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The accuracy of aspiration cytology in the diagnosis of rejection following orthotopic liver transplantation

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Abstract. The role of aspiration cytology (AC) and the total corrected increment (TCI) in the diagnosis of hepatic rejection was assessed in 30 patients following 36 liver transplants. A total of 174 AC specimens were "blindly" evaluated. Patients underwent protocol AC twice weekly and when biochemical or clinical parameters suggested rejection. Hepatic rejection was only confirmed when clinical and biochemical changes were accompanied by positive histological diagnosis. In all, 103 specimens were matched against histology, the remainder assessed against retrospective clinical and biochemical diagnoses. There were 80 cytological diagnoses of rejection, confirmed in 69 specimens, and 94 diagnoses of no rejection, confirmed in 73 specimens. These figures give a sensitivity of 76.7%, a specificity of 86.9% and a positive predictive value of 86.3%. Overall, 39.7% of specimens taken more than 2 months after grafting proved to be incorrectly diagnosed. However, the accuracy was higher in 145 specimens taken within 8 weeks of transplantation, with a sensitivity of 81.3%, a specificity of 90%, a positive predictive value of 89.7% and an accuracy of 85.5%. Although histology remains the gold standard in the diagnosis of acute rejection after hepatic grafting, AC using a TCI with a positive predictive value of 86.3% may prove to be of value in monitoring liver transplant patients in the first 2 months after grafting.

Key words: Liver transplantation - Aspiration cytology - Rejection - Fine needle aspiration - Total corrected increment.

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Hepatic dysfunction following orthotopic liver transplantation may be due to a number of causes [7], including rejection, biliary leaks or obstruction, hepatic ischaemia or infection. The diagnosis of rejection is made primarily by the exclusion of other causes [12] and secondarily by liver biopsy. The latter may be associated with both morbidity and mortality [4]. Fine needle aspiration (FNA) cytology diagnosis of renal allograft dysfunction is a well-established procedure and represents the standard investigation in many renal transplantation centres [2].

Although aspiration cytology (AC) has been used to diagnose rejection after liver transplantation [9, 13], the accuracy of such a diagnosis in patients has yet to be confirmed. The aim of this study was to evaluate the accuracy of AC compared with that of both histology and retrospective clinical diagnosis.

Patients

Group 1: control patients

Two control groups of patients were studied after informed consent had been obtained. Group A patients ($n = 10$) were not in the liver transplant programme but were under investigation on the liver unit for hepatic dysfunction. They were examined by FNA under vision at the time of laparotomy or by Menghini biopsy followed by flushout with the needle; these patients were not biopsied for study purposes alone. Group B consisted of FNAs from eight excised livers following hepatectomy and orthotopic transplantation.

Group 2: transplanted patients

A total of 30 patients were studied by FNA and washout cytology from Menghini biopsies [14] after informed consent had been obtained. Seven patients had undergone transplants for primary

