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Clinical Study

Immunohistochemical expression of OCT4 in primary central nervous system germ cell tumours

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Abstract

OCT4 is a POU-domain transcription factor that is expressed in embryonic stem cells and germ cells. OCT4 has been detected in specific types of testicular germ cell tumour (GCT), including seminoma and embryonal carcinoma. The aim of this study was to evaluate the role of OCT4 expression in the diagnosis of primary central nervous system (CNS) pure and mixed GCT. Seventeen formalin-fixed, paraffin-embedded tissues of primary CNS GCT were immunohistochemically studied. The 12 pure GCT samples comprised germinoma (5), yolk sac tumour (3), mature teratoma (2), and immature teratoma (2). The five cases of mixed GCT contained various components as follows: yolk sac tumour (4), embryonal carcinoma (3), mature teratoma (1), germinoma (2), polyembryoma (1) and immature teratoma (1). Diffuse and strong nuclear staining indicating OCT4 expression was detected in all cases of pure germinoma (5), and in all cases of mixed GCT containing embryonal carcinoma (3) and/or germinoma (2). There was no corresponding staining in pure GCT of yolk sac tumour, mature teratoma, or immature teratoma except in a primitive neuroectodermal component, or in mixed GCT containing components of yolk sac tumour, mature teratoma or immature teratoma. In conclusion, we found that OCT4 immunostaining is a useful diagnostic tool to assist in the identification of primary CNS embryonal carcinoma and germinoma. In CNS mixed GCT, OCT4 expression can be detected provided that the components include embryonal carcinoma and/or germinoma.

Keywords: OCT4; Central nervous system; Germinoma; Embryonal carcinoma; Mixed germ cell tumours

1. Introduction

OCT3/4, also known as *otf3* and *pou5fl*, is a POU-domain transcription factor. The *Oct3* gene is expressed in totipotent and pluripotent stem cells of the murine and human embryo and primordial germ cells (PGC) and in maturing and ovulated oocytes, but not in the resting oocytes.[1–7] It is believed that the *oct3* gene is an octamer-binding transcription factor that is related to the regulation of early embryogenesis and is required for primordial germ cell survival.[8] It is downregulated during differentiation and is no longer expressed in day 8–16 embryos or in any adult organs.[1–7]

In recent studies OCT4 expression has been detected in testicular germ cell tumour, particularly seminoma and embryonal carcinoma,[9,10] intratubular germ cell neoplasia,[11] ovarian dysgerminoma, gonadoblastoma and clear cell carcinoma,[12] central nervous system (CNS) germ cell tumour (GCT),[10,13] and metastatic testicular GCT in lymph nodes.[14]

The aim of the present study was to assess the diagnostic role of OCT4 expression in identification of primary CNS germinoma and embryonal carcinoma, and to establish whether expression of OCT4 in mixed GCT with the above components is similar to the pure form.

2. Materials and methods

In total, 17 primary CNS tumour samples were selected for OCT4 staining. Of these, the pure GCT samples (12)

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comprised germinoma (5), yolk sac tumour (3), mature teratoma (2), and immature teratoma (2). The five cases of mixed GCT comprised various components of yolk sac tumour (4), embryonal carcinoma (3), mature teratoma (1), germinoma (2), polyembryoma (1) and immature teratoma (1).

All slides, including hematoxylin and eosin-stained slides and immunohistochemically stained slides were reviewed. Immunohistochemical staining for placental alkaline phosphatase (PLAP)(polyclonal; Dako, Carpinteria, CA, USA; 1:50) and α-fetoprotein (AFP) (polyclonal; Dako, 1:50) was performed using formalin-fixed paraffin-embedded tissue using the avidin-biotin peroxidase method with the Ventana autostaining system (Ventana Medical Systems Inc., Tucson, AZ, USA). Additional paraffin sections of the selected block were used for immunostaining of OCT4. The antibody used was anti-OCT4 antibody (C20, sc8629; Santa Cruz Biotechnology, Santa Cruz, CA, USA; 1:250 dilution, 60 min at room temperature). The positive control tissue was testicular seminoma and the negative control was normal brain tissue. Since OCT4 is a nuclear transcription factor, only cells with strong nuclear staining were considered to be positive.

