別紙様式第2-1

No. 15

医薬品 研究報告 調査報告書

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一般的名称	人全血液	研究報告の公表状況	ABC Newsletter, No. 38. 2008 Oct 17.	公表国
販売名(企業名)	人全血液-LR「日赤」(日本赤十字社) 照射人全血液-LR「日赤」(日本赤十字社)			イタリア

研究報告の概要

○イタリアで久々に発生したWNV症例

2008年、イタリアで久々にヒトのウエストナイルウイルス(WNV)脳炎が2例報告された。

1例目は、最近ウマ(6例)のWNV確定症例およびトリ(13例)のWNV陽性が特定されているフェラーラとボローニャの間に位置する農村地帯在住の80歳代の女性患者である。患者に渡航歴はなく、9月5日に発熱および複数回の嘔吐を発症した後、高熱、嘔吐、意識障害、幻覚を呈し、9月19日にイモラの病院に入院したが救急室で痙攣状態となった。その後回復したが、ELISAによるWNV特異抗体検査で急性WNV感染が示され、さらに追加検査によりWNV特異抗体が確認された。10月9日のユーロサーベイランスレポートは、検査結果はWNVに対する抗体反応であり、WNV神経侵襲性感染の仮説を裏づけると述べている。患者の家から2、3km以内の場所には、数種類の鳥類集団が生息し、蚊(イエカ、ヒトスジシマカ)が発生している大きな沼がある。

神経浸襲性WNV疾患の2例目は、フェラーラ在住の60歳代後半の男性で、10月3日にボローニャで特定された。患者は、高熱を伴う急性髄膜脳炎の症状を発現し、血清および脳脊髄液検体はWNV特異IgG、IgM抗体陽性で、2回の血清RT-PCR検査は陽性だった。

WNV髄膜脳炎の積極的サーベイランスプログラムが開始され、当該地域で供血者スクリーニング用核酸増幅検査が導入された。また、イタリアの国立血液センターは、全血液センターに対し、当該地域に1日以上滞在したことのある供血者を28日間供血延期とするように指導した。

報告企業の意見	今後の対応
2008年、イタリアで久々にヒトのウエストナイルウイルス(WNV)脳炎が2例報告されたため、WNV髄膜脳炎の積極的サーベイランスプログラムが開始され、供血者スクリーニング用核酸増幅検査の導入、28日間供血延期措置がとられたとの報告である。	日本赤十字社では、輸血感染症対策として問診時に海外渡航歴の有無を確認し、帰国(入国)後4週間は献血不適としている。また、ウエストナイルウイルス感染の発生に備え、平成17年10月25日付血液対策課発事務連絡に基づき緊急対応の準備を進めている。今後も引き続き情報の収集に努める。

使用上の注意記載状況・その他参考事項等

人全血液-LR「日赤」
照射人全血液-LR「日赤」

血液を介するウイルス、細菌、原虫等の感染
vCJD等の伝播のリスク

19

WNV Case in Italy is First There in Many Years

Two human cases of West Nile Virus (WNV) encephalitis have been reported in Italy in the last month, the first human cases in that country in many years.

On September 20, the laboratory of the Regional Reference Center for Microbiological Emergencies in Bologna, Italy, reported the detection of specific IgM and IgG antibodies against WNV in the serum of a female patient in her 80s who lives in a rural area between Ferrara and Bologna.

Six confirmed cases of WNV disease in horses have recently been reported in this area, and 13 birds (six crows and seven magpies) have been identified as positive for WNV. Subsequently, an active surveillance program for possible human cases of WNV meningoencephalitis began.

> **Nucleic acid amplification testing has been introduced for blood donor screening in the provinces of Bologna and Ferrara. The Italian National Blood Center also has instructed all blood centers to defer for 28 days donors who have been for at least one night in the subject areas.**

No Travel Reported. The patient had fever and repeat vomiting episodes on September 5. A first diagnosis of suspected urinary tract infection was made and the patient was given medication, but the symptoms remained and the patient was admitted to an Imola hospital on September 19 with high fever, vomiting, impaired consciousness, and hallucinations. The patient went into convulsions in the emergency room. She has regained consciousness and has almost completely recovered, though she remains hospitalized as a safety precaution.