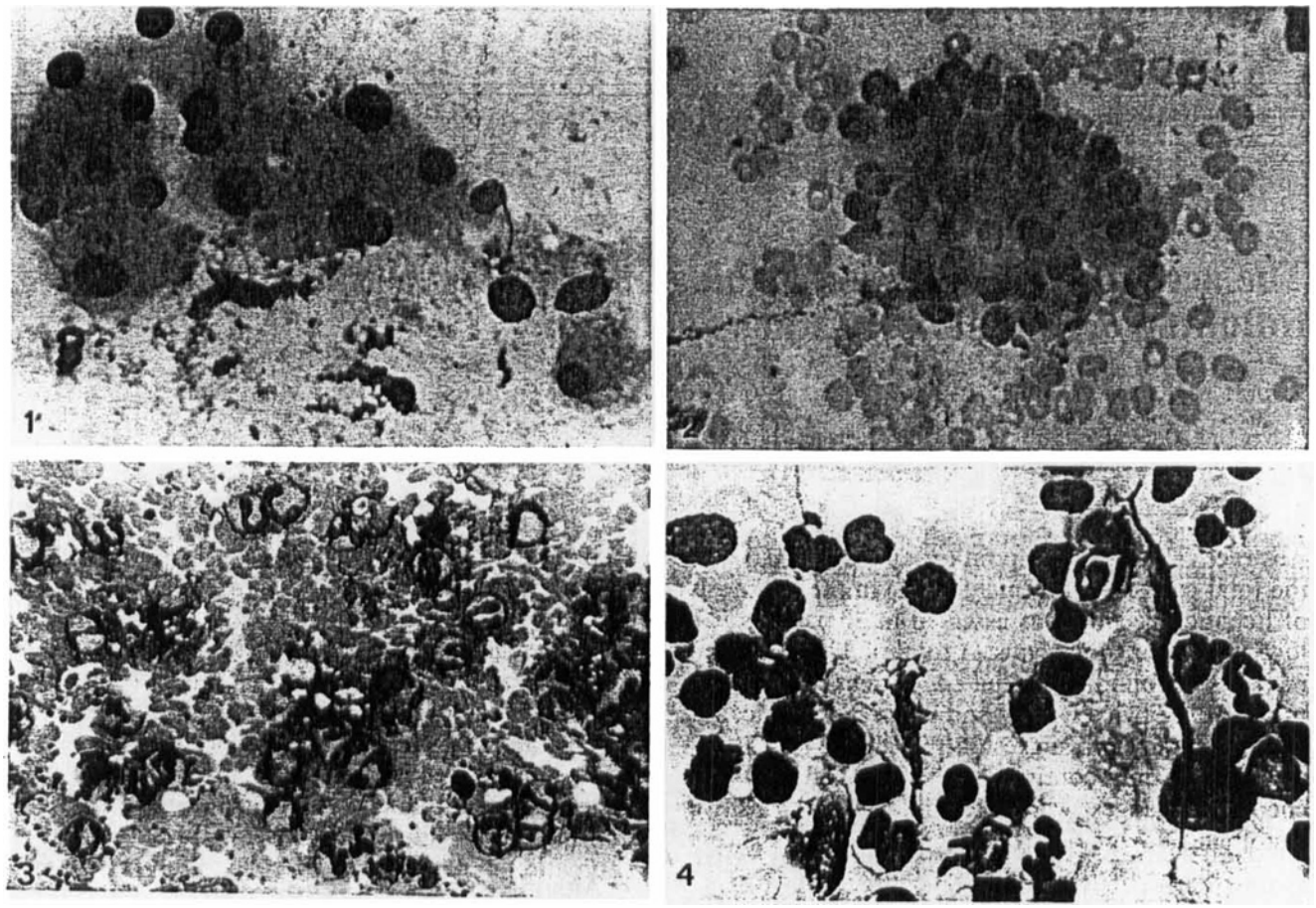

Fig. 1. Normal finding of hepatic aspirate. Note the small sheet of hepatocytes against a background of bile pigment. May-Grünwald-Giemsa, × 600

Fig. 2. Normal finding of hepatic aspirate. Note the group of well-preserved bile duct epithelial cells. May-Grünwald-Giemsa, × 600

Fig. 3. Acute inflammation due to infection. Note the numerous polymorphonuclear leucocytes mixed with erythrocytes and platelets. There is no evidence to suggest rejection. May-Grünwald-Giemsa, × 600

Fig. 4. Acute rejection. A large degenerate hepatocyte showing cytoplasmic vacuolation, surrounded by cells of the lymphoid series and occasional eosinophils and neutrophils. May-Grünwald-Giemsa, × 1070

hepatic malignancy, 2 patients for subacute massive necrosis, and the remaining 21 for chronic liver disease. The mean age of patients in this group was 37.3 years (range, 11-59). There were 20 females and 10 males. Two children under the age of 14 were examined by Menghini biopsy only at times of hepatic dysfunction. Three further patients were investigated with single biopsies at a time of suspected dysfunction (two suspected episodes of rejection and one tumour recurrence). The remaining 25 patients were followed from the time of surgery and were examined both at times of suspected dysfunction and according to the postoperative management and trial protocols. Six patients were regrafted during the period of the study. Three patients were regrafted for chronic rejection at 40, 55 and 103 days after the first operation and three for graft failure at 12, 13 and 30 days after the initial graft.

