

# KASABACH MERRITT SYNDROME IN KAPOSII HEMANGIO-ENDOTHELIOMA

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## ABSTRACT

Kasabach Merritt syndrome (KMS) is also known as hemangioma- thrombocytopenia syndrome. It is a rare disorder characterised by profound thrombocytopenia, microangiopathic hemolytic anemia, subsequent consumptive coagulopathy in association with vascular tumours -especially kaposiform hemangioendothelioma/ tufted angiomas. KMS is usually caused by kaposiform hemangio-endothelioma or tufted angioma and other vascular tumours like infantile hemangioma. KHE and tufted angioma are intermediate locally aggressive childhood vascular tumours that are locally aggressive and often spread to the area around tumour. Pathophysiology of KMS is poorly understood and complicated. The proposed mechanism involves both primary and secondary hemostatic mechanisms leading to platelet trapping, platelet activation/ aggregation and platelet consumption within the abnormal vascular structures. We report a case of two-day old male child presented with multiple areas of petechial haemorrhage on plantar aspect of both feet, right leg, both upper limbs, forehead and bilateral cheeks and large hemangiomas in left lower limb, lateral pelvic wall and abdominal wall. Hemogram showed thrombocytopenia with platelet count of 20,000/ cumm. Ultrasonography and MRI showed diffuse hemangioma in left leg extending in pelvis along left lateral pelvic wall, medial to the iliacus muscle and extending in the retroperitoneum, encasing aorta upto the level of renal hilum. Diagnosis of kasabach meritt syndrome in Kaposi hemangio-endothelioma was made.

**Keywords:** Kasabach Merritt syndrome, haemangioma, thrombocytopenia, kaposiform hemangio-endothelioma, tufted angioma

## Introduction

Kasabach Merritt syndrome (KMS) is also known as hemangioma- thrombocytopenia syndrome. It is a rare disorder characterised by profound thrombocytopenia, microangiopathic hemolytic anemia, subsequent consumptive coagulopathy in association with vascular tumours - especially kaposiform hemangioendothelioma/ tufted angiomas.<sup>1</sup>

KMS was first described by Kasabach (a radiologist) and Merritt (a pediatrician) in 1940 characterised by a coagulation abnormality in vascular tumours causing haemorrhage, infections, multiple organ failure and death, occurring in 12-24% of patients.<sup>2</sup>

Mortality rate of KMS is about 30 percent.<sup>3,4</sup>

KMS is usually caused by kaposiform hemangio-endothelioma or tufted angioma and other vascular tumours like infantile hemangioma. KHE and tufted angioma are intermediate locally aggressive childhood vascular tumours that are locally aggressive and often spread to the area around tumour.<sup>5</sup>

## Case Report

A two day old male child presented with multiple areas of petechial haemorrhage on plantar aspect of

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both feet, right leg, both upper limbs, forehead and bilateral cheeks. He was a full term, caesarean delivery with birth weight of 2.5 kgs. Skin in left leg and thigh upto groin appeared thickened and showed diffuse lesion with purplish discoloration with indistinct margins. Findings were suggestive of large cutaneous hemangioma (Fig. 1). There was no active bleeding elsewhere. Left foot and right hand were deformed in shape with lack of development of 2<sup>nd</sup> to 5<sup>th</sup> digits and right thumb.



**Figure 1:** Plantar surfaces of both feet (A) and skin in left leg and thigh upto groin (B) appeared thickened and showed diffuse lesions with purplish discoloration and indistinct margins, suggestive of large cutaneous hemangiomas.

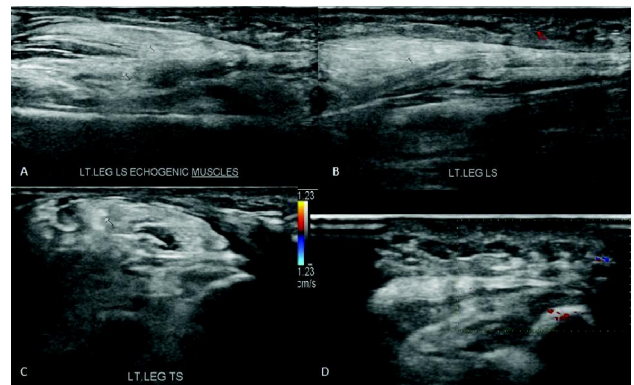
Hemogram showed thrombocytopenia with platelet count of 20,000/ cumm. Prothrombin time 15.7 sec (control - 13.6 sec), APTT is 29 seconds (20.1-30 sec). C reactive protein was negative. Hemoglobin was 11.8gm%. Total leukocyte count was 21,000/ cumm. Polymorphs-30%, lymphocytes-61%, eosinophils-4%, monocytes-5%. PCV - 36%, MCV-109.1 fl, MCH-34.5 pg, MCHC - 31.7. Toxic granules were also seen.

