

IgA-MM 患者血清双 M 蛋白分析与实验室指标检测对骨髓移植疗效预测价值研究

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摘要: **目的** 探讨 IgA 型多发性骨髓瘤 (IgA multiple myeloma, IgA-MM) 患者血清双 M 蛋白分析与实验室指标检测对骨髓移植疗效预测价值。**方法** 选择 2019 年 1 月~2022 年 1 月于中国人民解放军中部战区总医院收治的 60 例出现双 M 条带的 IgA-MM 患者为研究对象, 比较患者血清蛋白电泳及免疫固定电泳 (immunofixation electrophoresis, IFE) 图谱资料; 采用 2-巯基乙醇 (2-dimercaptoethanol, 2-DE) 处理 IgA-MM 双 M 蛋白带的血清, IFE 鉴定双 M 蛋白带; 比较两种双 M 蛋白类型患者免疫学试验指标, 包括免疫球蛋白 A (immunoglobulin A, IgA)、免疫球蛋白 G (immunoglobulin G, IgG)、免疫球蛋白 M (immunoglobulin M, IgM)、血清游离轻链 (serum free light chain, sFLC) 和本周蛋白 (Bence Jones protein, BJP); 并且比较二种双 M 蛋白类型患者的常规实验指标; 对两种 IgA 型双 M 蛋白血症骨髓瘤多发性骨髓瘤国际分期系统 (international staging system, ISS) 分期及疗效进行比较; 采用 Kaplan-Meier 法和 LOG-rank 检验分析两种双 M 蛋白类型的患者生存率。**结果** IFE 显示, 单克隆轻链型和 IgA 聚合体型为 IgA-MM 血清双 M 蛋白带的两种类型。单克隆轻链型患者相较于聚合体型 sFLC ($2\,970.14 \pm 876.82$ mg/L vs 118.68 ± 74.10 mg/L) 及 BJP (6.22 ± 3.01 g/L vs 0.55 ± 0.12 g/L) 水平更高, 差异具有统计学意义 ($t=21.684, 12.659$, 均 $P<0.05$); 单克隆轻链型患者相较于聚合体型血清 β_2 -微球蛋白 (β_2 -microglobulin, β_2 -MG) (7.88 ± 2.14 mg/L vs 4.65 ± 1.56 mg/L)、血清钙 (calcium, Ca) (2.64 ± 0.24 mmol/L vs 2.32 ± 0.20 mmol/L)、肌酐 (serum creatinine, Scr) (182.85 ± 64.23 μ mol/L vs 90.52 ± 42.20 μ mol/L) 水平升高 ($t=21.684, 120.659, 6.400, 5.193, 6.473$), 血红蛋白 (hemoglobin, Hb) (74.32 ± 19.44 g/L vs 90.75 ± 15.52 g/L)、清蛋白 (albumin, Alb) (28.42 ± 3.64 g/L vs 31.72 ± 4.96 g/L) 水平降低 ($t=3.386, 2.428$), 差异具有统计学意义 (均 $P<0.05$); 与 IgA 聚合体型患者相比, 单克隆轻链型患者 ISS 分期更高、疗效更低 ($t=11.827, 4.519$, 均 $P<0.05$); 生存分析结果显示, IgA 聚合体型相较于单克隆轻链型生存率更高 ($\chi^2=4.482, P<0.05$)。**结论** IgA 型双 M 蛋白的两种类型在疗效和预后不尽相同, 故鉴定 IgA-MM 双 M 蛋白带类型尤为重要。

关键词: 免疫固定电泳; 双 M 蛋白带; 免疫球蛋白 A; 多发性骨髓瘤

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Study on the Value of Serum Double M Protein Analysis and Laboratory Index Detection in Predicting the Curative Effect of Bone Marrow Transplantation in IgA-MM Patients

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Abstract: **Objective** To investigate the value of serum double M protein analysis and laboratory index detection in predicting the efficacy of bone marrow transplantation in patients with IgA multiple myeloma (IgA-MM). **Methods** Sixty IgA-MM patients with double M bands admitted to the General Hospital of the Central Theater Command of the Chinese People's Liberation Army from January 2019 to January 2022 were selected as the study objects. The chromatographic data of serum protein electrophoresis and immunofixation electrophoresis (IFE) were compared. Serum with double M protein bands of IgA-MM was treated with 2-dimercaptoethanol (2-DE), and the double M protein bands were identified by IFE. Immunological test indexes of patients with two double M protein types were compared, including immunoglobulin A (IgA), immunoglobulin G (IgG), immunoglobulin M (IgM), serum free light chain (sFLC) and Bence Jones protein (BJP). The conventional experimental indexes of patients with two types of double M protein were compared. The staging and efficacy of multiple myeloma in the international staging system (ISS) were compared between two IgA types of double-M proteinemic myeloma. Kaplan-Meier method and LOG-rank test were used to analyze the survival rate of patients with two types of double M protein. **Results** IFE

