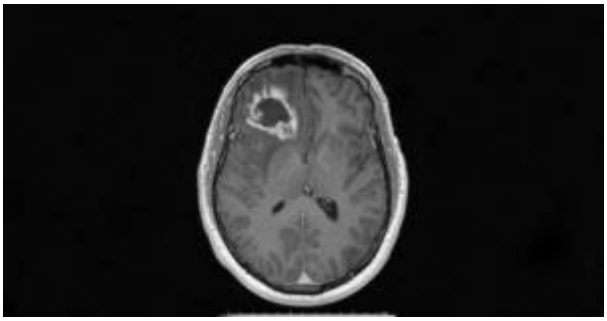
Glioblastoma in young adults



Young age is a favorable prognostic factor for patients with glioblastoma multiforme (GBM).

GBMs in young adults are a more inhomogeneous tumor group than GBMs occurring in old age patients and show features that overlap with both pediatric and adult GBMs [1].

High mitochondrial DNA copy number is associated with longer survival in young patients with glioblastoma [2].

Young GB patients (< 40 years old) may carry IDH1 mutation/IDH2 mutations or in rare instances, harbor H3F3A or HIST1H3B mutations. Other cases are wild-type for those genes and harbor gain of chromosome (chr) 7, loss of chromosome 10, and EGFR amplification (amp). IDH1/2 mutations are associated with longer survival (24 months) whereas histone H3F3A/HIST1H3B gene mutations are associated with shorter survival (9-12 months) [3]

Glioblastoma IDH Mutant (IDH1) were associated with a younger age at diagnosis, better clinical outcome, prominent oligodendroglial and small cell tumour cell morphology, pallisading necrosis and glomeruloid vascular proliferation in the absence of arcade-like structures. These features widen the phenotype of IDH1 mutation-positive primary glioblastoma in young adults and provide correlative evidence for a functional role of mutant IDH1 in the differential nature of neoangiogenesis in different subtypes of glioblastoma [4].

Leibetseder et al., reviewed the outcomes and molecular tumor characteristics of adolescent and young adult patients with GBM treated in 2 Austrian centers.

Data on patients with histologically proven primary GBM diagnosed from 18 through 40 years of age were retrospectively analyzed. All patients were treated with standard first-line therapy. The primary end points were overall survival (OS) and time to progression (TTP). IDH1-R132H mutation status was analyzed using immunohistochemistry, and MGMT promoter methylation was assessed using methylation-specific polymerase chain reaction.

They included 70 patients (36 men and 34 women) with a median age of 33 years. IDH1-R132H mutations were detected in 22 (39.3%) of 56 cases and MGMT promoter methylation in 33 (61.1%) of 54 cases with available tissue samples. In patients with wild-type IDH, median TTP was 8.2 months and median OS was 24 months, compared with 18 months and 44 months, respectively, observed in patients with mutated IDH. Neither IDH1 nor MGMT status showed a statistically significant association with TTP or OS. Of note, the social and economical situation of the young patients with GBM was alarming, because only 17% succeeded in staying employed after receiving the diagnosis.

They found a high frequency of IDH1 mutations and MGMT promoter methylation among young adult patients with primary GBM that may contribute to the generally favorable outcome associated with young age. The social and economic coverage of patients with glioma remains an unsolved socio-ethical problem [5].

In the study of Kleinschmidt-DeMasters et al., twenty-eight (74%) of 38 young-adult GBM patients had primary de novo tumors, two of which occurred in patients with cancer syndromes. Two additional GBMs were radiation-induced and eight (21%) were secondary GBMs. Seven patients were identified as long-term (>3 years) survivors. Six of 38 cases manifested unusual morphological features, including three epithelioid GBMs, one rhabdoid GBM, one gliosarcoma and one small cell GBM containing abundant, refractile, eosinophilic inclusions. MIB-1 index emerged as the most important prognosticator of survival ($P < 0.005$). Although there was a trend between extent of necrosis, TP53 immunohistochemical expression, and EGFR amplification status and survival, none reached statistical significance [6].

References

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