Immunosuppression

Patients were initially given 100 mg hydrocortisone b.i.d. and 1.5 mg/kg azathiaprine daily. Only when the patients were fully haemodynamically stable with good renal function was 5 mg/kg cyclosporin A begun IV as a 24-h infusion or by two 4-h infusions. Oral cyclosporin at 10 mg/kg was substituted when the patients started oral intake. Whole blood cyclosporin levels were monitored by radioimmunoassay with the aim of maintaining blood levels between 500 and 1000 mmol/l during the trough period. The oral maintainance steroid therapy was 20 mg prednisolone daily. Acute rejection was treated by a 3-day course of high-dose steroids, typically 200 mg prednisolone orally or 1 g methylprednisolone IV.

Materials and methods

A total of 198 cytological specimens were obtained for assessment: 24 were baseline studies taken at the time of operation, 71 were taken by percutaneous FNA, 103 with histological specimens, 92 with Menghini biopsies and 11 by FNA at a laparotomy subsequent to transplantation and at the same time as a trucut biopsy.

Fine needle aspiration

All FNAs at laparotomy were taken with a 21-gauge needle and a 20-ml syringe. Percutaneous aspiration was carried out with a Chiba "skinny" needle or a 23-gauge, 6-in. spinal needle (Steriseal) under local anaesthetic using a 20-ml syringe. The specimen was aspirated into 5 ml heparinized transport medium [Eagle minimum essential medium (modified) with Earles salts and 0.85 g/l sodium bicarbonate with glutamate (Flow Laboratories) to which 60 ml/l foetal bovine serum had been added].

Histology

Percutaneous needle biopsy was carried out using a Menghini needle under local anaesthetic. Suction was applied using a 20-ml syringe containing 5 ml heparinized transport medium prior to insertion of the liver. After removal of the core of liver tissue, the Menghini needle was flushed with the transport medium [14].

Processing and assessment

Two specimens from each sampling episode (liver aspirate and peripheral blood) were processed simultaneously and compared using the total corrected increment (TCI) method of von Willebrand and Häyry [3] for monitoring renal grafts. Air-dried specimens were stained with May-Grunwald-Giemsa. Examination of the dry slides was done using 400× magnification (Figs. 1-4).

The TCI was obtained by examining the percentages of different white cell types of the blood and hepatic aspirate specimens and subtracting the blood from the hepatic score. The cell types were given an incremental score:

lymphoblasts	×1	lymphocytes	×0.1
plasmablasts	×1	monocytes	×0.2
plasmacytes	×1	neutrophils	0
macrophages	×1	eosinophils	0

Higher peripheral blood increments were not scored. The total formed the TCI (see Table 1). The state of hepatocytes was noted at the same time (Figs. 1, 4), although it was highly dependent on the state of preservation. A TCI level of more than 3.5 was taken to indicate rejection.

During the study, a diagnosis of rejection was made only at a time of hepatic dysfunction with histological changes confirmed by needle biopsy [5, 7]. The AC specimens, although examined and scored prospectively, were not assessed until the conclusion of the study. They were then retrospectively examined together with the pattern of biochemical change and the knowledge of preceding and subsequent clinical and histological diagnoses to assess the true diagnosis at each sampling episode.

All the histological specimens were examined by one histopathologist (SGH). A diagnosis of acute rejection was made on the assessment of features including portal tract inflammation, infiltration of and damage to bile ducts and lifting of the endothelium of small vessels [5]. A diagnosis of chronic rejection was made on the disappearance of bile ducts and the appearance of arterial foam cells [5, 7]. All histology specimens were reported without knowledge of the cytological findings.

Results

The TCI for all main groups are demonstrated in Table 2. The cellular changes seen in the follow-up subgroups are shown in Table 3.

Table 1. An example of cytological aspirations demonstrating the TCI formula. Patient 15, 4 and 9 days after OLT

Day 4	LB	PB+ PC	L	N	E	B	Mo	Mph	TCI
Liver	3	3	30	63	0	0	1	0	
Blood	0	0	1	93	5	0	1	0	
Corrected Increment	3	3	2.9	0	0	0	0	0	8.9

Clinical condition: clinically well, rising liver function tests
Cytological diagnosis: acute cellular rejection

Day 9	LB	PB+ PC	L	N	E	B	Mo	Mph	TCI
Liver	0	1	5	90	2	0	2	0	
Blood	0	0	6	93	0	0	1	0	
Corrected Increment	0	1	0	0	0	0	0.2	0	1.2