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showed that monoclonal light chain type and IgA polymeric type were two types of double M protein bands in IGA-MM serum. Monoclonal light chain patients had higher levels of sFLC (2970.14 ± 876.82 mg/L vs 118.68 ± 74.10 mg/L) and BJP (6.22 ± 3.01 g/L vs 0.55 ± 0.12 g/L) than the polymeric type patients ($t=21.684, 12.659$, all $P<0.05$). Compared with polymeric type patients, serum β 2-MG (β 2-microglobulin) (7.88 ± 2.14 mg/L vs 4.65 ± 1.56 mg/L), serum Ca (calcium) (2.64 ± 0.24 mmol/L vs 2.32 ± 0.20 mmol/L) and serum Creatinine (Scr) (182.85 ± 64.23 μ mol/L vs 90.52 ± 42.20 μ mol/L) of monoclonal light chain patients were increased ($t=21.684, 12.659, 6.400, 5.193, 6.473$), while the levels of Hb (Hemoglobin) (74.32 ± 19.44 g/L vs 90.75 ± 15.52 g/L) and Alb (albumin) (28.42 ± 3.64 g/L vs 31.72 ± 4.96 g/L) of monoclonal light chain patients were decreased ($t=3.386, 2.428$), with significant differences (all $P<0.05$). Compared with IgA polymerized type patients, monoclonal light chain type patients had higher ISS stage and lower curative effect ($t=11.827, 4.519$, all $P<0.05$). Survival analysis showed that the survival rate of IgA polymerized type was higher than that of monoclonal light chain type ($\chi^2=4.482$, $P<0.05$). **Conclusion** The two types of IgA-type double-M protein differed in efficacy and prognosis, so identifying the type of IgA-MM double M protein band may be particularly important.

Keywords: immunofixation electrophoresis; double M protein band; immunoglobulin A; multiple myeloma

多发性骨髓瘤 (multiple myeloma, MM) 是一种恶性克隆性疾病, 可合成分泌单克隆免疫球蛋白 (immunoglobulin Ig) 或其轻链, 引起骨骼疼痛、骨折等表现^[1]。研究发现 MM 患者在移植后可出现 Ig 同型转换和 (或) 寡克隆蛋白条带, 即为异常蛋白条带 (abnormal prtein band, APB), 若出现 APB, 则表示预后良好^[2], 其中, Ig 同型转换则为新出现的 M 蛋白^[3]。血清蛋白电泳与免疫固定电泳 (immunofixation electrophoresis, IFE) 常用于检测 M 蛋白水平, 往往用来评估疗效^[4-5]。研究发现, 经化学治疗和细胞移植后, IFE 图谱中会出现其他 APB^[6-7]。在蛋白电泳时, MM 具有“窄底高耸”的单 M 蛋白峰, 而 IgA 型多发性骨髓瘤 (IgA multiple myeloma, IgA-MM) 有些存在双 M 蛋白带^[8-9]。临床上 IgA-MM 易出现高黏滞综合征, 且预后较差, 因此, 本研究比较二种双 M 蛋白类型的 IgA-MM 患者实验室指标以及骨髓移植疗效预测, 为临床治疗提供一定的参考价值。

1 材料与方法

1.1 研究对象 选择 2019 年 1 月~2022 年 1 月于中国人民解放军中部战区总医院收治的 60 例出现双 M 条带的 IgA-MM 患者为研究对象。其中男性 46 例, 女性 14 例, 年龄 45~70 (52.57 ± 9.66) 岁。本研究经我院医学伦理委员会审核批准且患者及家属知情同意。纳入标准: ①所有 IgA-MM 患者诊断均符合《血液病诊断及疗效标准》^[10] IgA 型 MM 的诊断标准; ②年龄 18~80 岁; ③纳入本研究的 IgA-MM 患者在初诊时出现双 M 蛋白条带; ④临床资料完整。排除标准: ①精神病患者; ②不愿意配合者; ③临床资料不完善者。多发性骨髓瘤国际分期系统 (international staging system, ISS) 分期参考文献^[10]。

1.2 仪器与试剂 全自动生化分析仪 (型号 AU5800, 美国贝克曼库尔特公司); 全自动血液分析仪 (型号 XE-5000); 全自动特定蛋白分析仪 (型

号: BN II, 德国 Simens 公司); Invitrogen 蛋白电泳系统。

1.3 方法

1.3.1 临床资料收集: 患者于初诊时清晨空腹状态下采集静脉血 8ml, 进行指标检测。采用 BN II 全自动特定蛋白分析仪及其配套试剂检测 (免疫透射比浊法) IgA, IgG, IgM, 本周蛋白 (Bene Jone protein, BJP); 采用 AU5800- 全自动生化分析仪及其配套试剂 (酶速率法) 检测血清 β 2-微球蛋白 (β 2-microglobulin, β 2-MG)、乳酸脱氢酶 (lactic dehydrogenase, LDH)、血清游离轻链 (serum free light chain, sFLC)、C 反应蛋白 (C reactive protein, CRP)、血清钙 (calcium, Ca)、清蛋白 (albumin, Alb)、血肌酐 (serum creatinine, Scr)、总胆固醇 (total cholesterol, TC)、尿酸 (uric acid, UA)、三酰甘油 (triglyceride, TG)、D-二聚体 (D-dimer, D-D) 和纤维蛋白原 (fibrinogen, FIB)。采用 XE-5000 全自动血液分析仪及其配套试剂 (化学发光免疫分析法) 检测白细胞计数 (white blood cells, WBC)、血小板计数 (platelet, PLT)、血红蛋白 (Hemoglobin, Hb) 和骨髓浆细胞比例。

