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Mini Review

Pediatric Metastasis and cIgE Antibodies -

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ABSTRACT

A common goal in pediatric oncology is a treatment protocol that minimizes risk and maximizes success. The overall survival rate of children with solid tumor metastasis (Stage IV) has shown little improvement in that the extent of the relocation of metastatic cells, and their progression, is not well understood. To better understand the limits of metastasis, an alternative treatment strategy is discussed; based on maladaptive immunity. A skin cream having natural and recombinant allergens, associated with immunologic adjuvants, is vectored into the cancer patient by topical dermal absorption. After that, humoral immunity increases the expression of cross-reactive Immunoglobulin-E (cIgE) primed effector cells, designed to decrease the incidence and prevalence of endogenous proteins that support the metastatic environment. The objective of this review is to explore an alternative cancer-immunotherapy intended to increase the overall survival rate and quality-of-life for children and adolescents struggling with solid tumor metastasis.

INTRODUCTION

Cancer is a tragic cause of death in children worldwide, and the recorded incidence tends to increase with time [1]. Treating metastatic cancer, primarily when it has spread to several different locations in the body, is an enormous challenge. Metastatic tumors are often unresponsive to existing therapies, and achieving long-term remission is far less likely than it is with localized cancer [2]. In the United States, approximately 1,800 children and adolescents die of cancer each year. Sarcomas that present with metastatic disease have much lower 5-year survival rates. [3].

Children and adolescents treated for solid-tumor metastasis need continuous medical surveillance throughout their lives because of the risk of complications related to treatments (eg. radiation therapy, chemotherapy). Health problems that develop after cancer treatments are known as late effects. A long-term follow-up analysis of a cohort of survivors of childhood cancer treated between 1970 and 1986 has shown that cancer survivors remain at risk of complications and premature death as they age, with more than half of the survivors experiencing a severe or disabling complication, or even death, by the time they reach 50 years old [4].

In children, immunotherapy is not a first-line treatment. If a child's cancer resists initial treatments, the care team decides if the type of cancer may respond to immunotherapy. It has been written that the ultimate contribution of immunotherapies to the outcome of pediatric cancer patients is uncertain. Although, the landscape of immunotherapy is likely to be quite different from traditional surgery, radiation, and chemotherapy. A variety of immunotherapies hold significant promise for children with cancer, both in terms of improving survival outcomes and reducing late effects. As we learn more about cancer cells, the immune system, and the tumor microenvironment, we are likely to devise novel ways in which to decrease immunosuppressive factors, interrupt pathways used for immune evasion, and identify useful biomarkers for treatment stratification and monitoring. Researchers are optimistic that the incorporation of immunotherapies into treatment regimens may increase survival and quality of life for children with cancer [5].

DISCUSSION

There are many different types of solid tumors in childhood cancer that can metastasize. The incidence pattern of solid tumors in children follows an age-specific pattern. In early childhood, embryonal type solid tumors are common, such as retinoblastoma, neuroblastoma, hepatoblastoma, Wilms tumor, and medulloblastoma. In adolescents, solid tumors often arise from bone and soft tissues (osteosarcoma, Ewing sarcoma), germ cells (germ cell tumor) and epithelial cells (thyroid carcinoma) [6].

The mechanism of why some solid tumors metastasize is not well understood. However, the metastatic cascade may be dependent on the loss of adhesion between cells, which results in the dissociation of the cell from the primary tumor, and subsequently, the ability of the cell to attain a motile phenotype via changes in the cell to matrix interaction [7].

Pediatric oncology treatment-protocols for metastatic cancer strive to be more beneficial and less toxic. Active immunotherapy using hyper-allergenic skin creams may inhibit solid-tumor metastasizing wherein immediate-type hypersensitivity decreases the incidence and prevalence of endogenous proteins that support a metastatic environment.

