Table 1. Serological homozygosity and molecular heterozygosity for DR locus in patients with infiltrating ductal carcinoma (IDC)

Patient	Serologic DR	Molecular DR (RFLP)
1	7 , —	1 , 7
2	7 , —	2 , 7
3	5 , —	5 , 6
4	10 , —	1 , 10
5	5 , —	2 , 5
6	6 , —	1 , 6
7	5 , —	4 , 5
8	5 , —	3 , 5

RFLP, restriction fragment length polymorphism.

phism with a specific β probe, with standard Southern blotting hybridisation and detection methods. Surprisingly, using RFLP typing, we obtained an heterozygous DNA profile in all serological homozygote patients tested (Table 1).

In conclusion, our results clearly indicate disequilibrium of HLA information between serology and molecular typing of PBL from IDC patients. Thus, it may be hazardous to conclude that a preferential decrease in the frequencies of some HLA antigens (B7 and DR4), as defined serologically, carry an increased risk of breast cancer. According to tissue studies, however, the possibility remains that certain HLA antigen expressions influence the development of cancer [6]; the reports on immune responses controlled by MHC genes provide support for this interpretation [7–10]. Finally, in our patients, we found an elevated serological homozygosity of the DR locus that is contradicted by RFLP analysis. Since serological HLA phenotype analyses on patient and control groups were performed under the same working conditions and were consequently a reliable comparison, we would suggest that these findings are a result of perturbation of HLA gene expression with loss or aberrant translation of some HLA antigen. Further molecular study may clarify these mechanisms.

1. Concha A, Esteban F, Cabrera T, Ruiz-Cabello F, Garrido F. Tumor aggressiveness and MHC class I and II antigens in laryngeal and breast cancer. *Semin Cancer Biol* 1991, **2**, 47–54.
2. Concha A, Cabrera T, Ruiz-Cabello F, Garrido F. Can the HLA phenotype be used as a prognostic factor in breast carcinomas? *Int J Cancer* 1991, **6**, (Suppl.) 146–154.
3. Song ST. Association of HLA with breast cancer and its ER status. *Chung Hua Chung Liu Tsa Chih* 1989, **11**, 19–21.
4. Yokoe T, Ishida T, Ogawa T, Iino Y, Izuo M. Relationship of breast cancer and HLA in Japanese females. *Gan No Rinsho* 1990, **36**, 29–33.
5. Bidwell J. DNA-RFLP analyses and genotyping of HLA-DR and -DQ antigens. *Immunol Today* 1988, **9**, 18–23.
6. Glew SS, Stern P, Davidson JA, Dyer PA. HLA antigens and cervical carcinoma. *Nature* 1992, **356**, 22.
7. Doyle C, Strominger JL. Interation between CD4 and class II MHC molecules mediates cell adhesion. *Nature* 1987, **330**, 256–259.
8. Dasgupta JD, Cemach K, Dubey DP, Yunis EJ, Amos DB. The role of class I histocompatibility antigens in the regulation of T cell activation. *Proc Natl Acad Sci USA* 1987, **84**, 1094–1098.
9. Norment AM, Salter RD, Parham P, Englehard VH, Littman DR. Cell-cell adhesion mediated by CD8 and MHC class I molecules. *Nature* 1988, **336**, 79–81.
10. Robbins PA, McMichael AJ. Immune recognition of HLA molecules downmodulates CD8 expression on cytotoxic T lymphocytes. *J Exp Med* 1991, **173**, 221–230.

Acknowledgments—This research was supported in part by Grant No. 92.02810.CT04 from the Italian Consiglio Nazionale delle Ricerche.

European Journal of Cancer Vol. 30A, No. 8, pp. 1208–1209, 1994.

0959-8049/94 $7.00 + 0.00

False Negative Testicular Biopsy in an Extragonadal Germ Cell Tumour

P. Albers, R. Moll and G.E. Voges

IN 60% OF patients with extragonadal germ cell tumours, testicular biopsy reveals a testicular intraepithelial neoplasia (TIN) [1]. We report a case of a patient with the primary diagnosis of extragonadal seminoma in whom an initial testicular biopsy was unremarkable. Fourteen weeks later a solid tumour in the left testicle was detected which proved to be a "burnt-out" seminoma.