1.3.2 血清蛋白电泳与 IFE: IFE: 患者于初诊时在早晨空腹状态下采集静脉血, 经离心处理后分离血清, 在 300 μ l 待测血清中加入 100 μ l 1% (v/v) 的 2-巯基乙醇 (2-dimercaptoethanol, 2-DE), 充分混匀, 进行 IFE^[13], 具体操作严格按照说明书进行, 经检测后发现, 60 例患者出现的双 M 蛋白条带分为单克隆轻链型 ($n=16$) 和 IgA 聚合体型 ($n=44$) 两种类型。

血清蛋白电泳: 取 10 μ l 血清标本于加样梳在琼脂糖凝胶板上电泳, 干燥, 染色, 脱色, 烘干, 扫描。

1.3.3 疗效评价: 所有患者接受至少 4 个疗程的治疗, 疗效参照国际骨髓瘤工作组制定的 MM 疗效判

定标准^[12],分为严格的完全缓解(stringent complete remission, sCR)、完全缓解(complete remission, CR)、很好的部分缓解(very good partial remission, VGPR)、部分缓解(partial remission, PR)、病情稳定(stable disease, SD)和病情进展(progressive disease, PD);达到sCR, CR, VGPR和PR者为治疗有效,达到SD, PD者为治疗无效^[13]。

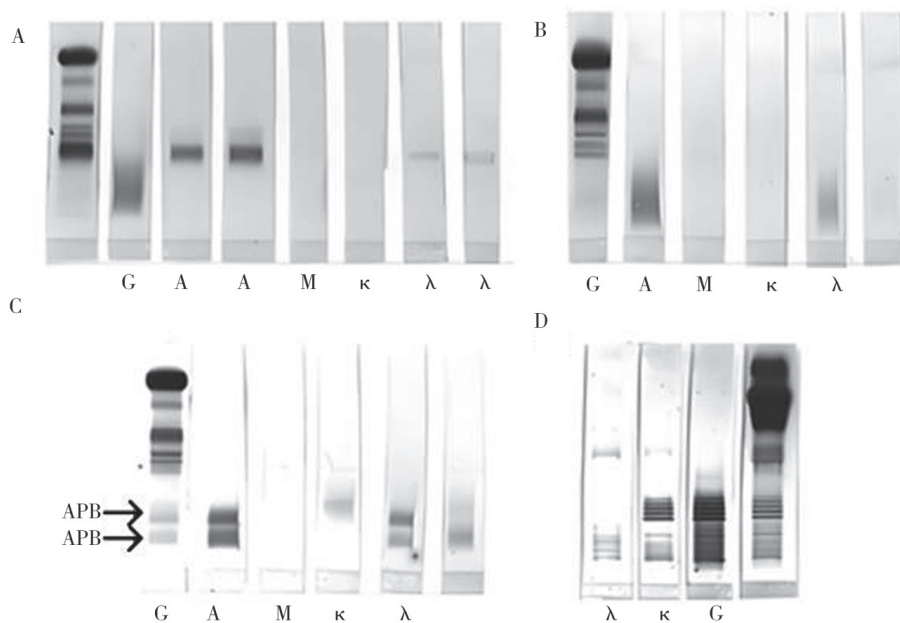
1.3.4 生存分析:以随访时间为横坐标、累计生存率为纵坐标绘制生存曲线,累计生存率50%所对应的生存时间为中位生存期。60例患者采取电话或门诊方式进行三年随访,随访时间均从治疗之日算起,随访终点为到达截止日期或患者死亡,60例患

者随访期内无失访。

1.4 统计学分析 利用SPSS 23.0统计软件进行数据统计分析,以均数 \pm 标准差($\bar{x}\pm s$)表示计量资料,采用 t 检验;使用百分数(%)表示计数资料,采用 χ^2 检验。生存分析采用Kaplan-Meier法,两种双M蛋白类型的患者生存率词语LOG-rank检验。 $P<0.05$ 为差异具有统计学意义。

