

Early Recognition and Treatment for Skin invasion by Glioblastoma Multiforme

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Glioblastoma multiforme (GBM) is the most common primary brain tumor and the most malignant of the astrocytomas, representing around 12-15% of all intracranial tumor and 50-75% astrocytomas. GBM is classified as the WHO grade IV astrocytoma and malignant astrocytoma. It has a poor differentiation and aggressive. Local spread is usually through the white matter. The mean survival time of affected patients is usually less than 2 years [1]. GBMs have numerous patterns of spread, including white matter metastases, CSF dissemination, ependymal and subependymal spread, skull-dura invasion and extra-CNS metastases. The most common route of GBM spreading is throughout the white matter, the “brain to brain” invasion. Extra-cranial lesion was less than 2% of cases and the common locations are lung and pleura, regional lymph node, spine, bone marrow and liver [2, 3]. For skin invasion is extremely rare, there are only 12 cases had been reports since 2002 in the literature review.

Importance for early recognition

From initial recognition of skin metastases by the GBMs, the estimated mean survival time is only 4.4 months. The patients didn't pass away from the skin metastases, but from the progression of intracranial lesion. The skin metastases often indicate rapid progression of the original lesion. If the patient presented with early signs of skin change, especially near the previous surgical area, we should be aware of the progression of primary brain lesion, even there are no clinical signs of neurological deterioration. The signs of skin metastases include well-defined erythematous infiltrated plaque, elastic to hard nodules or granulation, or chronic unhealed or erosive wound around the previous surgical site. We could have a skin biopsy for early pathological proof once the skin change was noted and follow up with brain image examination. s

The high correlation between skin metastases and previous surgical procedure

The cells type of GBMs is quite unique that most of the cells are hard to survive out of the brain tissues. Most of the spreads are the “brain to brain” invasion. Extra-cranial spreading is rare, no more than 0.4~2% [3, 4], even less for skin metastases. Surprisingly, up to 80% of these extra-cranial cases had been received the surgical procedure, such as craniotomy and ventriculo-peritoneal shunt [5-7].

As for the skin metastases, every patient had previous surgical intervention in our review. Because high proportions of extra-cranial skin spread have happened after the surgical procedures, there should be some relationship between the surgery and the change of brain microenvironments, which may account for such consequence. We proposed some hypotheses which may explain the skin metastases.

1. Local tumor seeding. We found that most of the skin metastases are near the previous surgical area. The skin at the surgical site should have more chances to be directly contacted and grafted by GBMs during the surgical procedures.
2. Break of the blood-brain barrier system. This thick basement membrane has no longer to offer intact physical barriers, the cells of GBM may escape from the intra-cranial to extra-cranial area through the lymphatic and vessel systems.

Because the direct contact and grafting of the tumor cell in the regional skin could be possible, the skin invasion of the GBMs should be no less than other distant spread location theoretically. In fact, these kinds of cases are extremely rare. We proposed another two hypotheses that could explain such situation. One is that the patients with GBMs, who will take the courses of whole brain radiotherapy after the brain surgery, and the radiotherapy may eliminate the tumor cell in the skin tissue. The other is that the microenvironments of the skin are extremely crucial for GBMs harvesting [8]. Glia cells are unique and require intracranial environments to survive.

Avoid the skin metastases

Since most of the extra-cranial metastases have relation with the previous surgical procedure, implantations of tumor cells by direct contact at the time of surgery have been reported in some cases [9-11]. We could lower the incidence of these kinds of metastases by some surgical technique, including the watertight approximation of the dura, replacement of the bone flap, and changing of surgical instruments once the intradural component of the surgery is completed. All of these procedures mentioned above may lower the rate of skin metastases [10].

Early recognition and treatment

Once the skin metastases happened, we noted the growth of such tumor is rapid that it could become unresectable just in a few weeks. Such patients could only undergo the partial resection or biopsy because of



delayed recognition and surgical resection, this unresectable scalp lesions often suffered the patients' appearance and end life of qualities. Most of the patients with skin metastases also accompanied with worsening of intracranial GBMs, we shall also plan the treatment for the GBMs at the same time. Early recognition for the skin lesion, early pathological proof, and followed by surgical management for both skin lesion and GBMs, radiotherapy, temozolomide, and chemotherapy are recommended and might be beneficial for the patients.

Conclusion :

Although glioblastoma multiforme accounts most in all of the primary malignant brain tumors, the extra-neural spread is not common, less than 2 %. For skin invasion is extremely rare. Once the regional skin invasion happened, it spreads rapidly and often indicates deterioration of primary brain lesion and short survival time. Early recognition of skin tumor, especially near the previous surgical site, is vitally important for patients with GBMs who had undergone the previous surgical intervention. Early surgical resection of intra-neural and extra-neural tumors, followed by chemotherapy and radiotherapy might be beneficial for the patients.

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