Serum samples were tested for WNV-specific antibodies using an enzyme-linked immuno-sorbent assay, which indicated an acute WNV infection. WNV-specific antibodies were further confirmed by additional serological tests on the first samples. The samples were tested for Japanese encephalitis virus (JEV) and tick-borne encephalitis virus (TBEV). "Results clearly demonstrated that the antibody response was mainly directed against WNV, thus corroborating the hypothesis of a WNV neuroinvasive infection," according to the *Eurosurveillance Report* (10/9/08).

The patient's relatives reported that she had not traveled outside the small village where she has lived for the past two years. The patient's home is located within a few kilometers from a large swamp that is home to a sizeable population of different bird species and is infested by mosquitoes (both *Culex* and *Aedes albopictus*).

A second human case of WNV neuroinvasive disease was identified in Bologna on October 3 – a man in his late 60s who lived in the province of Ferrara where WNV-positive horses and birds have recently been identified. The patient suffered from symptoms of acute meningoencephalitis with high fever. Serum and cerebrospinal fluid samples of this patient have tested positive for IgG and IgM antibodies against WNV and two different RT-PCRs performed on the serum were positive, though confirmatory laboratory testing was still pending.

WNV has been reported in Europe, the Middle East, Africa, India, parts of Asia, and Australia. Human WNV disease has been reported in the Mediterranean Basin: in Algeria in 1994, Morocco in 1996, Tunisia in 1997 and 2003, Romania in 1996 through 2000, the Czech Republic in 1997, Israel in 1999 and 2000, Russia in 1999 through 2001, and France in 2003. Enzootics involving horses were reported in Morocco in 1996 and 2003, Italy in 1998, Israel in 2000, and southern France in 2000, 2003, and 2004. (Sources: *Eurosurveillance Report*, 10/9/08; European Commission response to European Blood Alliance query, 10/6/08) ♦

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No. 22

医薬品 研究報告 調査報告書

識別番号・報告回数			報告日	第一報入手日	新医薬品等の区分	総合機構処理欄
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一般的名称	人全血液	研究報告の公表状況	Furtner M, Gelpi E, Kiechl S, Knoflach M, Zangerl A, Gotwald T, Willeit J, Maier H, Ströbel T, Unterberger U, Budka H. J Neurol Neurosurg Psychiatry. 2008 Feb;79(2):229-31.	公表国
販売名(企業名)	人全血液-LR「日赤」(日本赤十字社) 照射人全血液-LR「日赤」(日本赤十字社)			オーストリア

研究報告の概要

○ヒト成長ホルモンによる治療22年後に発症した医原性クロイツフェルト・ヤコブ病、臨床および放射線学的特徴
医原性のクロイツフェルト・ヤコブ病(iCJD)の多くは、プリオンに汚染されたヒト成長ホルモン(hGH)製剤の投与によるものである。
患者は、11歳でクッシング症候群と診断され、1984年9月から1985年11月まで死体から採取し市販用に製造されたhGH(クレスコモン、カビ社、現在は製造中止)の投与を受けていた。
2007年、神経学的兆候により入院後、状態は急速に悪化し、集中的な理学療法と言語療法にもかかわらず、患者は4ヵ月後に死亡した。
組織学的検査で海綿状の変化、神経細胞脱落、グリオーシスの特徴を示し、免疫組織学的検査は特異的なプリオン蛋白の沈着が見られた。医原性のリスクが認められたため、WHOの基準に従い確定iCJDに分類された。プリオン蛋白遺伝子(PRNP)には既知の突然変異は認められず、患者はPRNPコドン129、メチオニンホモ接合体であった。
疾患発症後の1、2、3ヵ月目に実施したMRIによる連続造影上の変化は、海綿状の変性を示しており、拡散強調画像の偽正常化は進行性の細胞死と関連していると推察された。
hGH投与22年後におけるCJD発症は、英国における一連のhGH-iCJD試験で推計された暴露後およそ20年というリスクのピークと一致する。
本症例は、hGHを投与された患者としては、オーストリアにおける初のCJD症例である。