In view of large hemangioma and thrombocytopenia, diagnosis of Kasabach Meritt syndrome was made. Treatment given was platelet concentrate human (RDP at 15cc/ kg).

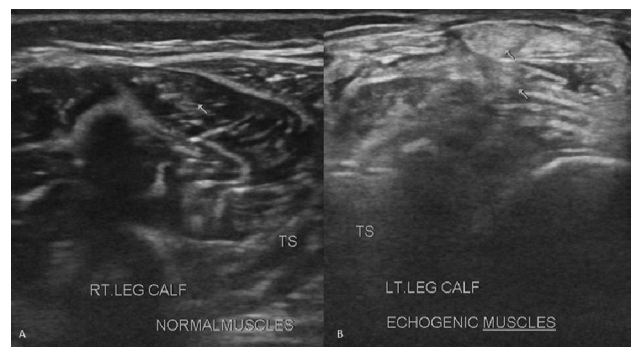
LFTs: Total Serum bilirubin - 7.2mg% (0.2-1mg%) ; Direct bilirubin - 0.2 mg% (0-0.3 mg%) ; SGPT - 19 IU/L(0-40 IU/L); SGOT- 78 IU/L(5-30IU/L); S. alkaline phosphatase - 85 IU/L(15-112 IU/L).

RFTs and serum electrolytes were normal. Serum proteins were normal.

Ultrasound of left leg, left calf, left thigh was done with linear high frequency probe (7-12MHz) (Fig. 2,3). There was diffuse thickening of skin and underlying subcutaneous fat with echogenic lesions showing

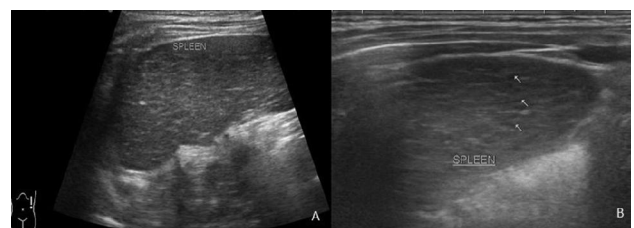


**Figure 2:** Ultrasound of left leg longitudinal (A,B) and transverse sections (C,D) with linear high frequency probe (7-12MHz) shows diffuse thickening of skin and underlying subcutaneous fat with echogenic lesions showing lack of vascularity on Colour Doppler. Muscles in left leg and calf were also involved and showed diffuse echogenic lesions suggestive of muscle involvement.

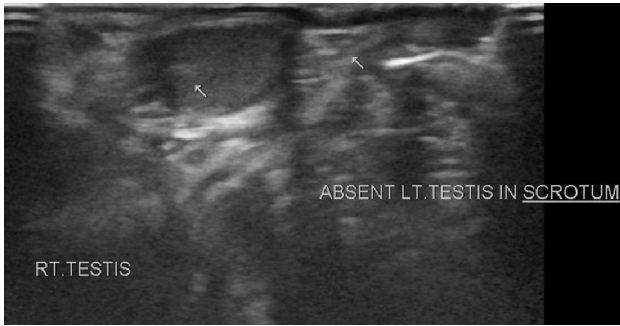


**Figure 3:** Ultrasound of right calf (A), left calf (B) transverse sections with linear high frequency probe (7-12MHz) shows diffuse thickening of skin and underlying subcutaneous fat in left calf with echogenic lesions, muscles in left calf were also involved and showed diffuse echogenic lesions suggestive of muscle involvement. Right calf was normal.

lack of vascularity on Colour Doppler. Muscles in left leg and calf were also involved and showed diffuse echogenic lesions. USG of abdomen (Fig. 4) showed multiple small hypoechoic lesions in entire spleen, suggestive of splenic involvement. USG of scrotum (Fig. 5) showed absence of left testis in left scrotum and left inguinal region.