Clinical condition: following course of high-dose steroids
Cytological diagnosis: no rejection

Table 2. Results of TCI - all samples

Group	*n*	TCI	SD	Min	Max
Controls	18	0.96	1.26	0	4.9
Baseline	24	1.15	1.16	0	3.5
Rejection (histological control)	73	5.15	2.44	0.2	11.2
Rejection (FNA)	17	4.96	1.99	2.3	8.4
Rejection (total)	90	5.11	2.35	0.2	11.2
No rejection (histological control)	30	3.08	1.99	0.3	8.5
No rejection (FNA)	54	1.83	1.50	0	7.3
No rejection (total)	84	2.27	1.79	0	8.5

Group 1: control patients

The specimens from group A, the non-transplanted control patients, all had a TCI of < 1.5 (mean, 0.45). The mean TCI in group B was 1.6 (range, 0-4.9).

Group 2: transplant patients

Baseline at time of grafting. The baseline specimens had a mean TCI of 1.15 ± 1.16 (range, 0-3.5); all were below the level regarded as indicative of acute rejection. There was no statistical difference between the results in the control group and the baseline group ($P = 0.3$, Student's *t*-test).

Five baseline specimens had a TCI of ≥ 2 (mean, 2.72). All the livers in this group were later affected by severe disease either necessitating urgent retransplantation ($n = 4$) or resulting in the patient's death ($n = 1$). Seven of the remaining 19 livers developed chronic rejection or severe ischaemia,

Table 3. Cell types. PB, Plasmablasts; PC, plasma cells; LB, lymphoblasts; Mph, macrophage; SD, standard deviation; Min, minimum; Max, maximum

Group	*n*	Plasma cells and plasmablasts				Lymphoblasts				Hepatic macrophage counts			
		Blood		Liver		Blood		Liver					
		PB/PC	SD	PB/PC	SD	LB	SD	LB	SD	Mph (%)	SD	Min	Max
Acute rejection (FNA)	16	0.06	0.25	2.19	1.72	0.37	0.81	0.93	1.12	0.87	1.46	0	1
Acute rejection (histology)	57	0.16	0.82	1.93	1.73	0.21	0.55	1.00	1.06	0.25	0.45	0	8
Acute rejection (total)	73	0.14	0.73	1.99	1.72	0.25	0.62	0.99	1.07	0.75	1.33	0	8
Chronic rejection (total)	17	0	0	1.18	1.24	0.18	0.39	0.71	1.16	2.35	1.54	0	6
No rejection (FNA)	46	0.02	0.14	0.76	0.85	0.19	0.58	0.19	0.50	0.09	0.29	0	1
No rejection (histology)	17	0	0	1.37	1.20	0.06	0.25	0.25	0.45	0.19	0	0	2
No rejection (total)	63	0.02	0.13	0.92	0.99	0.16	0.52	0.21	0.48	0.14	0.44	0	2
Graft failure (FNA)	8	0	0	0.71	1.25	0	0	0.14	0.38	0.57	0.79	0	2
Graft failure (histology)	13	0.23	0.83	1.08	2.18	0.38	0.51	0.38	0.65	0.92	1.12	0	3
Graft failure (total)	21	0.14	0.65	0.91	1.84	0.24	0.44	0.29	0.56	0.76	0.99	0	3

leading to regrafting or the death of the patient. This was statistically significant ($P<0.05$, χ^2 with Yates' correction and Fisher exact test). Macrophages were seen at two baseline aspirations (1%), both from livers that developed graft necrosis.

Follow-up. Eighty specimens in 26 patients demonstrated a rise in TCI of >3.5, indicative of acute rejection. Sixty-four of these were taken from washouts following Menghini needle biopsy or with a trucut comparison and were therefore directly comparable by histology. The remainder were taken by FNA.

Histology

There were 73 histological diagnoses of rejection. The mean TCI of these specimens was 5.15±2.44 (range, 0.2-11.2). This group was subdivided into those with acute rejection ($n=57$), with a mean TCI of 5.14±2.62 (range, 0.2-11.2), and those with chronic rejection ($n=16$), with a mean TCI of 5.20±1.70 (range, 2.0-8.4). Fifty-seven of the 73 specimens had a TCI of ≥3.5 and 16 had a TCI of <3.5.