報告企業の意見	今後の対応
ヒト(死体)由来のヒト成長ホルモン(hGH)製剤の投与を受けた患者が、22年後にクロイツフェルト・ヤコブ病を発症し、4ヵ月後に死亡し、確定医原性CJDに分類されたとの報告である。 なお、日本においては1995年以降には、すべてリコンビナントヒト成長ホルモン製剤に切り替わった。	日本赤十字社では、CJDのリスクのある血液を排除する目的から、献血時にhGH製剤投与の有無を確認し、該当するドナーを無期限に献血延期としている。今後もCJD等プリオン病に関する新たな知見及び情報の収集に努める。

使用上の注意記載状況・その他参考事項等

人全血液-LR「日赤」
照射人全血液-LR「日赤」

血液を介するウイルス、細菌、原虫等の感染
vCJD等の伝播のリスク

⑩

A novel mutation (c.64_65delGGinsAACC [p.G21fsX66]) in the *GTP cyclohydrolase 1* gene that causes Segawa disease

DYT5 dystonia (Segawa disease) is an autosomal-dominant inherited progressive dystonia that is evoked by mutations/deletions of the *GTP cyclohydrolase 1* (*GCH1*) gene,[1–5] which codes for the rate-limiting enzyme of tetrahydrobiopterin (BH_4) synthesis. Segawa disease is a rare disorder with an estimated prevalence of 0.5 per million. We report a clinical course caused by a novel mutation of the *GCH1* gene in a 25-year-old Caucasian female presenting in our outpatient clinic. The patient was born to healthy parents with no history or signs of neurological diseases. She described the development of a gait disturbance beginning at the age of 5 years. She was increasingly unable to walk at her soles, but was only walking at the outer edges of her feet (*pedes equinovarus*), causing a monstrous callus, within years. The feet cramped after only a few steps, which was relieved after some rest. Several stays in hospital did not reveal the final diagnosis, so that the gait disturbance was initially classified as a psychogenic disorder. The patient was then introduced to our movement disorder outpatient clinic just before an operation of the feet abnormalities. Clinical examination showed focal crampi of both feet with relevant relief only by inactivity. The feet were severely adducted and suppinated. Neurophysiological examinations, including somatosensory and magnetic-evoked potentials, were normal. A magnetic resonance imaging scan of the cervical and thoracic spine revealed only a short hydromyelia with no signs of inflammation or neoplasma. Analyses of the biogenic amines and pterins in the cerebrospinal fluid, according to the methods of Curtius and Hyland,[4 5] revealed highly decreased dopamine (homovanillic acid 48 nmol/l; normal values: 115–455) and serotonine metabolites (5-hydroxyindoleacetic acid 20 nmol/l; normal values: 51–204). Similarly, all pterines were markedly reduced (tetrahydrobiopterin: below detection level [normal value: 18–53 nmol/l]; total neopterin: 6 nmol/l [normal value: 10–31]). Folate metabolites were normal. To confirm the diagnosis of Segawa disease, GTP-cylcohydrolase I (GTPCH) enzyme activity was determined in skin fibroblasts according to Bonafé *et al.*,[6] which showed only 34% activity (0.99 µU/mg protein) compared with healthy controls (reference value: 2.6±0.53 µU/mg protein). Treatment with low doses of levodopa was capable of resolving the symptoms completely. Sequencing of exons 1–6 of the *GCH1* gene revealed a heterozygous deletion of two guanines at positions 64 and 65 and an insertion of 4 bases (AACC; fig 1), leading to a frameshift from amino acid 21 and subsequent termination of the protein after amino acid 66 within exon 1 (c.64_65delGGinsAACC [p.G21fsX66]). Multiplex ligation-dependent probe amplification (MRC, Amsterdam, The Netherlands) of the whole *GCH1* did not detect any further deletions. The clinically unaffected parents did not show any mutation in the *GCH1* gene (fig 1), confirming that the mutation in the patients represents a *de novo* mutation. This novel combined deletion-insertion mutation leading to protein truncation within exon 1 has not been reported before, despite up to more than 100 abnormalities of the *GCH1* gene being reported—including exon (start point change, missense, nonsense and frameshift mutations) and intron mutations, and deletions.