**Figure 4:** USG of spleen showing multiple hypoechoic lesions scattered in entire spleen.



**Figure 5:** USG of scrotum showing absence of left testis in scrotum.

Radiograph of right hand showed absence of phalanges in 3<sup>rd</sup> to 5<sup>th</sup> digits, absence of 1<sup>st</sup> metacarpal and phalanges of thumb. Radiograph of left foot showed absence of phalanges in 2<sup>nd</sup> to 5<sup>th</sup> toes (Fig. 6).

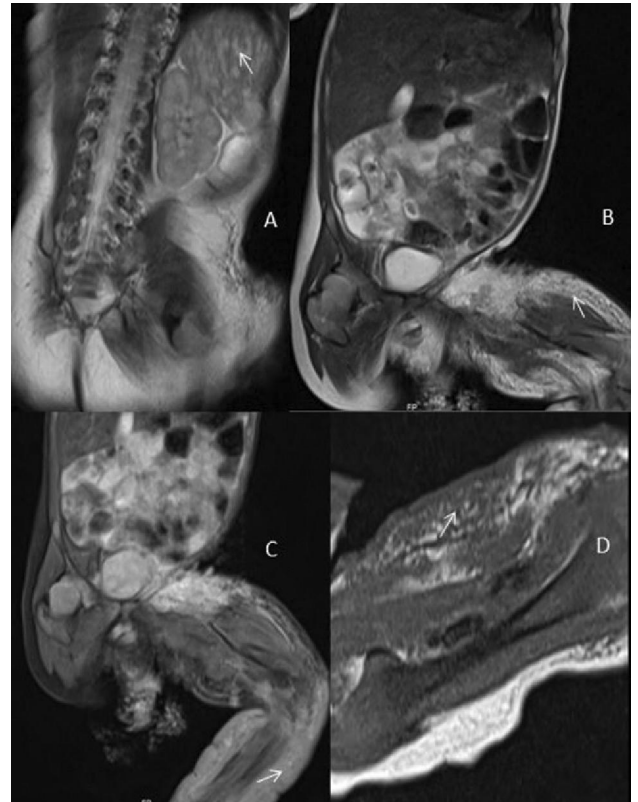


**Figure 6:** Radiograph of right hand (A) showing absence of phalanges in 3<sup>rd</sup> to 5<sup>th</sup> digits, absence of 1<sup>st</sup> metacarpal and phalanges of thumb. Radiograph of left foot (B) showing absence of phalanges in 2<sup>nd</sup> to 5<sup>th</sup> toes.

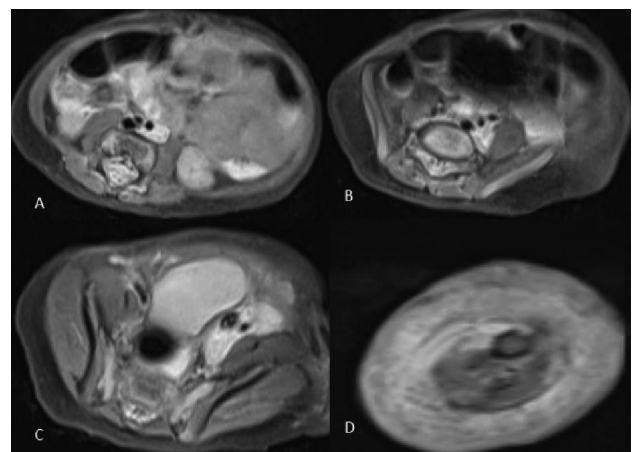
MRI left lower limb, pelvis and lower abdomen, showed diffuse thickening of skin and subcutaneous fat in thigh and leg by diffuse hyperintense lesion on T2WI appearing hypointense on T1WI and showing intense and near homogenous contrast enhancement in post contrast fat sat images. Diffuse hemangioma was extending in pelvis along left lateral pelvic wall, medial to the iliacus muscle and extending in the retroperitoneum, encasing aorta upto the level of renal hilum (Fig. 7-9). Diagnosis of Kaposi hemangio-endothelioma was made.

