



Pediatric Intracranial Germinoma: Use Chemotherapy First

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To the Editor;

We read with interest the recent report of five cases of intracranial germinoma by Abdallah et al.(1) in which 80% survival was observed with one case of surgery-related mortality. Unlike most central nervous system tumors where surgical resection plays a pertinent role in treatment with curative intent, germinoma requires a different approach as it is exquisitely chemo-sensitive. Our experience of 100% event-free survival in 10 children with a chemotherapy-based management approach may discourage heroic surgical interventions in this unusual subgroup of central nervous system malignancies.

From 1998 to 2016, seven boys and three girls were treated consecutively at our center for primary intracranial germinoma. Their mean age was 14.0 (range 9.1–18.9) years. The tumor was suprasellar (n=5), pineal (n=4), or both (n=1) in location. None had signs of neuraxis dissemination. Except for three cases of pineal primary, all children were affected by panhypopituitarism and central diabetes insipidus. Two children with pineal germinoma had significant hydrocephalus and required emergency placement of a ventriculoperitoneal shunt.

Two children received upfront surgery with resection of the primary tumor from which the histopathology of germinoma was confirmed. Five children underwent stereotactic biopsy as the basis for diagnosis. In another two children, the diagnosis was based on mild elevation of human chorionic gonadotropin (HCG) in the serum or cerebrospinal fluid. In the remaining child, the diagnosis was based on radiation sensitivity. The latter child sustained an acute subdural hematoma following the initial shunt placement that precluded further surgery.

All children received four 3-week cycles of chemotherapy consisting of carboplatin 560 mg/m² on day 1 and etoposide

120 mg/m² on days 1 to 3. Treatment was delivered on an outpatient basis without the need of vigorous hydration. The preferred radiotherapy consisted of periventricular irradiation with an involved field boost. No spinal radiation was used. Conventional cranial irradiation was used instead of periventricular irradiation if the patient preferred a cheaper alternative. In eight children, two cycles of chemotherapy was used upfront followed by the radiotherapy and the remaining two cycles of chemotherapy were given four weeks after completion of irradiation. In the remaining two children, radiotherapy was used upfront followed by the four cycles of chemotherapy. An interim assessment by imaging was done after the second cycle of chemotherapy, prior to the radiotherapy if it had not been given, in all cases.

At the interim assessment, five children had complete remission and the other five children had minimal residual on magnetic resonance imaging. The five cases of complete remission all occurred in children who had received chemotherapy upfront, including the two children who had surgical resection. In the five cases of minimal residual lesions, the solid component of the original tumor had disappeared and repeat imaging on subsequent follow-up did not show much change afterwards (Figure 1A-C). These findings indicate that the maximal radiologic response from treatment is evident after the second cycle of chemotherapy in all cases.

Of note, the chemotherapy was well tolerated. No exacerbation of fluid and electrolyte disturbance occurred in any of the patients with diabetes insipidus and hence no alteration in the dosing of desmopressin was required. All patients were given oral ciprofloxacin and two doses of filgrastim during the neutropenic phase. Re-admission for treatment of febrile neutropenia was required in one (2.5%) of the 40 cycles of chemotherapy. The complication was related to delayed occurrence of hypothyroidism as reported previously (2).



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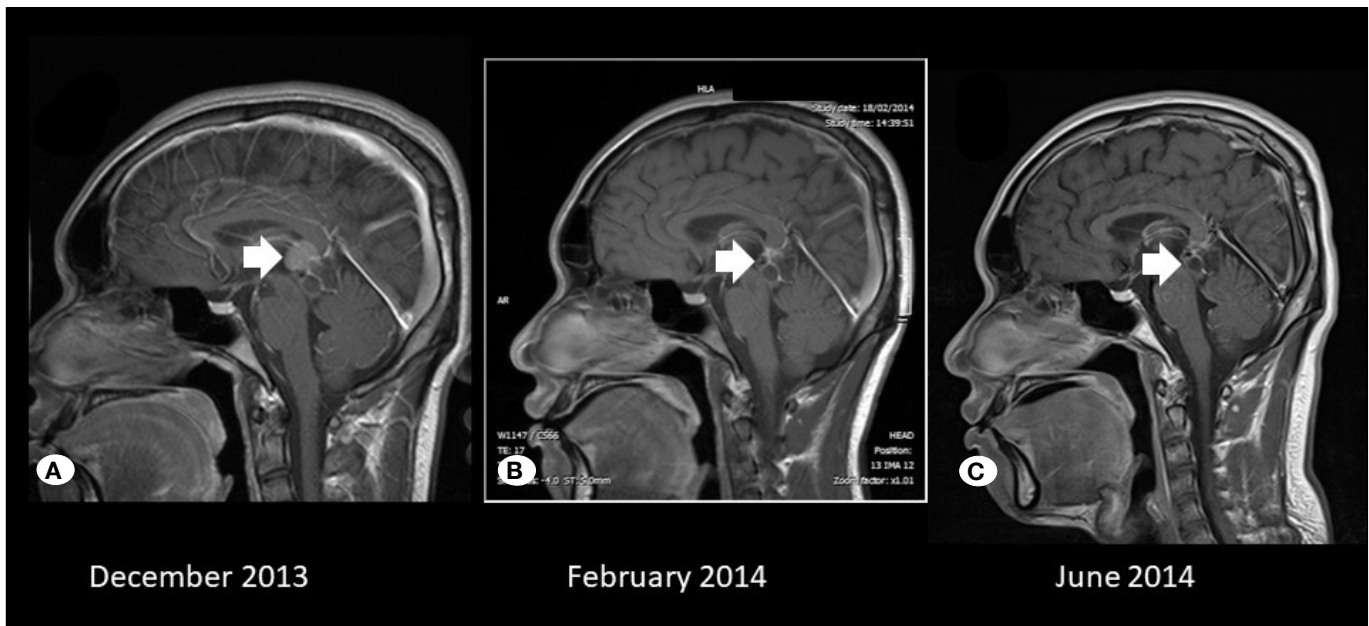


Figure 1: Serial magnetic resonance imaging in an 18-year-old boy with pineal germinoma at initial diagnosis (A), following 2 cycles of chemotherapy before radiotherapy (B), and at 6 months following initial diagnosis (C). Note the initial solid component of the tumor has completely resolved after chemotherapy while a minimal residual cystic lesion remains stable 3 years after completion of treatment (not shown).

At a median of 6.6 (range 0.8–9.3) years of follow-up, all patients remain well with no signs of recurrence. Thus, our experience of a chemotherapy-based approach in the management of pediatric intracranial germinoma is highly successful. Heroic surgery should be avoided. An initial diagnosis based on biopsy or tumor markers followed by combination chemotherapy with sandwiched radiotherapy is recommended.

REFERENCES

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