Immediate-type hypersensitivity is a maladaptive immune response towards allergens that occurs within minutes of exposure. Repeated exposure to allergens induces the human body to form B-cells, IgE antibodies, and IgE- primed effector cells, which bind to the allergen to begin the process of elimination and removal. Suppression of metastatic cancer is suspected with IgE antibodies in that they are exceptionally biologically active despite being present in relatively low concentrations in the bloodstream, i.e., approximately one-thousandth of a percent. B-cells produce IgE antibodies that bind to high-affinity receptors on the surface of effector cells (eg. mast cells, basophils, and eosinophils) to provide IgE-primed effector cells. A review article describes cancer immunotherapy wherein allergens that have structural homology to endogenous proteins, based on conformational and linear epitopes, can be used to form cross-reactive Immunoglobulin-E (cIgE) antibodies. An allergy blood test or skin prick test, using native antigens, can be used to determine the expression of cIgE antibodies. The resulting cIgE-primed effector cells may bind to homologous endogenous-proteins that support a metastatic environment [8].

Older children with neuroblastoma presenting metastasis have a poor prognosis in all cancer treatment programs. Neuroblastoma may metastasize to other parts of the body, such as the lymph nodes, bone marrow, liver, skin, and bones. Close to seventy percent (70%) of children diagnosed with neuroblastoma experience metastatic disease [9].

An investigative hyper-allergenic skin cream designed to inhibit Stage-IV neuroblastoma may propose the following allergens:

A natural cysteine-protease allergen (30 kDa.) from Kiwi (Food of Plant Origin) or a recombinant cysteine-protease allergen (27 kDa) from Dermatophagoides (Mites) may induce the humoral immune system to produce cIgE antibodies that inhibit the expression of human cysteine protease cathepsin-B (31 kDa.) and human cysteine protease cathepsin-L (32 kDa.). The inhibition of cathepsin-B and cathepsin-L blocks the growth and invasive properties of many different tumor cells, including neuroblastoma [10,11].

A recombinant enolase allergen (45 kDa.) from Alternaria (Mold) may induce the humoral immune system to produce cIgE antibodies that inhibit the expression of human alpha-enolase ENO1 (48 kDa.). EN01 is a glycolytic enzyme expressed in most tissues. The overexpression of ENO1 is associated with neuroblastoma [12].

A recombinant phospholipase-A2 allergen (16 kDa.) from Honeybee (Venom) may induce the humoral immune system to produce cIgE antibodies that inhibit the expression of human phospholipase A2 (~14 kDa.) isoforms. Phospholipase A2 (PLA2) belongs to a family of enzymes that catalyze the cleavage of fatty acids from the *sn*-2 position of phospholipids. Most neuroblastoma tumor cells contain elevated levels of PLA2, and increased production of eicosanoids affects cellular growth [13].

A recombinant aspartic-protease allergen (36 kDa.) from cockroach may induce the humoral immune system to produce cIgE antibodies that inhibit the expression of human aspartic protease cathepsin-D (48 kDa.). Cathepsin-D is an aspartic endo-protease that degrades proteins and activates precursors of bioactive proteins in pre-lysosomal compartments. The inhibition of cathepsin-D increases the sensitivity of SK-N-BE2 neuroblastoma cells to doxorubicin (chemotherapy) and attenuates their migratory properties [14].

A recombinant glutathione-s-transferase allergen (23 kDa.) from cockroach may induce the humoral immune system to produce cIgE antibodies that inhibit the expression of human GSTP1-1 (27.4 kDa.). Glutathione S-Transferases (GSTs) belongs to a family of metabolic isozymes. Cytosolic GSTP1-1, an isozyme of the mammalian GST family, is expressed primarily in the heart, lung, and brain tissues. The overexpression of GSTP1-1 plays a role in the development of cancer and its potential resistance to drug treatment [15,16].

A recombinant rubber elongation factor allergen (14.6 kDa.) from Hevea Brasiliensis may induce the humoral immune system to produce cIgE antibodies that inhibit the expression of human GTPases that are members of the Rho family [17]. The Rho family of GTPases is a group of small (~21 kDa) signaling G proteins and is a subfamily of the Ras superfamily. The overexpression of proteins from the Rho family of GTPases has a role in multiple types of cancer [18].

CONCLUSION

Skin creams that support humoral immunity, and the production of cross-react IgE (cIgE) antibodies, may provide cancer immunotherapy for children and adolescents that inhibit solid tumor metastasis while limiting toxicity to healthy cells and tissues.

