DOI: 10.7860/JCDR/2014/10361.5299

Short Communication

Dentistry Section

Emperipolesis – A Review

VARUN RASTOGI[1], RACHNA SHARMA[2], SATYA RANJAN MISRA[3], LALITA YADAV[4], VANDANA SHARMA[5]

ABSTRACT

Emperipolesis is an uncommon biological process, in which a cell penetrates another living cell. Unlike in phagocytosis where the engulfed cell is killed by lysosomal enzymes of the macrophage, the cell exists as viable cell within another in emperipolesis and can exit at any time without any structural or functional abnormalities for either of them. This process can either be physiological or pathological and may be a pathognomonic feature of certain diseases. Histiocytes and Megakaryocytes are involved in Emperipolesis normally but tumour giant cells in Hodgkin's disease and Rosai-Dorfman disease are pathologic conditions in which this process is seen. We report a mini review as this process is rare and not much reported in the literature.

Keywords: Giant cells, Macrophage, Uncommon biologic process

INTRODUCTION

Emperipolesis is derived from the Greek (em – inside; peri – around; polemai – wander about) and was defined by Humble et al., [1] as "The active penetration of one cell by another which remains intact." It differs from phagocytosis in that an engulfed cell exists temporarily within another cell and with an intact normal structure while in phagocytosis, the engulfed cell is destroyed by the protective action of lysosomal enzymes. Recently, Overholtzer et al., reported a homogenous cell – in – cell phenomenon that bears a striking similarity to emperipolesis and named it as Entosis [2]. The cells involved in Emperipolesis are mainly histiocytes and megakaryocytes but can also be seen in association with tumour cells and Reed Sternberg cells. Lymphocytes both in the physiological and pathological conditions have been involved in emperipolesis [3]. In addition plasma cells, myeloid cells, erythroblasts and neutrophils can also be engulfed in histiocytes or megakaryocytes cell cytoplasm.

DISCUSSION

Emperipolesis is a hallmark feature of Rosai – Dorfman disease (RDD) also called Sinus Histiocytosis with Massive Lymphadenopathy (SHML) but can also be part of other malignant conditions such as hematolymphoid disorders (Hodgkin's disease, leukaemia, acute and chronic myeloid leukaemia, Non – Hodgkin's lymphoma, myeloproliferative disorders, myelodysplastic syndrome) and Non haematological malignancies (multiple myeloma, nueroblastoma, Rhabdomyosarcoma) [4,5].

The histiocytes in SHML are characterized by round to oval vesicular or hyperchromatic nuclei with distinct nucleoli and abundant amphophilic to eosinophilic granular or clear cytoplasm. These histiocytes shows features of antigen presenting cell or Langerhans cell (S100 positive) and phagocytic histiocytes (α1 – antitrypsin, lysozymes, CD 68, MAC – 378 positivity and CD 1a negativity) [6].

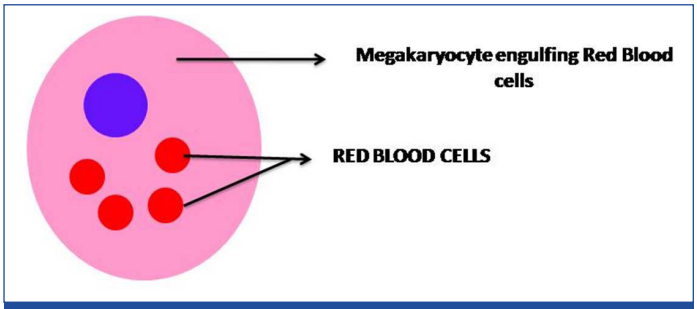
According to Wang and Li, emperipolesis act as a medium or pathway to mediate natural killer cell – mediated tumour cell death. This interaction requires target cell membrane fluidity for its binding with natural killer cells. Once inside the host tumour cells, the natural killer cell undergoes mitosis. They also demonstrated that after the emperipolesis of natural killer cell, tumour cell disintegration is mediated via lysosome – mediated degradation pathway at the ultra - structural level. This requires extracellular free calcium, adhesion molecules, and actin – based cytoskeleton [3]. The predominant fate of the invading cell in emperipolesis can be any of the following: 1. Cannabalism – invading cell disintegration via lysosome mediated pathway. 2. Host cell death via lysosome mediated pathway. 3. Transcytosis 4. Sncytial – both the invading cell and recipient cell undergo cell division.

In SHML, the hypothesis for Emperipolesis is due to the recruitment of marrow monocytes from the peripheral blood and their early transformation to immunophenotypically distinct histiocytes while in myeloproliferative diseases, it may be due to the increased expression of P – selectin (cell adhesion molecule) that results in neutrophils sequestration on the outer surface of megakaryocytes, thus promoting increased neutrophils – megakaryocytes interactions [7].