2 结果

2.1 患者初诊时出现双M蛋白条带情况 见图1。以某王姓患者为例,初诊时出现Ig同型转换及寡克隆蛋白条带在血清蛋白电泳及IFE图谱的具体情况。

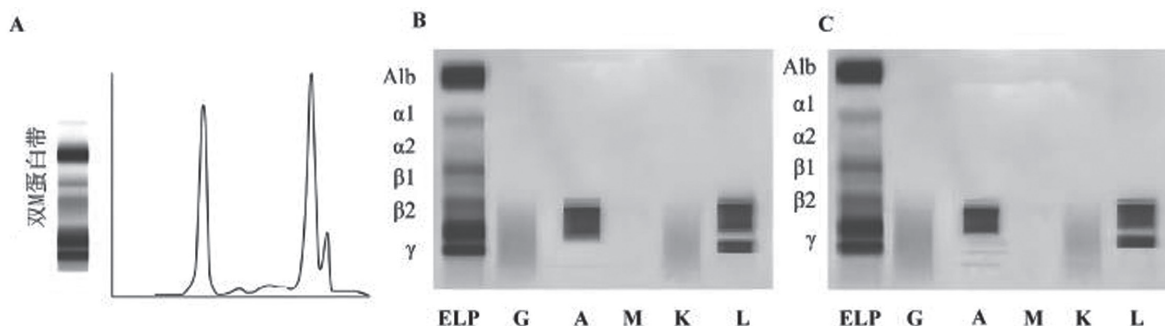


A为该病例初诊时异常蛋白类型为IgA λ ;B为APB消失;C为出现2条其他少量IgG;
D为经IFE图谱分析,新条带为单克隆IgG κ 及IgG λ 条带。

图1 患者初诊时出现双M蛋白条带图示

2.2 IgA-MM患者血清双M蛋白分析 经IFE可见,双M蛋白可分为单克隆轻链型(图2, $n=16$)和IgA聚合体型(图3, $n=44$):其中单克隆轻链型

由单体IgA和单克隆轻链组成,处理前后IFE图谱无变化;IgA聚合体型由IgA聚合体和IgA单体型组成,处理后,IFE图谱变成单M带。

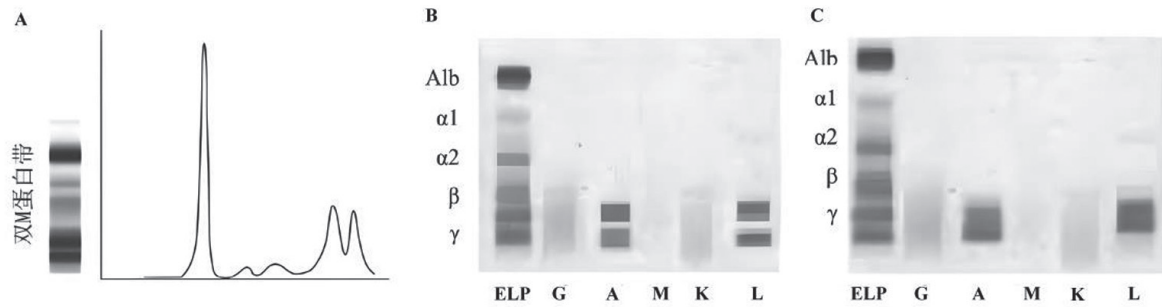


A为血清蛋白电泳;B为2-DE处理前IFE;C为2-DE处理后IFE。

图2 单克隆轻链型

2.3 两种不同类型双M蛋白骨髓瘤患者初诊时免疫学实验指标比较 见表1。单克隆轻链型患者

sFLC及BJP水平明显高于IgA聚合体型患者,差异具有统计学意义(均 $P<0.05$)。



A 为血清蛋白电泳；B 为 2-DE 处理前 IFE；C 为 2-DE 处理后 IFE。

图3 IgA 聚合型

表1 两种不同类型双 M 蛋白骨髓瘤患者初诊时

免疫学指标比较 ($\bar{x} \pm s$)

项目	单克隆轻链型 (n=16)	IgA 聚合型 (n=44)	t 值	P 值
IgG (g/L)	3.82 ± 2.30	4.25 ± 2.16	0.670	0.505
IgA (g/L)	28.57 ± 14.32	30.15 ± 16.63	0.337	0.737
IgM (g/L)	0.50 ± 0.22	0.61 ± 0.36	1.143	0.258
sFLC (mg/L)	2 970.14 ± 876.82	118.68 ± 74.10	21.684	<0.001
BJP (g/L)	6.22 ± 3.01	0.55 ± 0.12	12.659	<0.001

2.4 两种不同类型双 M 蛋白骨髓瘤患者初诊时常规实验指标比较 见表2。与 IgA 聚合型患者相比，单克隆轻链型患者 β 2-MG, Ca 和 Scr 水平明显高于 IgA 聚合型患者，Hb, Alb 水平明显低于 IgA 聚合型患者，差异具有统计学意义（均 $P < 0.05$ ），两种类型患者其余指标间比较差异无统计学意义（均 $P > 0.05$ ）。

表2 两种不同类型双 M 蛋白骨髓瘤患者初诊时

常规实验指标比较 ($\bar{x} \pm s$)

项目	单克隆轻链型 (n=16)	IgA 聚合型 (n=44)	t 值	P 值
β 2-MG (mg/L)	7.88 ± 2.14	4.65 ± 1.56	6.400	<0.001
LDH (U/L)	235.20 ± 45.47	228.36 ± 45.83	0.512	0.610
CRP (mg/L)	3.95 ± 0.21	4.18 ± 1.02	0.890	0.377
Ca (mmol/L)	2.64 ± 0.24	2.32 ± 0.20	5.193	<0.001
Hb (g/L)	74.32 ± 19.44	90.75 ± 15.52	3.386	0.001
Alb (g/L)	28.42 ± 3.64	31.72 ± 4.96	2.428	0.018
Scr (μ mol/L)	182.85 ± 64.23	90.52 ± 42.20	6.473	<0.001
UA (mmol/L)	342.17 ± 32.55	346.64 ± 30.43	0.494	0.623
TC (mmol/L)	4.12 ± 0.33	4.20 ± 0.54	0.554	0.581
TG (mmol/L)	1.24 ± 0.16	1.19 ± 0.14	1.178	0.244
WBC ($\times 10^9/L$)	11.76 ± 1.28	12.05 ± 1.32	0.758	0.451
PLT ($\times 10^9/L$)	157.95 ± 16.52	160.30 ± 18.17	0.453	0.652
FIB (g/L)	2.86 ± 0.31	3.02 ± 0.33	1.687	0.097
D-D (μ g/ml)	0.37 ± 0.04	0.40 ± 0.06	1.851	0.069
骨髓浆细胞比例 (%)	42.82 ± 9.21	39.26 ± 8.45	1.409	0.164