There were 30 histological diagnoses of no rejection, with or without another form of post-operative graft dysfunction. Thirteen of the histological specimens revealed non-immunological graft failure, ischaemic changes or necrosis. The remainder showed no rejection, minimal portal tract inflammation (taken as no rejection) ($n=11$), biliary obstruction ($n=2$) and cholangitis ($n=4$). The mean TCI of the "no rejection" group as a whole was 3.08±1.99 (range, 0.3-8.5). The TCI of the group with necrosis or graft failure was 3.08±1.67 (range, 0.9-5.9) and that of the remainder was 3.08±2.34 (range, 0.3-8.5). Twenty-three of the cytological diagnoses from this group were of no rejection, including the high TCIs already discussed. There were, however, seven specimens with a TCI of >3.5, with a cytological diagnosis of acute rejection; these were taken to be false positives. There was a highly significant difference between the results in the "rejection" and "no rejection" groups ($P<0.0001$, Student's *t*-test).

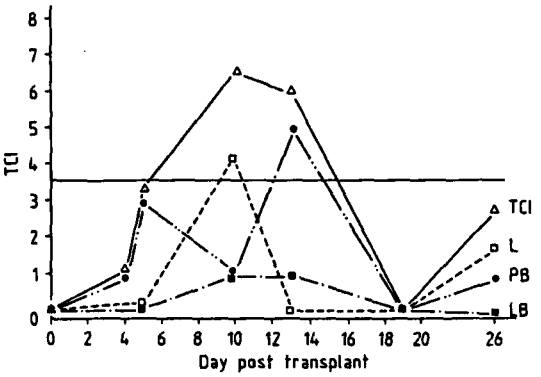

Fig. 5. Cellular changes seen in acute cellular rejection. The graph demonstrates the cytological changes in the first 26 days after OLT. Acute rejection was confirmed by histology on day 5 and treated by high-dose immunosuppression. Although the TCI had increased to 3.1, mostly because of a rise in plasmablasts, it had not reached the level adequate for a cytological diagnosis of rejection. By 10 days, the lymphocyte differential count had risen, with a resultant rise in TCI

Fine needle aspiration

Following the retrospective assessment of 71 FNA episodes, 17 biopsies were assessed as "rejection probable" and 54 as "rejection unlikely".

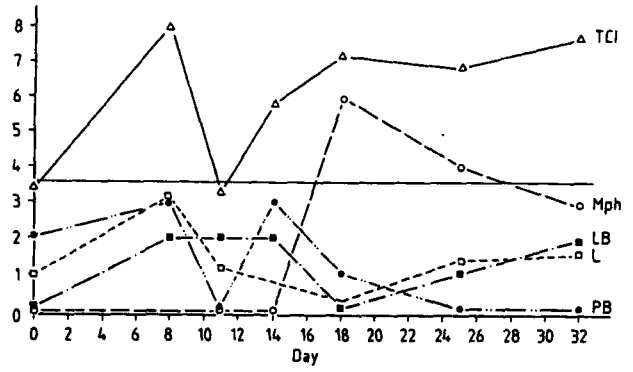

Fig. 6. Cellular changes in chronic rejection. The TCI of the first post-operative biopsy increased because of a rise in blast cells and lymphocytes in the hepatic aspirate. (Acute rejection was confirmed by histology.) The TCI dropped after treatment with high-dose steroids but rose again after 14 days and remained elevated, despite further courses of high-dose steroids, because of a high macrophage count. This patient required regrafting. (Note the high baseline TCI)

Table 4. Accuracy of cytology results

a Histology. $P<0.0001$ (χ^2 with Yates' correction)

Cytology	Histology rejection	No rejection
Rejection	57	7
No rejection	16	23

b Retrospective clinical diagnosis (cytology). $P<0.0001$ (χ^2 with Yates' correction)

Cytology	Retrospective diagnosis	
	Rejection	No rejection
Rejection	12	4
No rejection	5	50

c Combined. $P<0.0001$ (χ^2 with Yates' correction)

Cytology	Histology/retrospective diagnosis	
	Rejection	No rejection
Rejection	69	11
No rejection	21	73

d Combined (first 2 months). $P<0.0001$ (χ^2 with Yates' correction)

