非血縁者間同種臍帯血移植後の造血系・免疫系再構築の検討

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研究要旨　臍帯血のドナープールの拡大と共に、臍帯血移植が成人でも高頻度に行われつつある。臍帯血移植の問題点として生着遅延、拒絶、免疫再構築があげられる。本研究では、移植後末梢血細胞亜分画のマイクロサテライトDNAを用いた高感度キメリズム解析とT細胞受容体β鎖CDR3領域のスペクトラタイピングにより造血系・免疫系再構築過程を検討した。その結果、生着症例では移植後21～28日で完全キメラとなっており、興味深いことに白血球生着前に微量末梢血を用いた解析でキメリズムを確認できた。また、亜分画のキメリズム解析は生着遅延、拒絶の予知と確認に重要であることも明らかとなった。T細胞受容体レパトワの解析では移植後1ヶ月で顕著な多様性の減少を認めた。

A．研究目的

臍帯血移植後の造血系・免疫系再構築過程を解析することで、臍帯血移植の大きな課題である生着遅延および拒絶を回避することを目指す。

B．研究方法

非血縁者間同種臍帯血移植症例より末梢血を採取し、免疫磁気ビーズ法でCD3、CD14/CD15、CD56亜分画に分けた後、4種理のマイクロサテライトDNAをプローブとしてPCR法によりcapillary electrophoresis法でキメリズム解析を行った。T細胞受容体レパトワ解析は24種類のT細胞受容体Vβに特異的なプライマーを用いてPCR後、サイズスペクトラタイピングにより行った。

C．研究成果

生着症例でのキメリズム解析では移植後21～28日目で完全キメラとなっていた。さらに、移植後14日目頃の白血球生着前（200～300/μl）であっても、キメリズム解析は可能であり、生着遅延あるいは拒絶を予知することができ、特にCD3陽性T細胞のキメリズムが重要であった。T細胞受容体レパトワは移植後1ヶ月で多様性の減少が顕著となりGVHDの出現とともに、特定のVβ3やVβ12などT細胞受容体を有するクローンが出現した。

D．考　察

成人における臍帯血移植後の生着遅延、拒絶、免疫系再構築過程を解析することは増加しつつあるこの分野において重要である。高感度キメリズム解析を白血球生着前に実施することで、生着遅延および拒絶を予知できることが明らかとなり、CD3陽性T細胞のキメリズムが重要であることが確認されたことの臨床的意義は大きい。今後、より早期に回復し、造血細胞の拒絶に密接な関連を有しているCD56陽性NK細胞のキメリズム解析も検討されるべきと考えられる。

T細胞受容体レパトワ解析では移植後1ヶ月目の多様性の減少が顕著であることより、従来の同種造血幹細胞移植と同様の結果が得られた。一方、GVHDを発症した症例では特定のT細胞受容体を有するT細胞の出現が認められ、この点に関しても同種骨髄あるいは同種末梢血幹細胞移植と類似した結果であった。しかし、その後の回復過程に関してはまだ不明であり、さらなる解析が必要とされる。この解析を通して、移植後のGVHDを含む種々の合併症の回避とその治療に有用な情報が提供されるものと考える。

E．結　論

臍血帯移植後の生着遅延および拒絶の予知に、白血球生着前CD3陽性T細胞のキメリズムが重要であることが確認された。さらに、臍血帯移植後T細胞受容体レパトワ解析は免疫系再構築と

種々の合併症との関連で重要であると考えられた。

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G．知的所有権の取得状況

1. 特許取得
   該当なし
2. 実用新案登録
   該当なし
3. その他
   該当なし

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平成15年度の本研究に当たってなされた研究業績のうち既発表または印刷中の原著論文、学会発表抄録、単行本を関連分野別に区別し、原則として英文、和文の順序で、それぞれを原著、抄録に整理し、班構成員名簿の記載順に配列した。

著者名のアンダーラインは本研究班の構成員を示し、通し番号の肩につけた＊印は抄録を示す。

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