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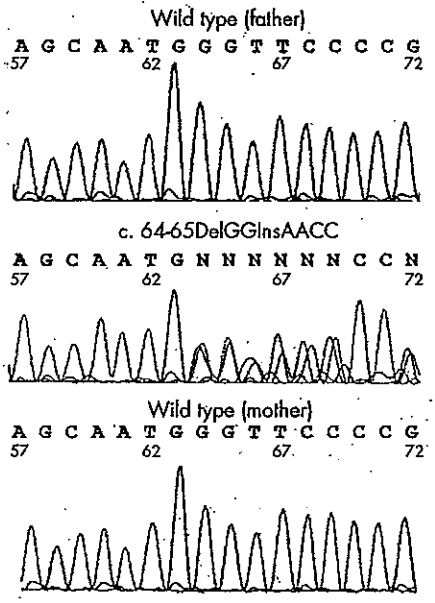

Figure 1 Genomic sequences of the index patient (middle panel) and both parents (father: upper panel; mother: lower panel), revealing a heterozygous deletion of two guanines at positions 64 and 65 and an insertion of the four bases AACC in the index patients, but wild-type sequences in both parents. The sequence abnormalities lead to a frame shift from amino acid 21 and subsequent termination of the protein after amino acid 66 within exon 1.

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Iatrogenic Creutzfeldt–Jakob disease 22 years after human growth hormone therapy: clinical and radiological features

Creutzfeldt–Jakob disease (CJD) is a human transmissible spongiform encephalopathy or prion disease. Although CJD is most frequently sporadic, numerous acquired or iatrogenic CJD (iCJD) cases have been reported, about half of which are attributable to prion-contaminated human growth hormone (hGH) preparations.[1] Cadaveric hGH was provided by public and commercial sources up to 1985, when recombinant GH became available. Incubation periods of hGH-iCJD peak at a median of 12 (range 5–30) years after exposure.[2 3]

We report the first Austrian case of hGH-associated autopsy-proven iCJD and discuss clinical features and serial magnetic resonance imaging (MRI) findings.

CASE REPORT

Clinical history

A 39-year-old man presented with right-sided clumsiness and dysaesthesia, which had started in his leg 3 weeks prior to admission and had spread to his right arm. No impairment of cognitive function and no involuntary movements were present. There was no family history of neurological disease. The patient had been healthy until the age of 11 years, when progressive obesity and growth impairment had been noticed and a diagnosis of Cushing syndrome had been made. The patient moved to Austria at the age of 15 years (1982) and was subsequently diagnosed with a hormone-producing pituitary adenoma, which was removed by transsphenoidal hypophysectomy. The frontal skull base defect was covered with

autologous connective tissue (fascia lata). Due to persistent Cushing syndrome symptoms, bilateral adrenalectomy was performed. To promote body growth (height <3rd percentile), he received commercially manufactured cadaveric hGH (Crescormon®, Kabi Pharma, now discontinued) from September 1984 (2 IU IM three times per week, which was later reduced to 2 IU IM twice a week). The treatment was continued until November 1985 and resulted in an increase of body height of 13.5 cm.

In 2003, a recurrency of the pituitary adenoma causing Cushing symptoms was diagnosed and transsphenoidal resection was performed, again with an autologous fascia lata graft.

On admission, the patient's neurological exam showed coarse bilateral gaze nystagmus, vertical gaze palsy and mild right-sided hemiparesis. Tendon reflexes in both lower extremities were exaggerated, whereas pyramidal signs were negative. Gait was paraspastic, with a deviation tendency to the right, but unaided walking was still possible. Cerebellar tests revealed bilateral ataxia in the upper and lower limbs and dysdiadochokinesia of both hands. Testing for infectious, parainfectious, as well as neoplastic or paraneoplastic neurological diseases, was negative, as was metabolic screening.

Serial cerebral MRI was performed in months 1, 2 and 3 (fig 1). Electroencephalographic recordings (EEGs) in months 1 and 2 showed diffuse slowing with generalized delta activity and intermittent rhythmic delta-theta runs with a right fronto-central accentuation. EEG in month 3 revealed further slowing and some non-periodic bilateral sharp/slow wave complexes.

Cerebrospinal fluid (CSF) examinations in week 1 and week 6 after admission exhibited divergent results. In the first sample, 14-3-3 protein was undetectable; protein content, as well as cytology, were normal. In the second CSF sample, a strong signal in the molecular weight range of the 14-3-3 protein was detected.