## Discussion

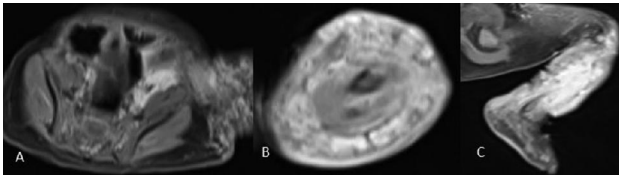
According to International Society for the Study of Vascular Anomalies (ISSVA) for the study of vascular



**Figure 7:** MRI of abdomen coronal T2WI (A) showing multiple hyperintense lesions in spleen, MRI of abdomen with thigh coronal T2WI (B) showing diffuse hyperintense lesions in subcutaneous plane in left thigh, MRI of left thigh with leg coronal STIR (C) showing diffuse hyperintense lesions in subcutaneous plane in left thigh and left leg, MRI of left thigh coronal T1WI (D) showing diffuse hypointense lesions involving skin and subcutaneous fat due to Kaposi's hemangio-endothelioma.



**Figure 8:** MRI of abdomen and pelvis and left thigh axial STIR (A-D) showing diffuse Kaposi hemangio-endothelioma seen as hyperintense lesion in the retroperitoneum encasing aorta (A,B), extending in pelvis along left lateral pelvic wall, medial to the iliacus muscle (C), diffuse thickening of skin and subcutaneous fat in left thigh due to Kaposi hemangio-endothelioma (D).



**Figure 9:** MRI post contrast T1 fat sat of pelvis (A), left thigh (B), left leg (C), showing diffuse enhancement of hemangioendothelioma in retroperitoneum, subcutaneous fat and underlying muscles.

anomalies are classified into vascular tumours and malformations. Vascular tumours show neoplastic growth of vascular endothelial cells while vascular malformations are vascular structural anomalies with no neoplastic proliferation of endothelial cells.<sup>2</sup>

Vascular tumours are- (a) Infantile hemangiomas - these grow rapidly from birth up to the age of 1 year followed by regression. (b) Congenital hemangiomas- develop during fetal life and manifest at birth. These can be rapidly involuting congenital hemangiomas (RICH) which rapidly involute after birth and non-involuting congenital hemangioma (NICH) which do not involute.

Vascular malformations grow steadily and become conspicuous with age. Aggravating factors of this disorder are- traumatic, injury, surgery, puberty and pregnancy.

KMS and KM-like phenomenon are two different entities. KMS is an entrapment coagulopathy which occurs when coagulation factors and platelets are trapped between vascular tumour cells. These occur in KHE and tufted angiomas (TA). Management is resection, corticosteroids, chemotherapy, embolization, interferon and radiation therapy. KM-like phenomenon is a consumptive coagulopathy which occurs when coagulation factors consumed after haemorrhage has occurred. It occurs in venous and other types of malformations. Treatment is with blood coagulation factors. Thus, KMS and KM-like phenomenon are two different conditions requiring different treatment.<sup>2</sup>

KMS occurs in TA, KHE, hemangioma, angiosarcoma and rarely aneurysms. KHE and TA are rare. The incidence of KHE is 0.07 per 10 lakh children per year.<sup>6,7</sup>

The incidence of KMS in KHE is 70 percent while in TA it is 10 percent.<sup>8,9</sup>

KHE is a locally aggressive tumour involving superficial and deep soft tissues. In adults, KMS is rare and

occurs as complication in hemangiomas, hemangiomatosis and angiosarcomas.<sup>10</sup>

Tumour can be found in the upper and lower extremities, trunk, retroperitoneal and in the cervical and facial areas.<sup>5</sup>

KHE and TA are rare proliferative tumours that present at or shortly after birth. Both lesions can occur in the extremities, trunk, head, neck, retroperitoneum and rarely other locations. Expansion into soft tissues and regional lymph nodes is commonly seen in KHE but distant metastasis does not occur. The imaging characteristics are similar. KHE tends to be larger, infiltrative and ill-defined and often associated with flow voids due to numerous feeding and draining vessels. KHE may be associated with secondary destructive bony changes. Both may be associated with KMS due to platelet sequestration. The presence of KMS indicates poor prognosis with mortality rate of 30 percent in KHE and hence is an indication of aggressive treatment. Due to aggressive behaviour of KHE, wide local excision and supportive treatment are the mainstay of therapy. On histology, KHE consists of irregular infiltrating nodules of compressed vessels and show both vascular and lymphatic components. TA shows vascular tufts of tightly packed capillaries in a canon-ball pattern. Immuno-staining of patterns of mono-clonal antibody D2-40 helps in distinguishing KHE from TA.<sup>2</sup>