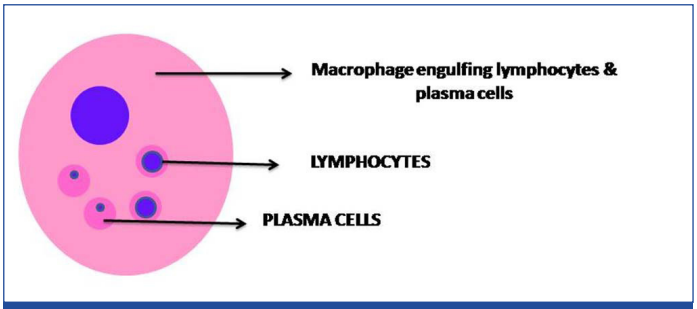
CLASSIFICATION

Depending on the engulfment of cells by histiocytes or megakaryocytes, Emperipolesis is classified as follows:

1. Engulfment of hematopoietic cells (erythroblast, myeloid cell, neutrophils) by megakaryocytes is called Megakaryocytic Emperipolesis [Table/Fig-1]. This is seen in hematolymphoid disorders - Hodgkin's disease, leukaemia, acute and chronic myeloid leukaemia, Non – Hodgkin's lymphoma, myeloproliferative disorders, myelodysplastic syndrome [4,5].
2. Engulfment of inflammatory cells (lymphocytes and plasma cells) by histiocytes is called Histiocytic Emperipolesis [Table/



[Table/Fig-1]: Megakaryocyte engulfing red blood cells



[Table/Fig-2]: Macrophage engulfing lymphocyte & plasma cells

Features	SHML	LCH
CD 68	++	--
CD 1a	--	++
Birbeck granules	--	++
Eosinophils as a component	--	++
Nuclear lobation	--	++
Indentation/ Longitudinal grooving	--	++

[Table/Fig-3]: Difference between histiocytes in SHML & LCH

Features	SHML	MM
S100	++	++
HMB – 45	--	++
Emperipolesis	Present	Absent

[Table/Fig-4]: Difference between histiocytes in SHML & MM

Features	SHML	HD
Matted lymph nodes	--	++
Capsular fibrosis	--	++
Reed – Sternberg cells	--	++
CD 15	--	++

[Table/Fig-5]: Difference between histiocytes in SHML & HD

Fig-2]. This is seen in Rosai – Dorfman disease (RDD) also called Sinus Histiocytosis with Massive Lymphadenopathy (SHML) [6].

DIFERENTIAL DIAGNOSIS

The histiocytes seen in SHML must be differentiated from Langerhans Cell Histiocytosis (LCH), Malignant Melanoma (MM) and Hodgkin's disease (HD) [8-10] as shown in [Table/Fig-3-5].

CONCLUSION

Phagocytosis, Emperipolesis, and Entosis are physiological and pathological phenomenon which is characterized by the engulfment of one cell into another cell i.e. cell – in – cell phenomenon. The exact mechanism for emperipolesis is unknown; it has only been hypothesized that the natural killer mediated lysosomal degradation pathway is involved in emperipolesis. Further studies and research at the molecular level due to the scarcity of the cases, along with the use of recent imaging techniques is needed to figure out the molecular ensemble facilitating the intercellular communications and thus, unchain the underlying mechanism and physiology of emperipolesis.

REFERENCES

[1] Humble JG, Jayne WHW, Pulvertaft RJV. Biological interaction between lymphocytes and other cells. *Br J Haematol*. 1956;2:283-94.
[2] Overholtzer M, Mailleux AA, Mouneimne G, et al. A nonapoptotic cell death process, entosis that occurs by cell – in – cell invasion. *Cell*. 2007;131:966-79.
[3] Xia P, Wang S, Guo Z, Yao X. Emperipolesis, entosis and beyond: Dance with fate. *Cell Research*. 2008;18:705-07.
[4] Lee KP. Emperipolesis of hematopoietic cells within Megakaryocytes in Bone Marrow of the rat. *Vet Pathol*. 1989;26:473-78.
[5] Sable MN, Sehgal K, Gadage VS, et al. Megakaryocytic emperipolesis: A histological finding in myelodysplastic syndrome. *Indian Journal of Pathology and Microbiology*. 2009;52(4):599-600.
[6] Iyer VK, Handa KK, Sharma MC. Variable extent of Emperipolesis in the evolution of Rosai – Dorfman disease: Diagnostic and pathogenetic implications. *J Cytol*. 2009;26: 111-16.
[7] Osmani Z Saad, Susan H, Hedge P. Emperipolesis in giant cell carcinoma of lung. *Community Oncology*. 2010;17:233-35.
[8] Gnepp D. Diagnostic Surgical Pathology of the Head and Neck 2nd edition. Saunders, *Elsevier Health Sciences*. 2009. p. 739-40.
[9] Fletcher DM Christopher. Diagnostic Histopathology of Tumours 4th edition. Churchill Livingstone. 2013.p.150-51.
[10] Rosai J. Rosai and Ackerman's Surgical Pathology 10th edition. *Mosby, Elsevier*. 2011; 1911- 13.

PARTICULARS OF CONTRIBUTORS:
1. Reader, Department of Oral & Maxillofacial Pathology, Kalka Dental College, Meerut, Uttar Pradesh, India.
2. Senior Lecturer, Department of Oral & Maxillofacial Pathology, Seema Dental College & Hospital, Rishikesh Uttrakhand, India.
3. Reader, Department of Oral Medicine & Radiology, Institute of Dental Sciences, Bhubaneswar, Odisha, India.
4. Senior Lecturer, Department of Oral & Maxillofacial Pathology, Kalka Dental College, Meerut, Uttar Pradesh, India.
5. Senior Lecturer, Department of Oral & Maxillofacial Pathology, Kalka Dental College, Meerut, Uttar Pradesh, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Varun Rastogi,
Reader, Department of Oral & Maxillofacial Pathology, Kalka Dental College, Meerut, Uttar Pradesh, India.
Phone : 07417864865, E-mail : drvarunrastogi@gmail.com

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Jun 17, 2014**
Date of Peer Review: **Aug 08, 2014**
Date of Acceptance: **Aug 16, 2014**
Date of Publishing: **Dec 05, 2014**