



Decreased natural killer cells in diffuse intrinsic pontine glioma patients

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Received: 3 November 2019 / Accepted: 6 May 2020
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Abstract

Purpose Diffuse intrinsic pontine glioma (DIPG) remains the leading cause of death among pediatric brain tumor patients. Its pontine location and aggressive nature make developing effective treatment an ongoing challenge in pediatric oncology. Although studies have found that one of the hallmark features of glioma is immunosuppression, the immune status of DIPG patient is not clearly understood.

Methods We tested the lymphocyte profile in four radiologically diagnosed DIPG patients. All the four patients did not receive any steroids, radiotherapy, and chemotherapy before the collection of blood.

Results We found decreased natural killer (NK) cell level and increased B cell level in all four cases.

Conclusion These findings suggested that decreased NK cells and increased B cells may aid the tumorigenesis and growth seen in DIPG patient. Increased NK and decreased B cells may be the future direction for the treatment of DIPG patient.

Keywords Natural killer cell · NK · Diffuse intrinsic pontine glioma · DIPG

As one of the most lethal pediatric central nervous system (CNS) cancers, diffuse intrinsic pontine glioma (DIPG) remains the leading cause of death among pediatric brain tumor patients. Its pontine location and aggressive nature make developing effective treatment an ongoing challenge in pediatric oncology. Although studies have found that one of the hallmark features of glioma is immunosuppression, the immune status of DIPG patient is not clearly understood. To elucidate this problem, the lymphocyte profile had been routinely tested in peripheral venous blood of four radiologically diagnosed DIPG patients (two patients at the time of hospitalization; two patients at outpatient). All the four patients did not receive any steroids, radiotherapy,

and chemotherapy before the collection of blood. The four controls were chosen at the same range of 5 to 6 years old age. The decreased percentage of natural killer (NK) cell level and increased that of B cell level in all four patients comparing with that of the control. Lieberman et al. recently reported that DIPG

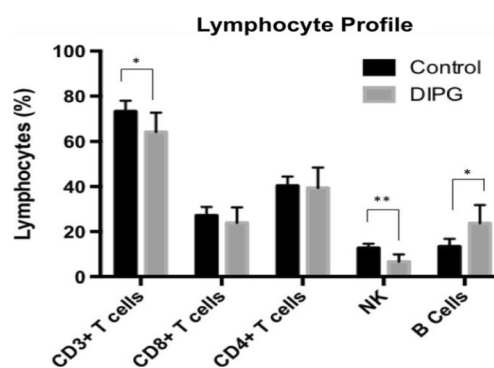


Fig. 1 Lymphocyte profile in DIPG patients. The lymphocyte profile was tested from the peripheral blood of DIPG patients ($n = 4$). The black columns indicated the control and grey ones represented the DIPG patients. There was significant decrease in the percentage of CD3+ T cells in DIPG group compared with that of control ($*p < 0.05$). There was no significant decrease in the percentage of CD8+ and CD4+ T cells. NK cells of DIPG patients were decreased compared with the control ($**p < 0.01$). The B cells of DIPG patients were elevated compared with the control ($*p < 0.05$)

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cells were not effectively targeted by activated allogeneic T cells, yet all DIPG cells could be lysed by NK cells [1]. In agreement with Lieberman's finding, our result suggested that decreased NK cell level may be one of the factors aiding the tumorigenesis and growth seen in DIPG patient. In Fig. 1, we found that in the DIPG group, there was significant decrease in the percentage of CD3+ ($p < 0.05$) compared with that of control. There was no significant decrease in the percentage of CD8+ and CD4+ T cells. However, the percentage of NK cell (CD56+ CD16+) were significantly reduced compared with that of the controls ($p < 0.001$). We also observed an increased CD19+ B cell percentage in the DIPG group compared with that of the controls ($p < 0.05$). The reason for this increase of B cell level was not clarified this time and it might be due to the increase of regulatory of B cells (Breg). Qin et al. had reported that B cells could inhibit induction of T cell-dependent tumor immunity [2]. So, the role B cells in DIPG patient was warranted for further study.

In summary, our findings suggest that decreased NK cell level in DIPG patients may reflect defective NK cell activity

and aid the tumorigenesis and growth seen in DIPG patient. NK cells may be focused for the treatment of DIPG patients in the future.

Compliance with ethical standards

Conflict of interest No conflict of interest.

References

1. Lieberman NAP, DeGolier K, Kovar HM et al (2019) Characterization of the immune microenvironment of diffuse intrinsic pontine glioma: implications for development of immunotherapy. *Neuro Oncol.* 21(1):83–94
2. Qin Z, Richter G, Schüler T, Ibe S, Cao X, Blankenstein T (1998) B cells inhibit induction of T cell-dependent tumor immunity. *Nat Med* 4(5):627–630

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