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Histogenetic Analysis of Ovarian Teratomas by DNA Fingerprinting

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THE HISTOGENESIS of ovarian teratomas has long been disputed, the main controversy being whether they originate from premeiotic or postmeiotic oocytes [1–4]. Recently, some investigators observed both heterozygosity and homozygosity of chromosome and enzyme markers in several ovarian tumours, and they postulated that these arise from germ cells in a number of different ways [5, 6]. Thus, the pathogenesis of ovarian teratomas has not been completely clarified by conventional cytogenetic methods, and remains to be investigated by more sensitive and specific techniques.

In the present study, we introduced a newly developed method of DNA fingerprinting for histogenetic analysis of ovarian teratomas. The minisatellite DNA probe 33.15 used in the present study can simultaneously detect highly variable regions widely dispersed in the human genome and can provide individual-specific restriction fragment length polymorphisms (RFLPs), called DNA fingerprints [7].

High molecular weight DNA was extracted from the tumour tissues and mononuclear cells of the patients as described elsewhere [8]. 5 μg of each DNA sample was digested with endonuclease *Hinf*I at 37°C for 3 h and electrophoresed on an 0.8% agarose gel, then transferred by blotting to nitrocellulose filters. After baking the filters in a vacuum at 80°C for 3 h, a ^{32}P-labeled minisatellite DNA probe was hybridised at 65°C for 12 h in Denhardt's solution, 1 mol/l NaCl, 50 mmol/l Tris-HCl (pH 7.4), 0.1% sodium dodecyl sulphate (SDS), 10 mmol/l EDTA and 0.1 mg/ml denatured and sonicated salmon sperm DNA. The filters were then washed once at room temperature in 2 × sodium chloride–sodium citrate (SCC), followed by two washes at 65°C in 1 × SCC containing 0.1% SDS for 30 min. They were autoradiographed using Kodak XRP-1 film at −80°C for 48 h.

Figure 1 shows the profiles of RFLP band patterns detected by the 33.15 probe in 4 sets of ovarian teratoma tissue specimens and the peripheral mononuclear cells of each host. In the 4–20 kb region, each patient displays about 10–20 polymorphic bands, constituting person-specific RFLPs, while fragments smaller than 4 kb do not show person-specific polymorphisms. In the three cases (cases 1–3) of mature teratoma (dermoid cyst), each DNA fingerprint was identical to that of the mononuclear cells from the host. On the other hand, in the one case (case 4) of grade II immature teratoma, some polymorphic bands

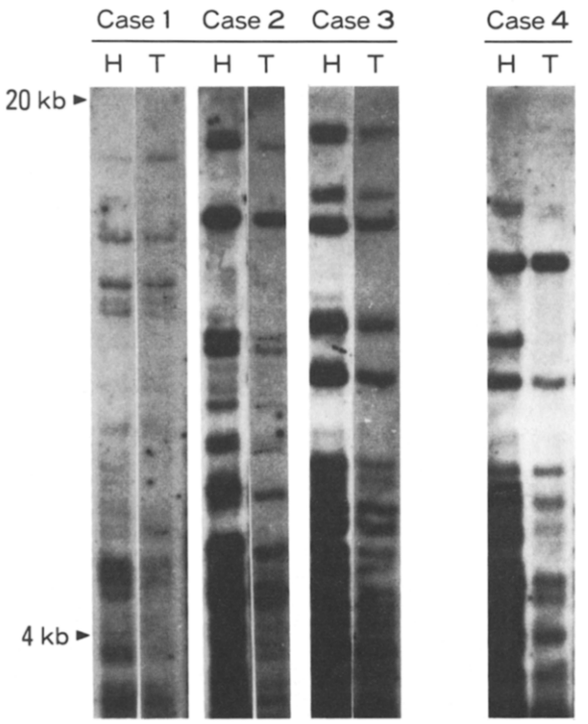

Fig. 1. Band patterns of restriction fragment length polymorphisms of DNA of 3 mature teratomas (cases 1–3) and 1 immature teratoma, grade II (case 4) in tumour tissues (T), and the mononuclear cells of the respective hosts (H) obtained with minisatellite probe 33.15.

observed in the host were deleted from the DNA fingerprinting of the tumour tissues.

It may be suggested that benign mature teratomas of the ovary arise from germ cells before meiosis 1, while immature teratomas arise from postmeiotic germ cells. Analysis of a larger series of cases is clearly needed. The recently developed method using the DNA minisatellite probe 33.15 definitely provides a useful and sensitive tool for cytogenetic analysis of germ cell tumours, including dysgerminomas, endodermal sinus tumours and teratomas.

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