the nodes was performed showed adenopathy in right and left parotid gland and along sternocleidomastoid muscle, further study with biopsy was recommended.

A decision was made to carry out excision biopsy which showed capsular and pericapsular fibrosis with normal lymph node architecture and lymph node sinuses were expanded (Fig 3) with proliferation of distinctive histiocytes (Fig 4) and emperipolesis noted (Fig 5). The tissue slides were stained for S100 (Fig 7) and CD 3(Fig 8)were positive for the former and negative for the later differentiating it from Langerhans cell histiocytosis and confirming it as a case of Sinus Histiocytosis with Massive Lymphadenopathy (SHML) or Rosai-Dorfman Disease

Discussion

RDD or SHML is rare but well defined, histiocytic proliferative disorder characterized by massive bilateral cervical lymphadenopathy, rarely involves other lymphatic regions and can also present with involvement of extra nodal sites[1,6,7]. In year 1969, Juan Rosai and Ronald Dorfman reported a histiocytic disorder in four patients with massive enlargement of the lymph nodes[9]. Mostly cases seen are Caucasian children, young adults and African ones. Literature reviews show hundreds of RDD cases in all races. The mean age of presentation is first and second decade of life and male to female ratio is 1.4:1[5, 10, 11]. The causative agents of this condition remains unclear but it is believed that it could be associated with viral infections like Epstein-Barr, measles, HHV 6 and some immunological disorders related with mono nuclear phagocyte and immunoregulatory effector system[5,12]. The disease can involve other lymphatic site and extra nodal sites, though the prognosis is excellent and disease is self limited, spontaneously regress. Some patients have been reported to progress to malignant lymphoma and amyloidosis[13]. The clinical presentation of RDD is cervical lymphadenopathy (87%) of the described cases. Extra nodal site affected and described in literature are skin and soft tissue (16%), nasal cavity (16%), eyes (11%), bones (11%), central nervous system (7%), salivary glands (7%), kidney (3%), airway (respiratory tract) 3% and liver 1%. In some cases, both lymph nodes and extra-lymphatic tissues are affected simultaneously [14].Systemic symptoms associated with RDD and described in literature include fever, sweating at night, malaise and loss of weight [12]. Leucocytosis, neutrophilia, polyclonal hypergammaglobulinemia and elevated erythrocyte sedimentation rate are other associated laboratory findings [5]. The diagnosis of RDD is based on histology of affected tissue obtained by fine needle aspiration or open biopsy. Dilated sinuses of lymph nodes that are filled with numerous big size histiocytes are observed in the histology. A characteristic finding is emperipolesis of histiocytes in which lymphocytes that are phagocytized by the histiocytes can move in the cytoplasmic vacuoles [15]. Immunochemistry should be performed and reveals positivity for protein S-100. Because of similar clinical and histologic findings, lymphoreticular malignancies such as lymphomas, Hodgkin's disease, Langerhans Cell Histiocytosis (positive for S100 and CD1a) and monocytic leukemia should be considered as differential diagnoses [5]. Reactive sinus hyperplasia (lack emperipolesis and S100 negative) and tuberculosis are other differentials. The treatment for RDD are nonspecific and include steroids, chemotherapy with combination of vinca-alkaloids and alkylating agents ,low dose interferon, antibiotic therapy, radiation therapy and surgical partial or total resection .

Conclusions

RDD is a rare disease with self limited course, benign pathology, in most cases there is spontaneous resolution and no special treatment is needed in most cases. In our case, patient was put on steroids and gradually the nodes started shrinking in size.

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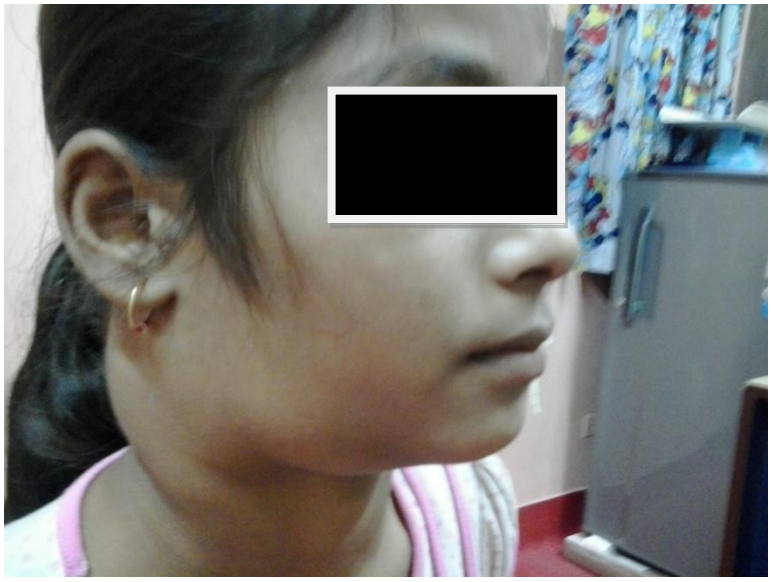

Figure 1. Lateral and frontal view of the Pre-auricular and Right side cervical lymphadenopathy.