A 37-year-old male patient was admitted to an outside hospital with persistent back pain. Physical examination demonstrated a palpable mass in his left upper quadrant. Ultrasound and computerised tomography (CT) of the abdomen showed a retroperitoneal tumour (6 × 3.2 × 2 inches). Fine needle aspiration was performed and suggested a Hodgkin's lymphoma. For definitive diagnosis, a staging laparotomy and partial resection of the tumour were carried out. Histology revealed a pure seminoma. The patient was referred to the Department of Urology, Mainz University Medical School for further treatment.

Sonographic examination of both testicles was unremarkable. Lactate dehydrogenase (LDH) was increased to 1344 U/l (normal value up to 215 U/l), α-fetoprotein (AFP) and β-human chorion gonadotropin (βHCG) values were normal. CT of the abdomen showed a residual tumour mass (3.2 × 3.2 × 1.6 inches). The patient was treated with three courses of BEP (bleomycin, etoposide, cisplatin) chemotherapy. Staging after chemotherapy demonstrated tumour markers in the normal range and a volume reduction of the retroperitoneal mass of 75%. Radical retroperitoneal lymph node dissection (RPLND) at that time showed complete necrosis without histological evidence of viable tumour cells. In addition, a single biopsy of each testicle demonstrated completely atrophic seminiferous tubules without any malignant cells or testicular intraepithelial neoplasia.

Fourteen weeks after RPLND, a palpable testicular tumour on the left side was detected. Ultrasound showed a hypoechoic inhomogeneous intraparenchymal mass occupying 70% of the testis. Tumour markers were normal. Magnetic resonance tomography (MRT) confirmed the ultrasound findings. In addition, the scar of the previous biopsy in both testicles was clearly visible. The left-sided biopsy at the medial edge of the testicle was opposite the tumour (Figure 1). A left-sided radical orchiectomy was performed. Histology showed a 1.0-inch parenchymal lesion within a 1.6-inch atrophic testicle which was diagnosed as a "burnt-out" seminoma. A vascular lesion as the cause of the atrophy and scar could clearly be ruled out by histology.

Correspondence to P. Albers.
P. Albers and G.E. Voges are at the Department of Urology; and R. Moll is at the Department of Pathology, Mainz University Medical School, Langenbackstr. 1, D-55101 Mainz, Germany.
Revised 10 Dec. 1993; accepted 14 Feb. 1994.

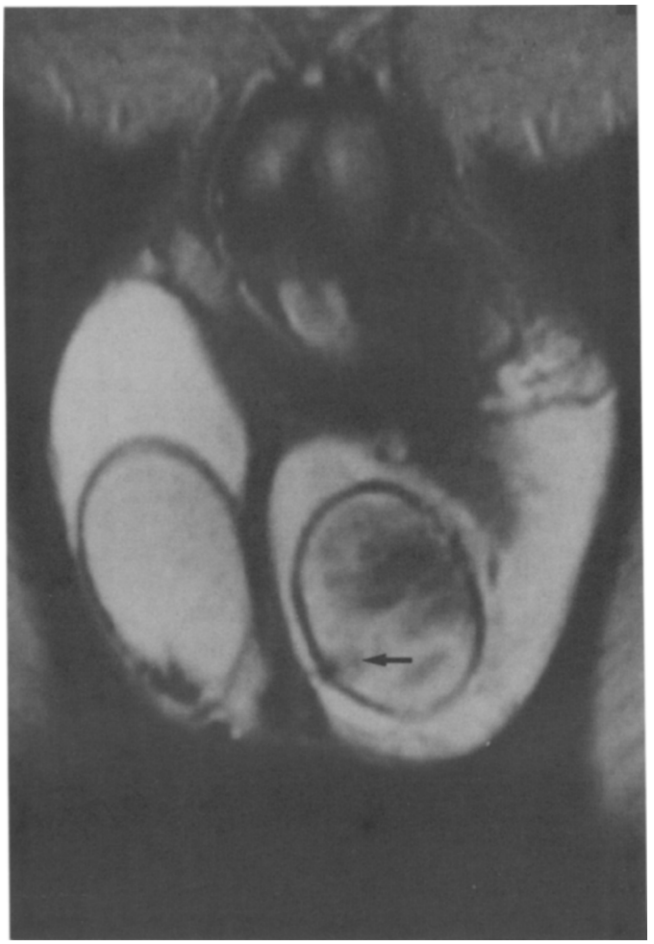

Figure 1. Magnetic resonance tomography of the left testicle 3 months after radical retroperitoneal lymph node dissection showing the tumour and the scar of the biopsy (arrow) opposite the tumour.