Neuropsychological examination 3 weeks after admission showed reduction of attentive functions, whereas memory was unimpaired. Over 3 months of hospitalization, the patients condition rapidly deteriorated. Myoclonus of both arms and legs emerged; the patient became bedridden after about 6 weeks. Speech was increasingly dysarthric, and severe dysphagia ensued. Hypostatic pneumonia required antibiotic treatment. Despite intensive physiotherapy and speech therapy, the patient's condition continued to worsen. The patient died after an overall disease course of 4 months.

Neuropathology

Histology showed the characteristic triad of spongiform change, neuronal loss and gliosis. Immunohistochemistry revealed characteristic prion protein deposits in cerebral and cerebellar cortices, confirming the diagnosis of CJD. Due to the recognised iatrogenic risk (hGH), the disease was classified as definite iCJD according to World Health Organization (WHO) criteria.[1] Western-blot analysis of proteinase K restistant PrP was not performed due to lack of adequate material.

Genetic analysis

Sequencing of the entire coding region of the prion protein gene (*PRNP*) performed after isolation of genomic DNA from peripheral blood showed no known mutations. The patient was methionine homozygous at codon 129 of the *PRNP*.

DISCUSSION

This case of definite iatrogenic CJD 22 years after hGH medication exhibits several noteworthy features.

MRI studies 1, 2 and 3 months after manifestation of disease revealed early bilateral cortical involvement of the mesial frontal lobes. Diffusion-weighted imaging (DWI) hyperintensities progressed to adjacent cortical areas and to the striatum, in line with clinical deterioration (fig 1). DWI has been recommended as the most sensitive test for early diagnosis of CJD,[5] but is not suggestive of a specific form of disease. HGH-iCJD cases have exhibited DWI hyperintensities mainly in the basal ganglia. Cerebellar malfunction is one of the most common early signs of iCJD after hGH treatment[1] and was one of the main clinical disturbances at disease onset in our patient. However, no corresponding MRI abnormalities were detected in the cerebellum. To our knowledge, no other hGH-iCJD case has been documented with early frontomesial DWI changes and progressive bilateral striate hyperintensities.

CSF 14-3-3 protein was negative on first testing and turned positive 4 weeks later. Of interest, DWI changes preceded CSF 14-3-3 protein conversion by weeks and had spread from the cortical distribution shown in figure 1A/B to a striatal DWI pattern that is commonly associated with sporadic CJD (fig 1B). It has been speculated that these changes on serial imaging indicate spongiform degeneration, but that the neurons are still viable in the early disease stages, and that a subsequent DWI pseudonormalization is related to progressive cell death.[6]

The clinical presentation, with paraspastic gait as one of the first striking features, also requires attention. This correlates well with the imaging findings and represents a bilateral parietal edge syndrome—that is, first motoneuron dysfunction in the leg areas of both precentral gyri.