Due to critical condition of KMS patients, biopsy and histology of lesions are usually not available before involution of the lesion unless surgical resection is performed as a curative procedure. In KHE, infiltrating sheets, lobules of spindle shaped or round endothelial cells with red cell- microthrombi and hemosiderin deposits are found.<sup>5</sup>

It is a low- grade, aggressive malignant tumour. In contrast, TA is a benign lesion characterised by discreet small vascular tufts of aggregates of round dilated capillaries showing canon ball distribution. Micro-thrombi and hemosiderin deposits are also seen as with KHE. Aberrant lymphatic vessels and distant areas of lymphangiomatosis can be found in both KHE and TA. KHE can be found in non-cutaneous sites like retroperitoneum, mediastinum and pelvis apart from skin with equal incidence in both sexes.<sup>5</sup> Cutaneous KHE are smooth, indurated, shiny, dark copper in color, tender and poorly delineated and usually single. Though multiple KHE have been repor-

ted. On MRI, KHE shows cutaneous thickening with strands of sub-cutaneous fat in cutaneous lesions, ill-defined margins, diffuse enhancement in contrast with small hemosiderin deposits and small feeding and draining vessels. Hemosiderin deposits in MRI is because of red cell destruction.<sup>5</sup>

Pathophysiology of KMS is poorly understood and complicated. The proposed mechanism involves both primary and secondary hemostatic mechanisms leading to platelet trapping, platelet activation/ aggregation and platelet consumption within the abnormal vascular structures. The site of platelet destruction is controversial.<sup>10</sup>

Indium 111 platelet scintigraphy study show platelet trapping in the vascular lesions. However the degree of thrombocytopenia doesn't correspond to the size of the lesion. Other studies involving platelet labelled with Tc 99m demonstrates lower level of platelet sequestration in vascular lesions compared to the spleen. Platelet destruction in spleen and not in vascular lesion can be explained by acquired platelet defects occurring in the vascular lesion leading to their subsequent destruction in spleen.<sup>11</sup>

The epicentre of KMS initiation is endothelial. Hemangioma derived endothelial cells show increased expression of E-selection, a cell adhesion molecule and diffuse distribution of CD 31 and von Willebrand factor (vWF), demonstrating an immature phenotype of the endothelium.<sup>10</sup>

Exposure of sub-endothelial collagen and tissue factor in rapidly changing endothelial cells leads to platelet binding by a glycoprotein (GP)- Ib-V-IX and vWF, with subsequent platelet activation. This leads to localized intra-vascular coagulopathy and hence life threatening disseminated intravascular coagulopathy (DIC).<sup>12</sup>

Platelet trapping leads to thrombocytopenia and hypofibrinogenemia, increased fibrinolysis causing intraleisional bleeding and tumour enlargement. Microangiopathic hemolytic anemia is also seen. Vascular endothelial growth factor alpha (VEGFA) play important role in tumour enlargement and is secreted by tumour cells, tumour stroma and platelets.<sup>10</sup>

Consumptive coagulopathy uses clotting factors and the fibrinogen and worsens bleeding. The coagulopathy can lead to DIC and even death. Hemolytic anemia occurs secondary to physical damage of the RBC (micro-angiopathic destruction) and can be mild, moderate or severe. Diagnostic workup in KMS

involves-

1. Imaging studies- ultrasound, doppler, MRI, CT scan, rarely angiography and nuclear medicine studies.
2. Blood counts and clotting studies.
3. Biopsy of the tumour.<sup>12</sup>

In vaso-proliferative disorders, there is increased endothelial cell turnover determined by the identification of mitosis on histology. Vascular malformations are structural anomalies of capillaries, venous, lymphatic and arterial system and do not have increased endothelial cell turnover. Ultrasonography (US), magnetic resonance imaging are the widely used modalities of choice for their detection.<sup>2</sup>