In this patient, the testicular origin of a supposed extragonadal germ cell tumour was diagnosed several weeks after the initial presentation. The testicular tumour was even missed by single testicular biopsy at the time of RPLND. Testicular seminoma was present all along, most probably as TIN.

There is a gradual transition from TIN to a malignant invasive tumour, and both entities are not detectable clinically or by ultrasound. During chemotherapy, these tumour cells may persist in the testicles [2]. TIN can only be diagnosed by open biopsy [3]. In extragonadal germ cell tumours, a bilateral testicular biopsy is necessary. Weißbach [1] recommends performing the biopsy on the upper medial side of the testis. According to Skakkebaek [4] and Maase [5], TIN is diffusely distributed within the testicle, therefore, a single biopsy should be sufficient.

This case report demonstrates the limits of reliability of a single testicular biopsy for the detection of TIN. MRT showed clearly that the biopsy scar was only superficial and opposite the tumour.

We agree with Walz [6] that multiple biopsies increase the chances of diagnosing tumour or TIN, although a more thorough exploration of the testicle bears the great risk of complete loss of functioning testicular parenchyma. Most probably, TIN in the testicle is not diffuse but multifocal [7]. Therefore, a single testicular biopsy can give false negative results. Additionally, Hoeltl and colleagues [8] and Giwercman and colleagues [9] have shown that in patients with a testicular tumour, biopsy of the contralateral testicle does not exclude the development of an asynchronous contralateral tumour.

We conclude that, despite negative biopsies in patients with a contralateral testicular germ cell cancer and extragonadal germ cell tumours, a regular and careful examination of the testicles is mandatory.

1. Weißbach L, Bussar-Maatz R. Pathogenese, Diagnostik und Therapie von Hodentumoren. *Urologe A* 1992, **31**, W25–33.
2. Dieckmann KP, Loy V. Persistent testicular intraepithelial neoplasia after chemotherapy. *Eur Urol* 1991, **20**, 258–260.
3. Mumperow E, Lauke H, Holstein AF, Hartmann M. Further practical experiences in the recognition and management of carcinoma in situ of the testis. *Urol Int* 1992, **48**, 162–166.
4. Shakkebaek NE, Berthelsen JG, Müller J. Carcinoma-in-situ of the undescended testis. *Urol Clin N Amer* 1982, **9**, 377–385.
5. v.d. Maase H, Rorth M, Walbom-Jorgensen S, *et al.* Carcinoma *in situ* of the contralateral testis in patients with testicular germ cell cancer: study of 27 cases in 500 patients. *Br Med J* 1986, **293**, 1398–1401.
6. Walz PH, Eitner S, Tan HK, Böhm E. Häufigkeit und Verteilungsmuster des Carcinoma *in situ* in tumorbefallenen Hoden. *Akt Urol* 1992, **23**, 73–77.
7. Loy V, Wigand I, Dieckmann KP. Incidence and distribution of carcinoma *in situ* in testes removed for germ cell cancer: possible inadequacy of random testicular biopsy in detecting the condition. *Histopathology* 1990, **16**, 198–200.
8. Hoeltl W, Gabriel CH, Marberger M. Asynchronous bilateral testicular tumour without previous carcinoma *in situ*. *Eur J Cancer* 1991, **27**, 110.
9. Giwercman A, Berthelsen JG, Müller J, van der Maase, Skakkebaek NE. Screening for carcinoma *in situ* of the testis. *Int J Androl* 1987, **10**, 173–180.

European Journal of Cancer Vol. 30A, No. 8, pp. 1209–1211, 1994.

0959–8049/94 $7.00 + 0.00

Vitiligo-like Lesions Following Immunotherapy With IFNα and IL-2 in Melanoma Patients

C. Scheibenbogen, W. Hunstein and U. Keilholz

SEVERAL FINDINGS support the concept of vitiligo as an autoimmune disease where destruction of melanocytes occurs. Most patients with active vitiligo have cytolytic anti-melanocyte antibodies [1–3]. The accumulation of activated T cells at the margins of the lesions has been demonstrated [4]. Vitiligo is associated with other autoimmune diseases such as primary hypothyroidism or type 1 diabetes mellitus [5, 6]. Thus, humoral and cellular immune mechanisms as well as a genetic predisposition may play a role in the disease's pathogenesis.

Correspondence to C. Scheibenbogen.
The authors are at the Dept. of Internal Medicine V, University of Heidelberg, Hospitalstr. 3, D-69115 Heidelberg, Germany.
Received 27 Jan. 1994; accepted 18 Feb. 1994.