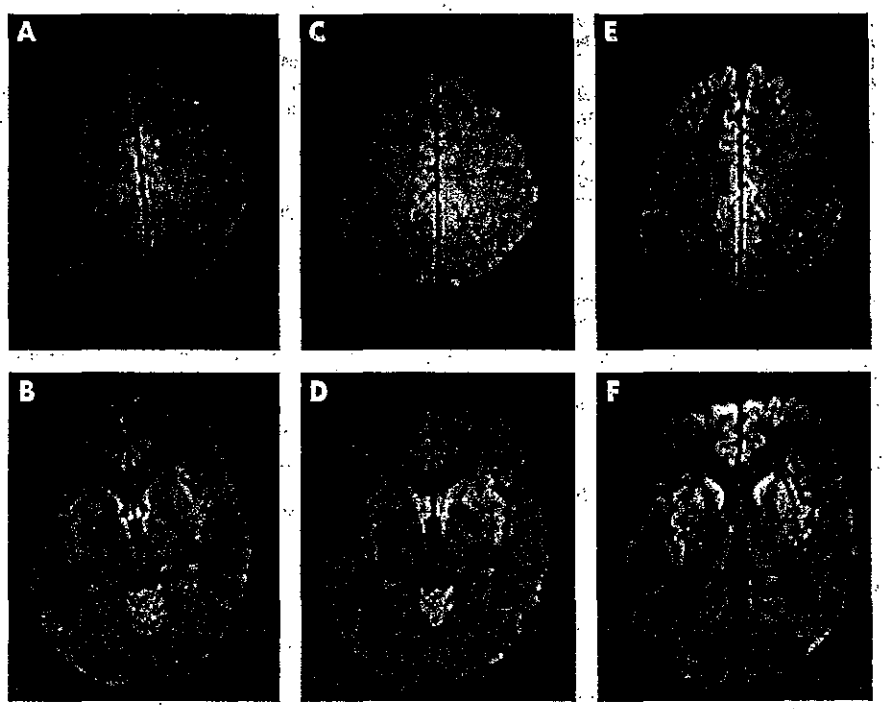

Figure 1 Magnetic resonance imaging (MRI) 1 month (panels A and B), 2 months (C, D) and 3 months (E, F) after onset. Diffusion weighted imaging (DWI) 1 month after onset revealed bilateral frontomesial hyperintensities (A), and moderate DWI signal increases in the medial portion of both caudate heads (B). Two months after onset, the bifrontal hyperintensities showed slight enlargement (C), and DWI signals were elevated in both caudate heads, the adjacent putamina and insular cortices (D). On follow-up MRI 1 month later, there was increased DWI signal in the frontomesial and frontopolar cortex (E,F) and marked DWI hyperintensity in both caudate heads, both putamina with accentuation in their rostral parts, and both insular ribbons (F). ADC maps and FLAIR images were inconspicuous (data not shown).

Occurrence of CJD 22 years after hGH administration is in line with the peak risk approximately 20 years after exposure calculated from a large hGH-iCJD series in the UK,[2] whereas the mean incubation period in French hGH recipients was considerably shorter at 9–10 years.[3] Differences of infectivity in hormone lots have been suggested as an explanation for this finding.

Some unusual circumstances and clinical features also deserve comment. First, iCJD associated with hGH has, so far, only been reported after administration of non-commercial hormone. The reports available, however, have excluded patients treated with commercially prepared hormone; hence, there are insufficient data on the CJD rate in these patients.[2 3] Second, the administration period of hGH and disease duration were both short for iCJD patients even though comparable cases have been reported in previous literature.[2 7]

In summary, this is the first CJD case from Austria in a patient having received hGH and only the third iatrogenic case detected in this country. The recognised iatrogenic risk (cadaveric hGH 22 years before onset) and the neuropathological confirmation of CJD meet the WHO criteria for definite iCJD, although the possibility of a sporadic methionine-homocygous juvenile CJD case without causal relation to hGH treatment cannot be definitely ruled out.

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APPENDIX

Histopathological examination

The total fixed brain weight was 1408 g. Macroscopically, moderate diffuse cerebral and cerebellar atrophy was observed. In addition, there were signs of diffuse oedema. On coronal sections, the cortical ribbon of the insular and parietal cortices was narrowed. Histology showed characteristic spongiform change, moderate neuronal loss and gliosis in cerebral cortex and basal ganglia (see Supplementary figure). The cerebellar cortex was severely affected with marked spongiform change of the molecular layer and neuronal loss of the granule cell layer (see Supplementary figure). The Purkinje cells and brain stem nuclei were comparatively better preserved. Immunohistochemistry using the antibody 12F10 (Cayman, Ann Arbor, Michigan, USA) revealed strong pathological prion protein (PrP^{sc}) deposits in cerebral and cerebellar cortices, and basal ganglia in a diffuse synaptic pattern (see Supplementary figure). In the brain stem nuclei, only discrete PrP^{sc} deposits were demonstrable. There were no PrP^{sc} plaques neither in the cerebellum nor in the cerebral cortex or white matter. These features confirmed the diagnosis of Creutzfeldt–Jakob disease (CJD). Due to the recognised iatrogenic risk (due to human growth hormone), the disease was classified as definite iatrogenically transmitted CJD, according to World Health Organisation criteria.