Ultrasound is useful for initial screening because of ease of availability, portability, lack of ionizing radiation, real time imaging, no requirement of sedation in children. It is non-invasive, simple and useful for evaluating superficial and/ or visceral lesions. It determines the basic type of lesion, useful for further imaging evaluation and helpful in management. Along with colour doppler and spectral doppler, it evaluates vascularity and type of vessel present. MRI further characterise sonographic findings, determines the extent of larger lesions, extension in retroperitoneum, involvement of viscera and useful in planning medical, surgical and interventional therapy.<sup>2</sup>

Computed tomography (CT) is helpful when urgent imaging is needed due to its speed and less need for sedation. The association of hemangiomas with regional and segmental anomalies has been described. Our patient had bony abnormalities suggestive of lumbar association.<sup>2</sup>

MRI is extremely useful in detecting vascular tumours and malformations. T2W images show a diffuse increase in signal involving skin and sub-cutaneous fat. Post-contrast T1FS images show diffuse enhancement of mass. It is useful in initial diagnosis and subsequent follow up after various treatments. Doppler studies differentiate a solid mass from a vascular lesion.<sup>10</sup>

KMS shows severe thrombocytopenia, microangiopathic hemolysis, low fibrinogen levels and high fibrin degradation products due to fibrinolysis.<sup>5</sup> Treatment is surgical resection, embolization to limit blood supply, medicines like corticosteroids, alfa interferon, chemotherapy like vincristine and radiation therapy.

## Conclusion

Kasabach Merritt syndrome (KMS) is a rare disorder characterised by profound thrombocytopenia, microangiopathic hemolytic anemia, subsequent consumptive coagulopathy in association with vascular tumours -especially kaposiform hemangioendothelioma/ tufted angiomas.

## References

1. Yadav D, Maheshwari A, Aneja S, Seth A, Chandra J. Neonatal Kasabach-Merritt phenomenon. *Indian J Med Paediatr Oncol.* Oct 2011; **32(4)**: 238-41.
2. Lowe LH, Marchant TC, Rivard DC, Scherbel AJ. Vascular malformations: classification and terminology the radiologist needs to know. *Semin Roentgenol.* Apr 2012; **47(2)**: 106-17.
3. Larsen EC, Zinkham WH, Eggleston JC, Zitelli BJ. Kasabach-Merritt syndrome: therapeutic considerations. *Pediatrics.* Jun 1987; **79(6)**: 971-80.
4. Osman NM. Kasabach - Merritt syndrome: A case report. *Sudan J Paediatr.* 2013; **13(1)**: 49-52.
5. Hall GW. Kasabach-Merritt syndrome: pathogenesis and management. *Br J Haematol.* Mar 2001; **112(4)**: 851-62.
6. Rodriguez V, Lee A, Witman PM, Anderson PA. Kasabach-merritt phenomenon: case series and retrospective review of the mayo clinic experience. *J Pediatr Hematol Oncol.* Jul 2009; **31(7)**: 522-6.
7. Ryan C, Price V, John P, Mahant S, Baruchel S, Brandão L, Blanchette V, Pope E, Weinstein M. Kasabach-Merritt phenomenon: a single centre experience. *Eur J Haematol.* Feb 2010; **84(2)**: 97-104.
8. Croteau SE, Liang MG, Kozakewich HP, Alomari AI, Fishman SJ, Mulliken JB, Trenor CC 3rd. Kaposiform hemangioendothelioma: atypical features and risks of Kasabach-Merritt phenomenon in 107 referrals. *J Pediatr.* Jan 2013; **162(1)**: 142-7.
9. Kelly M. Kasabach-Merritt phenomenon. *Pediatr Clin North Am.* Oct 2010; **57(5)**: 1085-9.
10. Master S, Kallam D, El-Osta H, Peddi P (2017) Clinical Review: Management of Adult Kasabach-Merritt Syndrome Associated with Hemangiomas. *J Blood Disord Transfus;* **8(5)**: 397
11. Wen S, Zhang W, Yang Y, Sun J. Angiosarcoma of the scalp and face associated with Kasabach-Merritt syndrome and disseminated intravascular coagulation. *Indian J Dermatol Venereol Leprol.* Jan-Feb 2016; **82(1)**: 96-7.
12. Mantovani A, Dejana E. Cytokines as communication signals between leukocytes and endothelial cells. *Immunol Today.* Nov 1989; **10(11)**: 370-5.