2.5 两种不同类型双 M 蛋白骨髓瘤患者 ISS 分期

及骨髓移植疗效比较 见表3。单克隆轻链型患者 ISS 分期明显高于 IgA 聚合型患者，疗效更差，差异具有统计学意义（均 $P < 0.05$ ）。

表3 两种不同类型双 M 蛋白骨髓瘤患者 ISS

分期及疗效比较 [n(%)]

类别	单克隆轻链型 (n=16)	IgA 聚合型 (n=44)	χ^2 值	P 值
ISS 分期 I	4 (25.00)	23 (52.27)	11.827	0.003
II	5 (31.25)	18 (40.91)		
III	7 (43.75)	3 (6.82)		
疗效 有效	11 (68.75)	40 (90.91)	4.519	0.034
无效	5 (31.25)	4 (9.09)		

2.6 生存曲线分析 见图4。生存分析结果显示，两种类型的中位生存期存在显著差异，IgA 聚合型生存率明显高于单克隆轻链型，差异有统计学意义（ $\chi^2=4.482$, $P < 0.05$ ）。

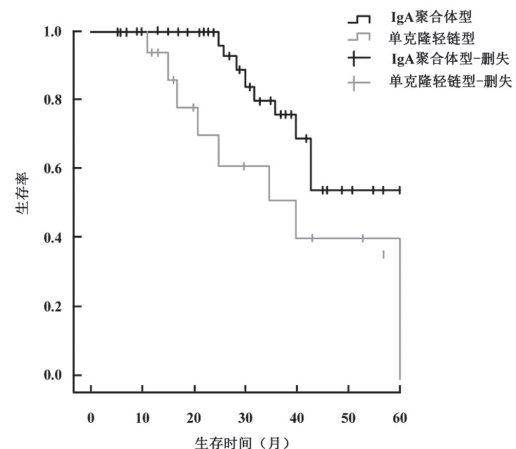


图4 单克隆轻链型与 IgA 聚合型双 M 蛋白患者生存分析

3 讨论

MM 作为一种恶性肿瘤，可产生单克隆免疫球蛋白或轻链蛋白（M 蛋白），发病率较高^[14]。通过检测 M 蛋白能够诊断 MM，而 M 蛋白的分型和鉴定往往采用 IFE^[15]。正常情况下，IgA 包括单体和二聚体，二聚体经 2-DE 处理后可分解成单体^[16]。MM 患者肿瘤细胞分泌的轻链 κ 或 λ 明显多于重

链,一部分轻链和重链形成完整的免疫球蛋白分子,另一部分未与重链结合的轻链,即为sFLC^[17]。正常人sFLC的量极少,通常在每升几毫克到十几毫克之间,当MM发生后,sFLC明显增多^[18]。既往研究^[19]表明,sFLC可能是产生于骨髓轻链亚克隆。免疫球蛋白由轻链和重链构成,sFLC异常增高表明Ig合成异常。这与本研究结果基本一致。相关研究^[20]表明,sFLC水平与MM病情及预后密切相关。近年来临床广泛开展sFLC检测,在MM诊断和治疗中发挥重要作用^[21-22]。BJP是游离的单克隆免疫球蛋白轻链,分 κ 和 λ 型,合成的轻链除了与重链形成完整的Ig分子外,约40%轻链呈游离状态,几乎全部从肾小球滤过^[23-25]。

此外, β 2-MG作为一种小分子球蛋白,分子质量为11800,广泛存在于体液中^[26]。与IgA聚合体型MM相比,轻链型MM反映肿瘤负荷的指标 β 2-MG增高明显,血钙水平较高,极易发生肾功能损害,提示轻链型MM患者预后较聚合体型患者差,本研究也有同样发现。轻链型MM患者会出现轻链明显多于重链的情况,可在血清中出现轻链型的M蛋白成分,过多的轻链从肾脏排出后,在尿中形成BJP,从而造成肾功能损伤^[27-28],这也是本研究中轻链型的Scr, β 2-MG比聚合体型有更明显升高的原因。文献显示MM患者机体内Hb水平会降低,易出现贫血^[29],本研究还发现单克隆轻链型患者Hb,Alb水平均显著低于IgA聚合体型患者,说明轻链型MM的Hb较IgA聚合体型MM减低更为明显,与既往研究^[30]相一致。Alb水平降低代表该类疾病患者预后不良^[31-33],Alb主要维持稳定的血液胶体渗透压^[34]。这与本研究结果基本一致。

除此之外,单克隆轻链型与IgA聚合体型ISS分期存在显著差异,相关研究^[35]发现,与IgA聚合体型MM相比,多数轻链型MM处于Ⅲ期。此外,本研究还发现两种类型MM有效率和生存率均存在显著差异。研究表明^[36],轻链型MM病情进展迅速,短期内全身多系统会受到损害,生存率明显降低。且有研究^[37]发现,轻链型患者骨髓移植后时常因同时累及心脏等其他脏器组织而出现损害,患者全身一般状况差,导致生存期降低。本研究基于IgA-MM患者的实验室指标的变化趋势,对骨髓移植疗效预测价值进行了探讨,为IgA-MM临床诊断以及评估预测骨髓移植疗效提供了价值参考。本研究局限性在于纳入的样本量较少,可能导致研究结果出现一定偏差,因此后续研究将继续扩大样本数作进一步研究。