AUTHOR DISCLOSURE

Michael J. Dochniak is cofounder of Alleam, LLC, Minnesota, USA. This commentary contains a discussion of an unapproved/ investigative hyper-allergenic skin cream designed to inhibit metastatic cancer.

REFERENCES

1. Steliarova Foucher E, Colombet M, Ries LAG, Moreno F, Dolya A, Bray F, et al. International incidence of childhood cancer, 2001-10: A population-based registry study. Lancet Oncol. 2017; 18: 719-731. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/28410997
2. National Cancer Institute. Overcoming the challenges of metastatic cancer: An interview with Dr. Rosandra Kaplan. http://bit.ly/2GJeDUe
3. National Cancer Institute. Cancer in children and adolescents. http://bit.ly/2OhEvuB
4. Armstrong GT, Kawashima T, Leisenring W, Stratton K, Stovall M, Hudson MM, et al. Aging and risk of severe, disabling, life-threatening, and fatal events in the Childhood Cancer Survivor Study. J Clin Oncol. 2014; 32: 1218-1227. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/24638000
5. Wedekind MF, Denton NL, Chen CY, Cripe TP. Pediatric cancer immunotherapy: Opportunities and challenges. Paediatr Drugs. 2018; 20: 395-408. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/29948928
6. Lee JA. Solid tumors in children and adolescents. J Korean Med Sci. 2018; 33: e269. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/30288160/
7. Tracey A Martin, Lin Ye, Andrew J Sanders, Jane Lane, Wen G Jiang. Cancer invasion and metastasis: Molecular and cellular perspective. In: Madame curie bioscience database [internet]. Austin (TX): Landes Bioscience. 2000-2013. **PubMed:** https://www.ncbi.nlm.nih.gov/books/NBK164700/
8. Dochniak MJ. Maladaptive immunity and metastasizing cancer. Cancer Med J. 2020; 3: 31-34. https://bit.ly/2GJnV2I
9. Cincinnati Children's Hospital Medical Center. Neuroblastoma in infants & children. https://bit.ly/3b32hEg
10. Olson OC, Joyce JA. Cysteine cathepsin proteases: Regulators of cancer progression and therapeutic response. Nat Rev Cancer. 2015; 15: 712-729. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/26597527
11. Colella R, Lu G, Glazewski L, Korant B, Matlapudi A, England MR, et al. Induction of cell death in neuroblastoma by inhibition of cathepsins B and L. Cancer Lett. 2010; 294: 195-203. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/20362389
12. Hsiao KC, Shih NY, Fang HL, Huang TS, Kuo CC, Chu PY, et al. Surface α-enolase promotes extracellular matrix degradation and tumor metastasis and represents a new therapeutic target. PLoS One. 2013; 8: e69354. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/23894455
13. Sun GY, Xu J, Jensen MD, Simonyi A. Phospholipase A2 in the central nervous system implications for neurodegenerative diseases. J Lipid Res. 2004; 45: 205-213. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/14657205
14. Gangoda L, Keerthikumar S, Fonseka P, Edgington LE, Ang CS, Ozcitti C, et al. Inhibition of cathepsin proteases attenuates migration and sensitizes aggressive N-Myc amplified human neuroblastoma cells to doxorubicin. Oncotarget. 2015; 6: 11175-11190. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/25883214
15. Laborde E. Glutathione transferases as mediators of signaling pathways involved in cell proliferation and cell death. Cell Death and Differentiation. 2010; 17: 1373-1380. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/20596078
16. Townsend DM, Tew KD. The role of glutathione-S-transferase in anti-cancer drug resistance. Oncogene. 2003; 22: 7369-7375. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/14576844
17. Michael J Dochniak. Rubber elongation factor and natural allergy-Oncology. BAOJ Cancer Res Ther. 2016; 2: 027. https://bit.ly/2UeSXqZ
18. Fritz G, Just I, Kaina B. Rho GTPases are over-expressed in human tumors. Int J Cancer. 1999; 81: 682-687. **PubMed:** https://www.ncbi.nlm.nih.gov/pubmed/10328216