Cytology	Histology/retrospective diagnosis	
	Rejection	No rejection
Rejection	61	7
No rejection	14	63

Sixteen of the "rejection probable" specimens were taken at a time of *acute* rejection. The mean TCI of this group was 4.81 ± 1.96 (range, 2.3-8.4). The remaining specimen was taken at a time of chronic rejection (TCI = 7.2). Twelve of the 17 samples had a TCI of ≥ 3.5, and the remaining 5 had a TCI of <3.5. There was a highly significant difference between the results in the "rejection probable" and "rejection unlikely" groups ($P<0.0001$, Student's *t*-test).

Table 5. Diagnosis of rejection - accuracy of FNA

		95% confidence intervals
Histological assessment		
Sensitivity	78.1%	± 9.5%
Specificity	76.7%	±15.1%
Positive predictive value	89.1%	± 7.6%
Negative predictive value	59.0%	±15.4%
Accuracy	77.7%	± 8%
Fine needle (retrospective clinical and biochemical assessment)		
Sensitivity	70.5%	±21.6%
Specificity	92.5%	± 6.9%
Positive predictive value	75.0%	±21.2%
Negative predictive value	90.9%	± 7.6%
Accuracy	87.3%	± 7.7%
Combined		
Sensitivity	76.7%	± 8.7%
Specificity	86.9%	± 7.2%
Positive predictive value	86.3%	± 7.5%
Negative predictive value	77.7%	± 8.4%
Accuracy	81.6%	± 5.8%
Combined first 2 months after transplantation		
Sensitivity	81.3%	± 8.8%
Specificity	90.0%	± 7.0%
Positive predictive value	89.7%	± 7.2%
Negative predictive value	81.8%	± 8.6%
Accuracy	85.5%	± 5.7%

Eight of the "rejection unlikely" specimens were taken at a time of graft dysfunction, ischaemia or necrosis. The mean TCI of this subgroup was 2.05 ± 2.06 (range, 0-5.6). The mean TCI of the remaining 46 samples in the "rejection unlikely" group was 1.77 ± 1.41 (range, 0-7.3). Fifty of the 54 specimens had a TCI of <3.5 and 4 had a TCI of >3.5 (Table 2).

There was a highly significant difference between the baseline group and both the post-operative rejecting and non-rejecting groups ($P<0.001$, Student's *t*-test). There was no difference between the FNA and histology control acute rejection groups ($P=0.32$) or between the chronic and acute rejection groups ($P=0.47$). There was, however, a difference between the FNA and histological control non-rejecting groups ($P<0.001$). When the differences were confined to those specimens taken from livers that were in graft failure or ischaemic, there was no difference between the two groups ($P=0.11$). There was a highly significant difference between the rejecting and non-rejecting groups, whether the groups were combined or taken singly ($P<0.0001$).

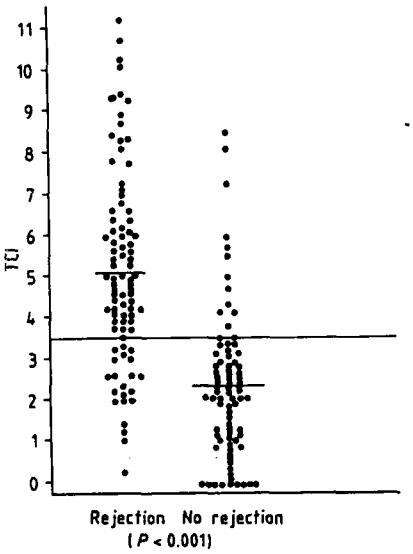

Fig. 7. The post-transplant follow-up specimens (both FNA and histology control), assessed as either "rejection" or "no rejection". There is a highly significant difference between the two groups, but all TCI values below the line in the "rejection" group represent false negatives, and the majority of those above the line in the "no rejection" group represent false-positive groups