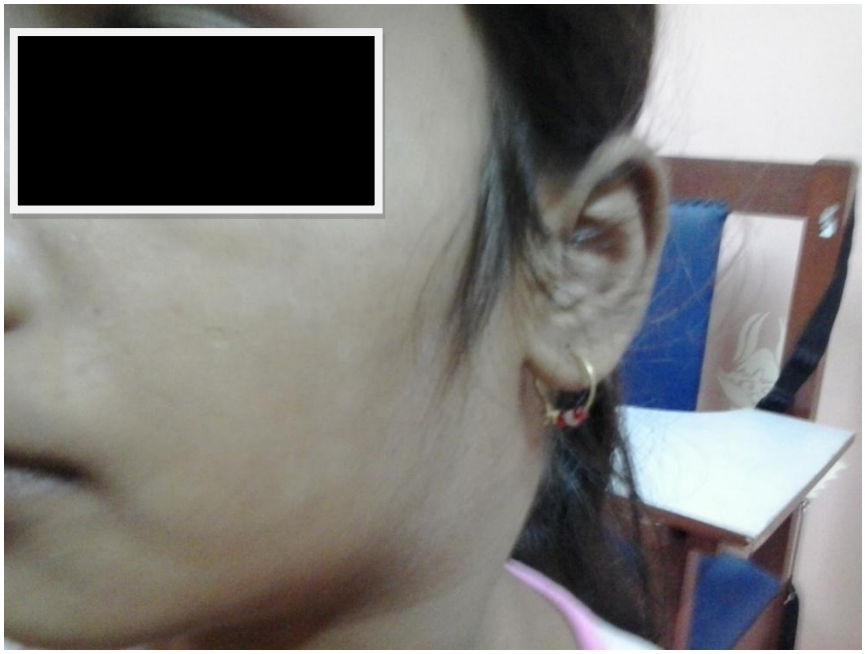

Figure 2. Lateral view showing left side neck lymphadenopathy

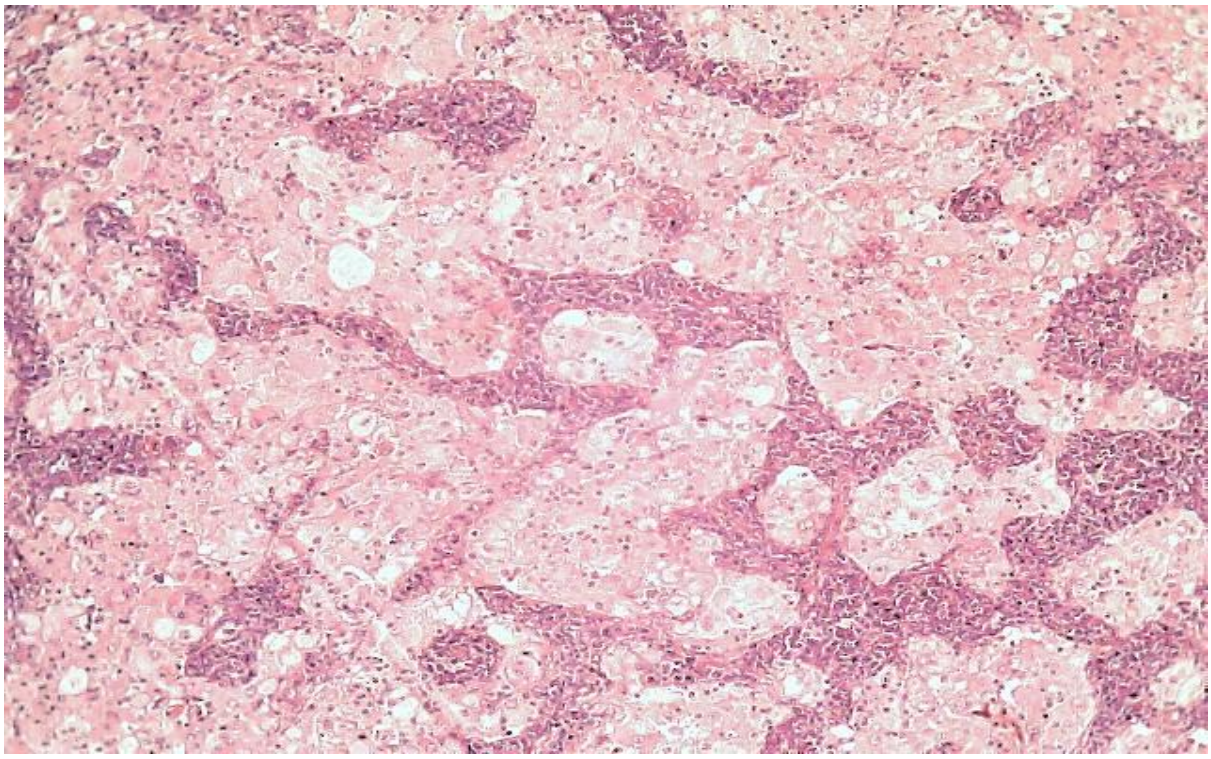

Figure 3. H&E Stained Sections of cervical Lymph Node Showing Dilated Sinuses and packed with macrophages

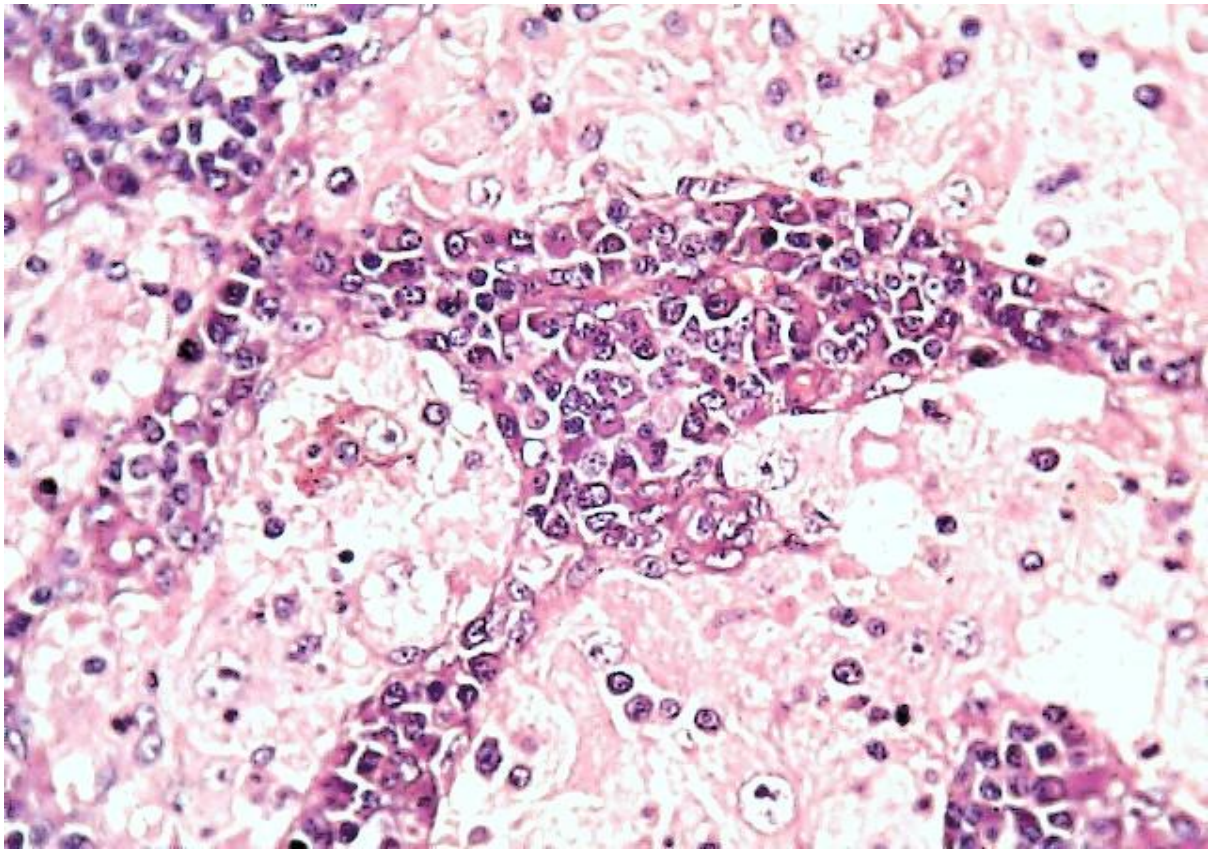

Figure4. H&E Stained Sections of Node Showing Dilated Sinuses and Multiple Giant Cells ,Histiocytes, Abundant pale eosinophilic cytoplasm ,Enlarged round or oval vesicular nuclei with well defined, delicate nuclear membranes and a single prominent nucleolus