3. Results

3.1. Clinical findings

Clinical information on the 17 patients is outlined in Table 1. The patients' ages ranged from 2 months to 41 years and 2 months (mean 14.99 years). The male to female ratio was 15:2. With respect to location, these 17 primary CNS GCT tumours were pineal (9), cerebellar (3), intracerebral (2), ventricular (2), and suprasellar (1). The duration of follow-up ranged from 0 to 62 months (mean 19.45 months). All 17 patients underwent surgical resection of the tumour. Ten patients had additional chemotherapy and seven had additional radiotherapy.

Of the 17 patients, six died of the disease or complications. The causes of death included diffuse tumour seeding or metastasis, tumour recurrence, tumour compression causing brainstem haemorrhage, pneumonia and meningoencephalitis. The mortality rate of mixed GCT was 60% (three out of five patients) as compared with 25% for the pure CNS GCT (three out of 12 patients).

3.2. Immunohistochemical findings

Diffuse and strong nuclear staining of OCT4 was noted in all samples of pure germinoma (5) (Fig. 1), and in all samples of mixed GCT containing components of embryonal carcinoma (3) (Fig. 2) and/or germinoma (2) (Table 2). Focal expression of OCT4 was found in the primitive neuroectodermal component of a pure immature teratoma (Fig. 3).

There was no staining in pure forms of yolk sac tumour, mature teratoma or one case of immature teratoma, or in those cases of mixed GCT with components other than germinoma and embryonal carcinoma.

4. Discussion

CNS GCT is a disease of childhood and adolescence with an incidence of 0.3–2%, as reported in various studies.[15–19] It predominantly occurs in the midline, particularly the pineal gland and suprasellar region. Other tumour locations include the basal ganglia, thalamus, bulbar region, cerebral hemisphere, intramedullary region and intrasellar region.[15–19]

In the present study, both germinoma and embryonal carcinoma had strong and diffuse nuclear staining for OCT4. Our findings suggest that expression of OCT4 in

Table 1
Clinical information and outcomes for 17 patients with central nervous system germ cell tumours

Case	Age	Sex	Tumour location	Follow-up (months)	Management	Outcome
1	13y 8m	M	Pineal	12	Surgery, C/T, R/T	A
2	21y 0m	M	Pineal	11	Surgery, R/T	A
3	18y 11m	M	Pineal	16	Surgery, R/T	A
4	12y	M	Pineal	26	Surgery, C/T, R/T	A
5	9y 2m	M	Pineal	36	Surgery, C/T	A
6	41y 2m	F	Left lateral ventricle	15	Surgery, C/T	D, infection
7	12y 9m	M	Bifrontal	12	Surgery, C/T	D, liver metastasis
8	9y 6m	F	Suprasella	31	Surgery, C/T, R/T	D, infection
9	1y 3m	M	Cerebellum	21	Surgery,C/T	A
10	17y	M	Intraventricular	3	Surgery, C/T, R/T	D, tumour seeding
11	18y 9m	M	Pineal	62	Surgery, C/T, R/T	A
12	4y 11m	M	Pineal	6	Surgery	A
13	2m	M	Cerebellum	0	Surgery	Lost to follow-up
14	39y 4m	M	Left temporal	50	Surgery	A
15	16y 0m	M	Pineal	2	Surgery	D, tumour bleeding
16	13y 10m	M	Cerebellum	23	Surgery, C/T	D, tumour recurrence
17	18y 3m	M	Pineal	0	Surgery	Lost to follow-up

y, years; m, months; C/T, chemotherapy; R/T, radiotherapy; A, alive; D, dead.