Fine-needle aspiration biopsy of the renal transplant—is it worthwhile or a waste of time?

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1. What is the advantage of fine-needle aspiration biopsy?

The method of fine-needle aspiration biopsy (FNAB) for the diagnosis of acute rejection in renal allografts has been reported as being quick and accurate [1–3]. A major advantage of FNAB in comparison with a core biopsy is the low risk of this relatively easy procedure, which allows for taking multiple samples, even daily, when close monitoring of the graft is indicated [1,3,4]. Another advantage is that FNABs can be taken in patients with a bleeding tendency, while in centres in which a histological diagnosis is not given within 24 h the rapid information of a FNAB can be very important. Pekka Häyry, Eva von Willebrand and their co-workers have successfully introduced the method of FNAB for renal allografts, and have described the cytological criteria for acute rejection, including a scoring system leading to a total corrected increment (TCI), that, when above a certain limit, is indicative for acute rejection [1,4]. Several other studies have shown that FNAB is a valuable diagnostic tool with good sensitivity and specificity [2,5]. In addition, the article of Manfro and colleagues in this issue [6] demonstrates that the method has a high diagnostic accuracy, as evaluated by comparison with the gold standard of histopathological examination in a multicentre study by Hökfelt [7]. In theory FNAB could therefore in many cases obviate the taking of a core biopsy. The key question that remains is: What has prevented FNAB from becoming used worldwide as the method of choice for the diagnosis of acute rejection?

2. Is there a role for fine-needle aspiration biopsy early on?

The diagnostic accuracy of FNAB is highest in the first 3 months after transplantation, the period with the highest incidence of acute rejection. Data on sensitivity and specificity are mostly derived from FNABs performed in this period. However, patients with deteriorating graft function early after transplantation...
usually need immediate diagnosis and treatment, and clinicians may not be willing to risk the delay caused by a non-representative or an inconclusive FNAB, after which a core biopsy still has to be taken. Because of the possible complications of anti-rejection treatment the clinician wants to be as certain as possible. To our knowledge only few centres use FNAB as a solitary diagnostic procedure, before actually initiating anti-rejection therapy, except in those cases in which strong clinical evidence for rejection is already present. From the advice of the most experienced centre that FNABs should be taken for monitoring of the graft and not as a substitute for a core biopsy [1,3], it can already be seen that a FNAB will seldom give decisive information in clinically difficult cases. Possibly, immunostainings can increase the accuracy of the cytological diagnosis [3,8,9]. Nevertheless, the information that can be obtained from a FNAB is essentially limited, since acute vascular rejection, with its immediate danger to the graft, can in general not be seen in the cytological specimen [1–3]. A prospective study of Gray et al., in which FNAB, core biopsy and immunohistology were blindly compared as diagnostic techniques in the management of the patients, showed that the core biopsy is the most reliable technique [10].

3. What is the role of fine-needle aspiration biopsy in late graft dysfunction?

After the first 3 months, declining graft function is not infrequently due to causes that cannot reliably be diagnosed by FNAB, such as chronic rejection or recurrence of the original renal disease. Although in such cases immediate therapy is not always indicated, which would make repeated FNABs acceptable, the chances that these will lead to a definite diagnosis are considerably less than in the first months [3], and most clinicians will prefer the more complete information that can be gained from histology.

4. Practical points

There are also practical reasons that prevent a more general clinical use of the FNAB method. Although the procedure is relatively simple to perform at the bedside, the technical preparation of the cytopsins and stainings is quite laborious. Following this, the differential counting of cells in peripheral blood and FNAB, with the calculation of the TCI, requires the effort of an experienced and dedicated pathologist/cytologist with expertise in both haematological and parenchymatous cytology [1,3,4]. We have the impression that most clinical centres that use FNAB as a routine procedure in clinical practice, have technicians and examiners available in close proximity to the clinical setting, and here usually the diagnosis will be based on a combination of clinical and cytological data. In those departments that depend on the service of a pathology or cytology laboratory, it may be difficult to motivate a technician and a cytologist/pathologist to drop other activities in favour of the immediate preparation and examination of a FNAB at irregular hours. Moreover, many pathologists will feel uneasy in making a definite diagnosis on a FNAB, unless the clinical data are already strongly pointing to rejection. When a pathologist is aware of the fact that about 30% of stable grafts show histological infiltrates suggestive of rejection, he may hesitate to base his diagnosis completely on the increase of mononuclear cells, without having information about tubulitis or endarteritis, which are the histological hallmarks of acute rejection. Moreover, the TCI is strongly influenced by the recognition of lymphoblasts, plasmacytoid cells, monoblasts and macrophages as these cells have a relative score 10 times higher than lymphocytes [3,4], while the differentiation of these cells from activated lymphocytes and monocytes is not always simple. Therefore, if the clinical data are equivocal, in most cases the cytological diagnosis will be made with reservations. When daily practice learns that after a suspect FNAB a core biopsy will still be necessary, both clinicians and pathologists will favour the method that most easily fits in the daily laboratory routine and that is also the most direct way to a complete and definitive diagnosis.

5. Balancing advantages and risks

From the above it can be concluded that FNAB usually cannot replace a core biopsy, but is more valuable for continuous monitoring of the graft early after transplantation, as has been emphasized by von Willebrand and Häyry [1,3,4]. This implies the taking of multiple samples, once or twice weekly, in patients with stable graft function, while in patients with declining function the frequency can be increased to daily samples or even more [4]. Despite the low risk of the method it is still an invasive technique, and many clinicians will prefer non-invasive methods for monitoring of graft function. As such the routine determination of serum creatinine remains the most informative parameter. Also, there seems to be a discrepancy between the workload of routine FNABs for clinicians and pathologists, and the actual consequences. While in some grafts a severe acute rejection may develop within a period of 24 h, and may thus be missed by weekly monitoring, in other grafts findings suggestive of rejection in the FNAB will have to await clinical signs of rejection before therapeutic measures are indicated. In a study in which renal allografts were monitored by FNAB during the period of conversion from cyclosporin treatment to azathioprine and prednisolone at six months after transplantation, Ubhi et al. found an increased TCI at some stage in more than 50% of the grafts, while in only 16.6% of patients did overt rejection occur [11].
Exit-site infection—is there an alternative to catheter removal?

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Continuous ambulatory peritoneal dialysis (CAPD) has gained wide acceptance as a treatment modality of end-stage renal failure. However, peritonitis and loss of the peritoneal catheter due to infection continue to be the major drawbacks of this technique. Coexisting exit-site infection (ESI) and/or tunnel infection is shown to be one of the variables (as well as advanced age, long duration of peritonitis, infection caused by Pseudomonas or fungi, elevated aspartateaminotransferase, and malnutrition) associated with catheter removal during peritonitis [1]. The leading causes of catheter infections and catheter losses in patients on CAPD are Staphylococcus aureus strains, touch contamina-tions and colonizations at the exit site, with subsequent periluminal spread of bacteria into the peritoneal cavity seeming to be the operative pathogenic events [2].

In 1984 the National CAPD Registry at National Institutes of Health (NIH) reported that 40% of the patients develop exit-site infection (ESI) during the first year and that about 50% of these patients will probably lose their catheters during this period [3]. More recently the incidence of ESI was calculated to be 28–46% in the first year [4,5]. Medical treatment is successful in only 65–70% of the cases [4,5], and recurrence occurs in the majority of the cases, especially when purulent discharge is present [5]. In fact ESI is involved in the majority of the catheter removals, with a history of ESI being present in more than 80% of...