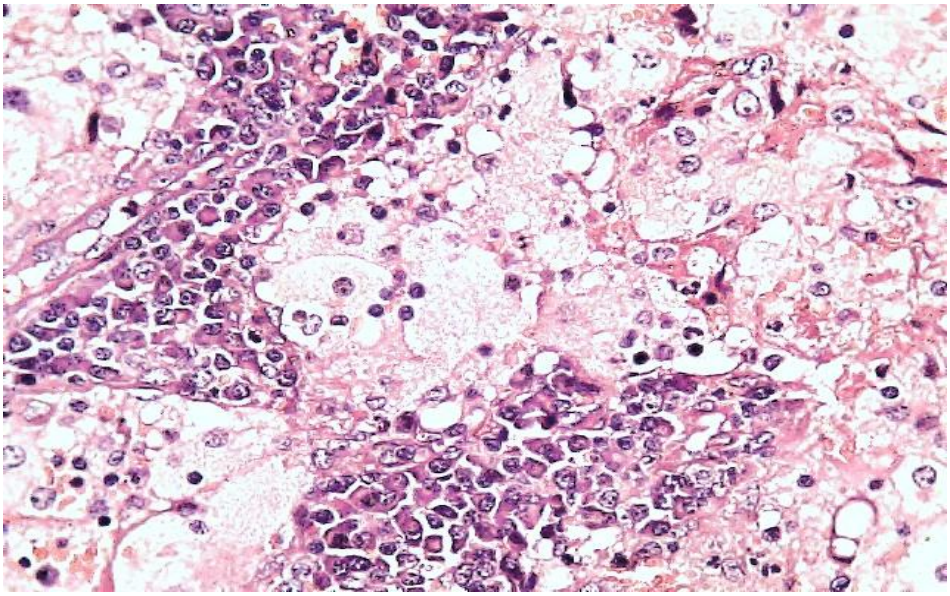

Figure 5. H&E Stained Sections of Cervical Lymph Node Showing Emperipolesis or lymphophagocytosis: Lymphocytic penetration and movement within another cell