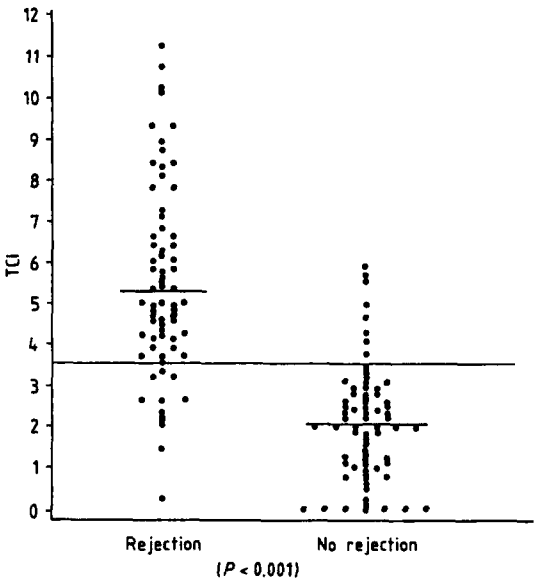

Fig. 8. All TCIs from specimens taken within 2 months of transplantation. There is still a highly significant difference ($P < 0.0001$, Student's t-test) between the two groups, but there are less false negatives and false positives compared with Fig. 7

Cell types

The patterns of cellular changes typically seen in acute and chronic rejection are demonstrated in Figs. 5 and 6. Table 3 shows the difference in cell types between the follow-up subgroups.

Accuracy (Tables 4, 5)

In total there were 21 false negatives and 11 false positives (Fig. 7). Nineteen (from 120 biopsies, 15.83%) of these were in the 1st month, 2 (from 25 biopsies, 8%) in the 2nd month, 2 (from 9 biopsies, 22.22%) in the 3rd month and 9 (from 20 biopsies, 45%) thereafter. If the cut-off is taken at the end of the 2nd month (Fig. 8), 37.9% of the cytological specimens were wrong beyond this time. During the first 2 months, 14.5% of the diagnoses were wrong; this difference was statistically significant ($P = 0.0067$, χ^2 with Yates' correction).

Three false-negative results were obtained with protocol or follow-up histological biopsies that were not treated for acute rejection. (Five histological specimens that revealed acute rejection were not treated.)

Two false-positive specimens were taken by Menghini washout with histological biopsies which, although reported as showing no rejection, contained occasional areas of portal tract inflammation. One cytological specimen was taken with a histological biopsy showing minimal inflammation; it was reported as not being diagnostic of rejection. Despite this, the following biopsy from the same patient revealed the final stages of chronic rejection with the disappearing bile duct syndrome. This patient was later regrafted (outside the study period) for chronic rejection.

All of the remaining specimens with a misleadingly high TCI were taken at a time of graft dysfunction. Two specimens were taken from patients with a bile leak and intra-abdominal abscess formation, one was taken from a patient with biliary obstruction secondary to biliary sludging, four were taken from two patients with idiopathic graft ischaemia that resulted in retransplantation and one was taken from a patient with graft ischaemia and a biliary-venous fistula.

Complications

There were no severe complications from FNA. Seventeen patients had multiple percutaneous FNAs, with a mean of 4 FNAs per patient. Four patients had one percutaneous FNA biopsy only. Two patients developed minor bruising and discomfort at the site of the biopsies (both FNA and Menghini). One patient found all diagnostic procedures worrying, but the remainder appeared to experience no discomfort from FNAs.

During this period, 101 Menghini needle biopsies were carried out with two significant complica-

tions. One patient with grossly altered clotting (PT 76/14 and PTT > 300) was biopsied as a known and understood risk to investigate severe graft dysfunction and required 6 units of blood. Another patient developed a haemothorax 2 days after liver biopsy and died 4 months later with an undiagnosed empyaema.

Discussion

The role of aspiration cytology (AC) after liver transplantation has yet to be determined. There are two options, not necessarily exclusive. The first is the routine monitoring of patients after grafting, and the second is the evaluation of hepatic dysfunction after grafting. This study has examined the accuracy of AC in the diagnosis of rejection rather than hepatic dysfunction as a whole. As such, it has been envisaged as a monitoring device to predict acute rejection and allow early treatment with high-dose immunosuppression. The predictability of rejection should be high, because the treatment for acute rejection, i.e. a course of high-dose steroids, is generally contra-indicated in other forms of hepatic dysfunction, such as cytomegalovirus (CMV) hepatitis.