综上所述,IgA型双M蛋白的两种类型在疗效和预后方面不尽相同,故鉴定IgA-MM双M蛋白

带尤为重要。

参考文献:

- [1] 蒋翔宁,陈俊峰,汪勇.血清游离轻链 κ/λ 比值联合免疫固定电泳在多发性骨髓瘤患者预后评估中的价值[J].中国实验血液学杂志,2020,28(1):191-195. JIANG Xiangning, CHEN Junfeng, WANG Yong. Value of serum free light chain Kappa/Lambda ratio detection combined with immunofixation electrophoresis in the prognosis evaluation of patients with multiple myeloma[J]. Journal of Experimental Hematology, 2020, 28(1): 191-195.
- [2] 范丽,马艳萍,晁瑶,等.老年多发性骨髓瘤肾损害患者的临床特征、预后及疗效分析[J].中国实验血液学杂志,2021,29(1):145-151. FAN Li, MA Yanping, CHAO Yao, et al. Clinical characteristic, prognosis and treatment outcome of elderly multiple myeloma patients with impaired renal function[J]. Journal of Experimental Hematology, 2021, 29(1): 145-151.
- [3] 喻垚,滕小娟,罗光丽,等.血清轻链在多发性骨髓瘤中的诊断及疗效评价中的价值[J].中国实验血液学杂志,2020,28(3):886-893. YU Yao, TENG Xiaojuan, LUO Guangli, et al. Value of serum light chain in diagnosis and evaluation of efficacy for multiple myeloma[J]. Journal of Experimental Hematology, 2020, 28(3): 886-893.
- [4] 蔡雨希,易呈凤,罗礼容,等.多发性骨髓瘤合并贫血患者的临床特征及危险因素分析[J].重庆医学,2021,50(4):577-581. CAI Yuxi, YI Chengfeng, LUO Lirong, et al. Analysis of clinical characteristics and risk factors of multiple myeloma combined with anemia[J]. Chongqing Medicine, 2021, 50(4): 577-581.
- [5] 张柳芸,向云会,李艳英,等.M蛋白在多发性骨髓瘤与淋巴瘤中的临床作用[J].中国实验血液学杂志,2022,30(4):1281-1285. ZHANG Liyun, XIANG Yunhui, LI Yanying, et al. Clinical role of M protein in multiple myeloma and lymphoma-review[J]. Journal of Experimental Hematology, 2022, 30(4): 1281-1285.
- [6] WHEELER R D, COSTA M V, CRICLOW A, et al. Case report: interference from isatuximab on serum protein electrophoresis prevented demonstration of complete remission in a myeloma patient[J]. Annals of Clinical Biochemistry, 2022, 59(2): 144-148.
- [7] THIRKETTLE S, RUSSELL J, WILSON S, et al. Implications for the monitoring of patients with multiple myeloma undergoing treatment with the anti-CD38 monoclonal daratumumab[J]. Annals of Clinical Biochemistry, 2020, 57(2): 178-181.
- [8] SCHNELLER A, ZOJER N, BOLOMSKY A, et al. Synergistic interaction between HDAC and MCL-1 inhibitors through downregulation of BCL-XL in multiple myeloma[J]. Haematologica, 2021, 106(9): 2516-2521.
- [9] PERES L C, HANSEN D K, MAURA F, et al. The

