

# Testicular cancer in three brothers

V. Raina, P.T. Young and M. Soukop

Department of Medical Oncology, Royal Infirmary, Glasgow G4 0SF, UK.

**Summary:** Three of four brothers in a family were diagnosed to have testicular tumour. All brothers were in their twenties at diagnosis and all had malignant teratoma, intermediate. One of the brothers, in addition, had a seminoma on the same side as the teratoma. The cases were unusual as there was no family history of cancer and no congenital abnormalities, such as cryptorchidism. Chromosomal analysis and HLA typing did not help in elucidating the cause of this rare familial occurrence of testicular tumour.

## Introduction

Most of the 100 cases of familial primary testicular malignant tumours reported so far relate to either identical twins, a pair of non-identical siblings, cousins or father and son relationship.<sup>1</sup> We report the first case of testicular cancer in three brothers from the UK and probably the third in the world.<sup>2,3</sup>

## Case reports

### Case 1

A 20 year old male presented in 1971 with left testicular swelling. Orchidectomy revealed a malignant teratoma intermediate. The patient was treated with adjuvant radiotherapy to abdomen and is relapse free and alive.

### Case 2

A 27 year old brother of Case 1 presented in 1974 with swelling of the left testis. Orchidectomy revealed malignant teratoma intermediate. The tumour was Stage III and treatment with abdominal radiotherapy and chemotherapy comprising of vincristine, adriamycin and methotrexate was given. The patient died of progressive disease in 1976.

### Case 3

A 26 year old brother of Cases 1 and 2 presented with swelling of the right testis in 1986. Orchidectomy revealed two tumours, a malignant teratoma intermediate in the lower pole, and a seminoma in the

upper pole of testis.  $\beta$ -Human chorionic gonadotrophic ( $\beta$ HCG) and  $\alpha$ -feto protein (AFP) were elevated. The patient had bulky Stage IV disease at presentation. Chemotherapy with cisplatin, vincristine, bleomycin, ifosfamide and VP16 was given. The patient went into remission and is alive.

There is one more brother who is in his twenties and healthy. There was no history of consanguinity in the parents and no deaths due to cancer in the family or first cousins. There was no evidence of cryptorchidism or any other congenital abnormality in any of the affected brothers. The remainder of the family, i.e., the unaffected brother and children of Cases 1 and 2, have been examined and screened for AFP and  $\beta$ HCG and are being followed up regularly. Chromosome analysis on the two surviving affected brothers and the remainder of the family showed normal karyotype.

The postulated specific marker for seminoma and testicular teratoma i (12p) using the Kirstein-Ras probe could not be looked for due to fixation of tumour at surgery.<sup>4</sup> It was negative in blood leucocytes. Oliver has found significant association of HLA DR5 and DR7 in testicular tumours.<sup>5</sup> Both affected surviving brothers were negative for HLA DR5 and DR7. In addition, HLA typing established these brothers to be non-identical.

## Discussion

Testicular tumours have twice been reported in three brothers.<sup>2,3</sup> There have also been two reports of testicular tumours in four brothers.<sup>6,7</sup> Arguments in favour of genetic aetiology of testicular tumours include occurrence in families, presence of seminoma *in situ* in contralateral testis in 1–2% of patients with

Correspondence: V. Raina, M.D., M.R.C.P.

Accepted: 7 March 1989

testicular tumours and association of such tumours with cryptorchidism, the latter increasing the risk of testicular tumour by 50%<sup>8</sup> In a case controlled study by Tollerud, 6 of 269 (2.2%) reported a first degree relative with testicular cancer compared to 1 of 259 (0.4%) controls.<sup>9</sup> Whether familial clustering involves an inherited susceptibility or a common familial exposure to cultural (including dietary) factors or other environmental stimuli (including exposure to an infectious agent) remains to be demonstrated. On the other hand, the small number of familial cases documented, the very occasional clustering of cases and lack of concordance in monozygotic twins are not sufficient to enable genetic influences to be regarded as a clearly established aetiological factor.<sup>10</sup> Moreover Gedde-Dahl and colleagues, after extensive investiga-

tions, were unable to support a genetic aetiology in their case of four brothers with testicular tumours.<sup>6</sup> It is, however, important to pay particular attention to family history in all new cases and to document all further cases in the literature, the objective being to define risk factors and to establish an individual cumulative risk calculation for a particular person by a combination of different risk factors, as has been done in breast cancer.<sup>11</sup>

#### Acknowledgement

The authors would like to thank Mrs J. Beckett for secretarial assistance.

#### References

1. Weisbach, L. & Widmann, T. Familial tumour of the testis. *Eur Urol* 1986, **12**: 104–108.
2. Mikulicek, I., Mikulastik, J. & Sobotka, P. Malignant testicular tumours in three brothers. *Int Urol Nephrol* 1976, **8**: 309–312.
3. Di Bella, N.J. Familial gonadal neoplasms. *N Engl J Med* 1983, **309**: 1389.
4. Haddad, F.S., Sorini, P.M., Somsin, A.P. *et al.* Familial double testicular tumours: identical chromosome changes in seminoma and embryonal carcinoma of the same testes. *J Urol* 1988, **139**: 748–750.
5. Oliver, R.T.D. HLA phenotype and clinicopathological behaviour of germ cell tumours: possible evidence for clonal evolution from seminomas to non seminomas. *Int J Androl* 1987, **10**: 85–93.
6. Gedde-Dahl, T., Hannsdal, E., Klepp, O. *et al.* Testicular neoplasms occurring in four brothers. A search for genetic predisposition. *Cancer* 1985, **55**: 2005–2009.
7. Gulley, R.M., Kowolski, R. & Neuhoff, C.F. Familial occurrence of testicular neoplasms. A case report. *J Urol* 1974, **112**: 620–622.
8. Mills, P.K., Newell, G.R. & Johnson, D.E. Familial patterns of testicular cancer. *Urology* 1984, **24**: 1–7.
9. Tollerud, D.J., Blattner, W.A., Fraser, M.C. *et al.* Familial testicular cancer and urogenital developmental anomalies. *Cancer* 1985, **55**: 1849–1854.
10. Diekmann, K.P., Becker, T., Jones, D. & Bauer, H.W. Inheritance and testicular cancer. *Oncology* 1987, **44**: 367–377.
11. Anderson, D.E. & Badzioch, M.D. Risk of familial breast cancer. *Cancer*. 1985, **56**: 383–387.