At present, histology must be regarded as the gold standard for the diagnosis of acute rejection following liver transplantation, and in this study the histological diagnosis of rejection coincided with clinical and biochemical evidence of rejection in 98.6% of the cases. A comparison of cytological and histological diagnoses therefore appeared to be valid.

AC using the TCI has been well demonstrated to be of value in the diagnosis of rejection after renal transplantation [2]. It might be questioned as to whether the same formula is of value after hepatic replacement, although no other reproducible quantitative scoring method has been suggested for this situation.

The use of a mathematical formula allowed a diagnosis to be made from the TCI score, so that we did not have to rely on previous experience in the interpretation of the pattern of rejection. For this reason, the investigation can easily be reproduced in centres where previous cytological assessment of transplants has not been the norm. Indeed, we had not used AC in the diagnosis of renal allograft rejection. AC using the TCI has proved to be a simple and straightforward method of assessing grafts.

No morbidity was seen as a result of FNA, and problems after percutaneous Menghini needle biopsy were not seen in any higher incidence (2%) than has been observed in any other series [1, 6, 10, 11, 15]. At times needle biopsy is essential, despite increased risks of poor coagulation, but FNA was not attempted under these circumstances in this study.

Overall, in this series of patients, there was a high incidence of acute rejection, with over 80% of the patients who survived more than 4 days developing rejection. In all, 51.7% of all biopsies were from patients rejecting at the time of sampling. This figure was higher in the histological control group (70.8%) than in the FNA group (23.9%) ($P < 0.0001$) because every suspected rejection episode was investigated by histological biopsy, whereas the majority of FNAs were carried out between or after such episodes.

Ultimately, every specimen can be assessed against a diagnosis of "rejection" or "no rejection". Using these parameters, the results may be examined at various stages. The control patients (group A) all had a TCI of < 1.5. One of the eight excised livers had a high TCI (4.9), but the remainder were below 2.5. Overall, this represents a specificity for this group of 94.4%. None of the 24 baseline investigations had a TCI of > 3.4, and when this group is combined with the control groups, there is a specificity of 97.6%. There was no statistical difference between the results in the control and baseline groups.

Despite the good separation between the TCI values of the rejecting and non-rejecting groups, there were a substantial number of false negatives and positives, but fewer in the first 2 months after grafting. False negatives sometimes occurred despite rising blast counts (Fig. 5), and false positives were often due to raised hepatic macrophage counts in degenerate livers. The specificity for the investigation after 2 months was 53.3% and the sensitivity was 71.4%. The accuracy of AC in the first 2 months was 85.5% and 62.1% thereafter ($P = 0.006$, χ^2). Despite analysis on a mainframe computer, this accuracy could not be improved by altering the Häyry/von Willebrand TCI formula. This formula would therefore appear to be relevant to liver grafting.

In this study there was no consistent cytological finding that predicted or confirmed ischaemia or graft failure. A baseline TCI of > 2 was associated with later graft failure ($P < 0.05$), but a low baseline TCI did not preclude later graft dysfunction. Severe hepatocyte degeneration in two follow-up specimens was associated with graft ischaemia, although it would have proved impossible to differentiate this from poor specimen preservation. A rise in TCI caused by the presence of macrophages was shown to be associated with graft failure [8], although a normal TCI did not preclude this.

It would appear to be unsafe to rely on AC and the TCI method as a diagnostic tool after the first 2 months following grafting. Unfortunately, the group of patients still requiring investigation during the period following grafting are precisely those whose problems become chronic and more difficult not only to diagnose, but also to manage. The straightforward patient will have been discharged by this time, and the majority of patients who die will have done so in the first 30 days after transplantation. Continuing the assessment of the patients after 2 months can only be done by the conventional methods, including histology.

Conclusions

AC using the TCI is an easily reproducible technique that may be used in the assessment of patients after liver transplantation. The cytological diagnosis of rejection using these methods has been shown to be sensitive and specific. Because there was a significant difference between the accuracy of the results from specimens taken in the first 2 months and those taken after this time, cytology should not be used to diagnose rejection after 2 months. Although cytology has not been used to diagnose non-immunological graft failure, where experienced histopathological help is not rapidly available, FNA may be of help in the assessment of hepatic dysfunction after liver replacement. Histology, however, remains the gold standard in the diagnosis of hepatic dysfunction after liver transplantation.

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