- knowns and unknowns of disparities, biology, and clinical outcomes in Hispanic and Latinx multiple myeloma patients in the U.S[J]. *Seminars in Oncology*, 2022, 49(1): 3-10.
- [10] 张之南, 沈悌. 血液病诊断及疗效标准 [M]. 3 版. 北京: 科学出版社, 2007.
ZHANG Zhinan, SHEN Ti. *Diagnosis and therapeutic effect criteria for hematological diseases*[M]. 3th Ed. Beijing: Science Press, 2007.
- [11] 龚盈盈, 闫晓爽, 王叶敏, 等. 多发性骨髓瘤患者的临床特征及预后因素分析 [J]. *中国实验血液学杂志*, 2021, 29(3): 772-780.
GONG Yingying, YAN Xiaoshuang, WANG Yemin, et al. Clinical features and prognostic factors of patients with multiple myeloma[J]. *Journal of Experimental Hematology*, 2021, 29(3): 772-780.
- [12] ENGELHARDT M, TERPOS E, KLEBER M, et al. European myeloma network recommendations on the evaluation and treatment of newly diagnosed patients with multiple myeloma[J]. *Haematologica*, 2014, 99(2): 232-242.
- [13] 杨光忠, 陈文明, 申曼, 等. BTd, MPT 方案序贯治疗新诊断的非移植多发性骨髓瘤患者的疗效分析 [J]. *白血病·淋巴瘤*, 2011, 20(6): 350-352.
YANG Guangzhong, CHEN Wenming, SHEN Man, et al. Sequential therapy of BTd and MPT regimen for the newly-diagnosed multiple myeloma patients no eligible for bone marrow transplantation[J]. *Journal of Leukemia & Lymphoma*, 2011, 20(6): 350-352.
- [14] LAI C, YING T, HO P J, et al. Successful kidney transplantation in a patient with stable multiple myeloma[J]. *Internal Medicine Journal*, 2020, 50(4): 492-494.
- [15] KOBARI L, AUCLAIR M, PIAU O, et al. Circulating cytokines present in multiple myeloma patients inhibit the osteoblastic differentiation of adipose stem cells[J]. *Leukemia*, 2022, 36(2): 540-548.
- [16] SUN Mengtian, CHENG Jingliang, REN Cuiping, et al. Differentiation of diffuse infiltration pattern in multiple myeloma from hyperplastic hematopoietic bone marrow: qualitative and quantitative analysis using whole-body MRI[J]. *Journal of Magnetic Resonance Imaging*, 2022, 55(4): 1213-1225.
- [17] SIM S, KALFF A, TUCH G, et al. The importance of frailty assessment in multiple myeloma: a position statement from the Myeloma Scientific Advisory Group to Myeloma Australia[J]. *Internal Medicine Journal*, 2023, 53(5): 819-824.
- [18] O'DONNELL E K, SHAPIRO Y N, YEE A J, et al. Quality of life, psychological distress, and prognostic perceptions in patients with multiple myeloma[J]. *Cancer*, 2022, 128(10): 1996-2004.
- [19] BANERJEE R, MIDHA S, KELKAR A H, et al. Synthetic control arms in studies of multiple myeloma and diffuse large B-cell lymphoma[J]. *British Journal of Haematology*, 2022, 196(5): 1274-1277.
- [20] 任梅, 石培民, 谢静, 等. 血清 CXCL9 和 IL-34 水平检测对多发性骨髓瘤患者的疗效监测及其预后价值 [J]. *现代检验医学杂志*, 2023, 38(5): 127-132.
REN Mei, SHI Peimin, XIE Jing, et al. Serum CXCL9 and IL-34 levels in multiple myeloma patients for monitoring efficacy and prognostic value[J]. *Journal of Modern Laboratory Medicine*, 2023, 38(5): 127-132.
- [21] FACON T, VENNER C P, BAHLLIS N J, et al. Oral ixazomib, lenalidomide, and dexamethasone for transplant-ineligible patients with newly diagnosed multiple myeloma[J]. *Blood*, 2021, 137(26): 3616-3628.
- [22] LIU Jianfang, ZENG Piaoe, GUO Wei, et al. Prediction of high-risk cytogenetic status in multiple myeloma based on magnetic resonance imaging: utility of radiomics and comparison of machine learning methods[J]. *Journal of Magnetic Resonance Imaging*, 2021, 54(4): 1303-1311.
- [23] SCHEUBECK S, IHORST G, SCHOELLER K, et al. Comparison of the prognostic significance of 5 comorbidity scores and 12 functional tests in a prospective multiple myeloma patient cohort[J]. *Cancer*, 2021, 127(18): 3422-3436.
- [24] HOU Yi, KUANG Wenbin, MIN Wenjian, et al. Design, synthesis, and biological evaluation of icaritin derivatives as novel putative DEPTOR inhibitors for multiple myeloma treatment[J]. *Journal of Medicinal Chemistry*, 2021, 64(20): 14942-14954.
- [25] ER J, ROUTLEDGE D, HEMPTON J, et al. Autologous stem cell transplantation in elderly multiple myeloma patients aged ≥ 65 years: a two-centre Australian experience[J]. *Internal Medicine Journal*, 2021, 51(2): 280-283.
- [26] USMANI S Z, GARFALL A L, VAN DE DONK N W C J, et al. Teclistamab, a B-cell maturation antigen \times CD3 bispecific antibody, in patients with relapsed or refractory multiple myeloma (MajesTEC-1): a multicentre, open-label, single-arm, phase 1 study[J]. *Lancet*(London,England), 2021, 398(10301): 665-674.
- [27] PAWLYN C, LOEHR A, ASHBY C, et al. Loss of heterozygosity as a marker of homologous repair deficiency in multiple myeloma: a role for PARP inhibition?[J]. *Leukemia*, 2018, 32(7): 1561-1566.
- [28] SOH K T, WALLACE P K. Evaluation of measurable residual disease in multiple myeloma by multiparametric flow cytometry: current paradigm, guidelines, and future applications[J]. *International Journal of Laboratory Hematology*, 2021, 43 (Suppl 1): 43-53.
- [29] 高晓云, 马艳萍, 晁瑶, 等. IgD 型多发性骨髓瘤患者临床特征及生存分析 [J]. *中国实验血液学杂志*, 2021, 29(2): 547-552.
GAO Xiaoyun, MA Yanping, CHAO Yao, et al. Clinical characteristics and survival analysis of patients with IgD multiple myeloma[J]. *Journal of Experimental Hematology*, 2021, 29(2): 547-552.