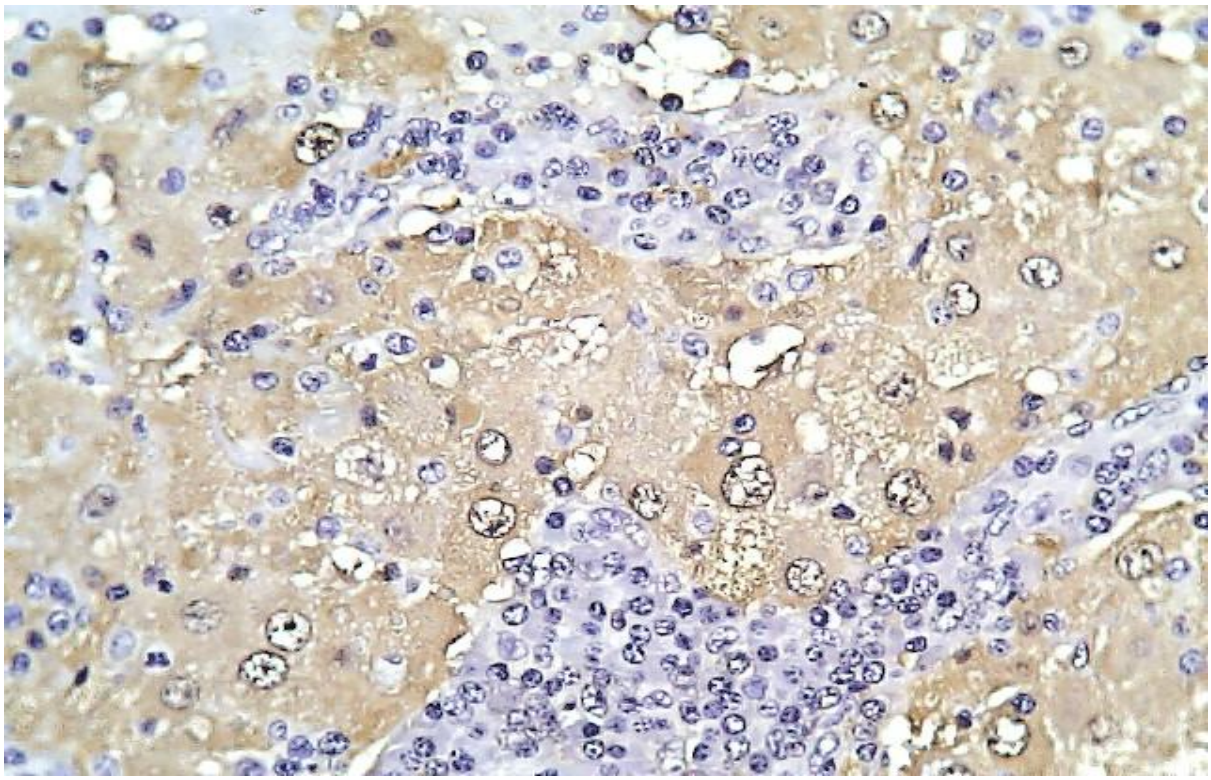

Figure 6. S 100 staining positive

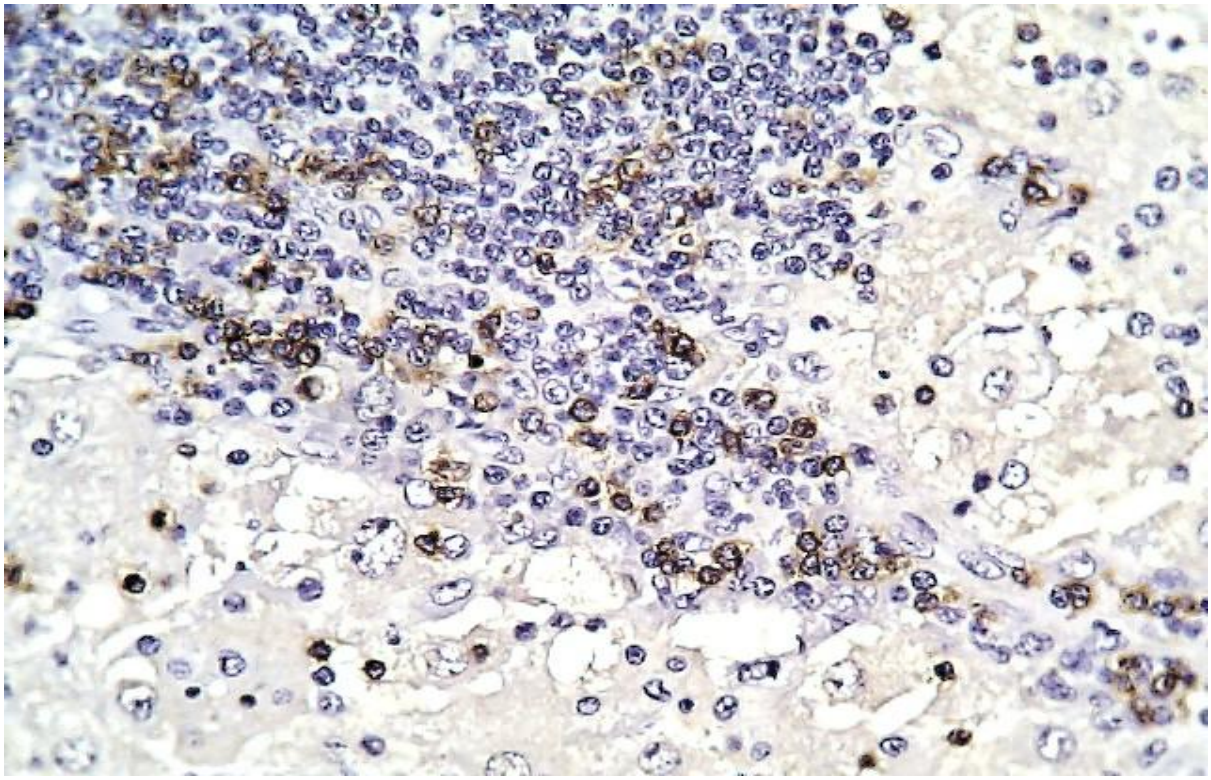

Figure 7. CD 3 staining Negative.

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