- 资质审核管理[J]. 医疗装备, 2021, 34(9): 60-62.
- WANG Jingyi, TIAN Shuang. Management of procurement qualification auditing of domestic in-vitro diagnostic reagents[J]. Chinese Journal of Medical Device, 2021, 34(9): 60-62.
- [15] 孙晶晶, 郭蕾, 蔡军, 等. 体外诊断试剂院内管理的风险分析与控制[J]. 中国医学装备, 2021, 18(5): 140-143.
- SUN Jingjing, GUO Lei, CAI Jun, et al. Risk analysis and control of in-hospital management of in vitro diagnostic reagents[J]. China Medical Equipment, 2021, 18(5): 140-143.
- [16] 陆锦贵. 浅谈供应链管理模式的 IVD 试剂质量监管[J]. 现代医院管理, 2021, 19(2): 26-29.
- LU Jingui. Discussion on quality supervision of IVD reagent in supply chain management mode[J]. Modern Hospital Management, 2021, 19(2): 26-29.
- [17] 贾昱晞, 周伟, 方沅湘, 等. 基于供应商绩效评价体系的体外诊断试剂精细化管理[J]. 中国卫生产业, 2021, 18(15): 190-193, 198.
- JIA Yuxi, ZHOU Wei, FANG Yuanxiang, et al. Refined management of in vitro diagnostic reagents based on supplier performance evaluation system[J]. China Health Industry, 2021, 18(15): 190-193, 198.
- [18] 曹群, 周伟, 方沅湘, 等. 医改背景下医院试剂供应商动态分级管理策略研究[J]. 中国医院, 2020, 24(12): 77-78.
- CAO Qun, ZHOU Wei, FANG Yuanxiang, et al. Research on the dynamic hierarchical management strategy of hospital reagent suppliers under the background of medical reform[J]. Chinese Hospitals, 2020, 24(12): 77-78.
- [19] 周伟, 贾昱晞. 医院试剂管理体系建设及质量控制[J]. 中国医疗管理科学, 2021, 11(6): 47-50.
- ZHOU Wei, JIA Yuxi. Hospital reagent management system construction and quality control [J]. China Medical Administration Sciences, 2021, 11(6): 47-50.
- [20] 徐晓辉, 高朦, 张伟, 等. 全周期可追溯试剂管理系统的设计与应用[J]. 中国数字医学, 2020, 15(6): 50-52.
- XU Xiaohui, GAO Meng, ZHANG Wei, et al. Design and application of the full-cycle traceable reagent management system[J]. China Digital Medicine, 2020, 15(6): 50-52.
- [21] 刘斌, 顾伟, 成月佳, 等. 基于多货主的体外诊断试剂二级库管理模式的探索[J]. 中国医疗设备, 2022, 37(5): 119-123.
- LIU Bin, GU Wei, CHENG Yuejia, et al. Exploration of the management mode of the secondary storeroom of in vitro diagnostic reagents based on multi-consignor[J]. China Medical Devices, 2022, 37(5): 119-123.

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- [30] 陈明真, 张学亚, 王美娥, 等. 多发性骨髓瘤患者血脂指标水平及预后意义[J]. 中国实验血液学杂志, 2022, 30(4): 1162-1169.
- CHEN Mingzhen, ZHANG Xueya, WANG Meie, et al. Serum lipid levels and their prognostic significance in patients with multiple myeloma[J]. Journal of Experimental Hematology, 2022, 30(4): 1162-1169.
- [31] 马柯娃, 孙超, 李建勇, 等. 多发性骨髓瘤预后因素的研究进展[J]. 中国实验血液学杂志, 2021, 29(4): 1346-1350.
- MA Kewa, SUN Chao, LI Jianyong, et al. Research progress on prognostic factors of multiple myeloma-review[J]. Journal of Experimental Hematology, 2021, 29(4): 1346-1350.
- [32] 何人可, 王欣, 罗小华, 等. 自体造血干细胞移植治疗多发性骨髓瘤 53 例的疗效评价及预后因素分析[J]. 第三军医大学学报, 2021, 43(6): 553-559.
- HE Renke, WANG Xin, LUO Xiaohua, et al. Efficacy and prognostic factors of autologous hematopoietic stem cell transplantation for multiple myeloma: clinical analysis of 53 cases[J]. Journal of Third Military Medical University, 2021, 43(6): 553-559.
- [33] ŠEGULJA D, ŠPARAKL T, ROGIĆ D. Applied capillary electrophoresis system affects screening for monoclonal gammopathy in serum: verification study of two eight-capillary systems[J]. Scandinavian Journal of Clinical and Laboratory Investigation, 2022, 82(2): 85-89.
- [34] KONISHI Y, SKLAVENTIS-PISTOFIDIS R, YUE Hong, et al. Attenuated response to SARS-CoV-2 vaccine in patients with asymptomatic precursor stages of multiple myeloma and waldenstrom macroglobulinemia[J]. Cancer Cell, 2022, 40(1): 6-8.
- [35] DECHOW T, ALDAOUD A, BEHLENDORF T, et al. Pomalidomide plus dexamethasone for patients with relapsed or refractory multiple myeloma: final results of the non-interventional study POSEIDON and comparison with the pivotal phase 3 clinical trials[J]. European Journal of Haematology, 2022, 108(2): 133-144.
- [36] RI M, IIDA S, MARUYAMA D, et al. HLA genotyping in Japanese patients with multiple myeloma receiving bortezomib: an exploratory biomarker study of JCOG1105 (JCOG1105A1)[J]. Cancer Science, 2021, 112(12): 5011-5019.
- [37] 李喆琪, 田卫伟, 郭雅芳, 等. 血清游离轻链比值及治疗后比值正常化对初诊多发性骨髓瘤患者诊断及预后的影响[J]. 中国实验血液学杂志, 2020, 28(4): 1245-1250.
- LI Zheqi, TIAN Weiwei, GUO Yafang, et al. Effect of serum free light chain ratio and normalization ratio after treatment on diagnosis and prognosis of patients with newly diagnosed multiple myeloma[J]. Journal of Experimental Hematology, 2020, 28(4): 1245-1250.

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