Skin reactions after intramuscular injection of Botulinum toxin A: a rare side effect

The use of Botulinum toxin (BTX) has been constantly increasing over the past years, not least on account of obtaining the license for the treatment of facial lines. It has proven a safe drug with only a few adverse effects. Local irritations at the injection site are not uncommon, whereas more widespread and generalised exanthemas were first described in 1992.[1] One dramatic case documents a lethal outcome due to treatment with a mixture of BOTOX® (BTX-A) and lidocaine.[2] In accordance with databases from the companies Allergan and Ipsen (SPC BOTOX®, Allergan, December 2005; SPC, DYSPORT®, Ipsen Pharma, April 2006), skin reactions seem to be a rare phenomenon with a frequency of less than 1:1,000. The Ipsen database (January 2007) mentions 5 cases of local and 4 cases of more widespread redness, bulging and pruritus in Germany, as well as 11 cases abroad. Here, we report on two further cases of rapid-onset skin reactions after injection of two different BTX-A products.

CASE 1

A 49-year-old woman developed a left-sided spastic hemiparesis after cavernoma exstirpation in 1997. Successful treatment of the spastic arm muscles was carried out with BOTOX® for about 5 years and with DYSPORT® for the last 4 years. She did not receive any other medication. Injection intervals ranged from 3 to 9 months. During the treatment session in April 2006, we applied a total dose of 1,000 Units DYSPORT® (250 MU into the left biceps muscle, 250 MU into the left flexor pollicis longus and extensor carpi radialis muscles, 500 MU into the left flexor digitorum superficialis muscle). Within 6 hours after intramuscular injection of BTX-A, a segmental or "pseudosegmental" fine-spotted pruriginous exanthema emerged in the region of the entire left shoulder, arm and left breast. Fever or other additional symptoms did not occur. Allergological tests, such as prick tests, and an intracutaneous test were normal. Treatment with DYSPORT® was repeated 3 months later with a dose reduction of 50% without any adverse effects. At a later visit, she received 1,000 Units DYSPORT®, which was well tolerated.

CASE 2

A 63-year-old man presented with right-sided limb spasticity due to a stroke 7 years ago. The patient received a stable medication consisting of gabapentine, tramadole, tetrazepam, clopidogrel and atorvastatin. From 2003, he was successfully treated with injections of 900–1,100 Units DYSPORT® at regular intervals of 3 months. In 2006, the therapy was changed to BOTOX®. Within

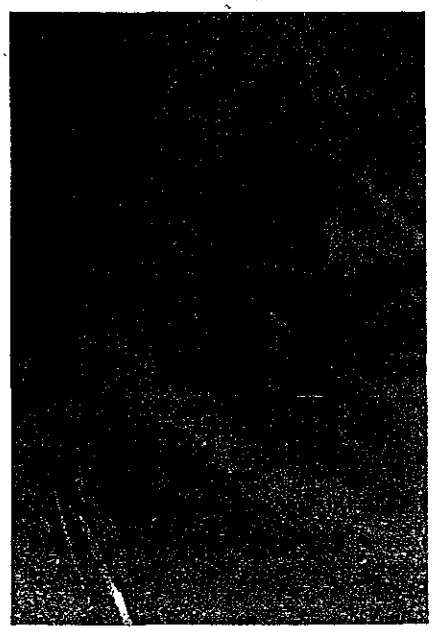

Figure 1 Photograph of the skin reaction as described in Case 2 about 1 hour after injection into the right brachial muscle. Informed consent was obtained for publication of this figure.

別紙様式第２－１

医薬品　研究報告 調査報告書

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研究報告の概要

重症筋無力症の治療として行ったアルブミンを交換液とした血漿交換の後に、パルボウイルス B19(以下「B19」)感染による赤芽球癆を発症した女性の症例を報告する。
アルブミン投与から 2 週間後に、患者は網状赤血球欠乏性貧血を発症し、骨髄穿刺を行ったところ、多数の巨大な前正赤芽球欠乏を伴う顕著な一連の低形成赤血球が示され、重度網状赤血球減少症を伴う貧血および骨髄の形態によって、B19 感染が原因の赤芽球癆が疑われ、IgM および IgG 型抗 B19 抗体により確認された。
患者は免疫グロブリン(0.4g/kg、4 日間)で治療したところ、貧血は徐々に回復した。
アルブミン、凝固因子、免疫グロブリンなどの血液製剤の感染性は除外できず、血液成分による B19 感染は依然未解明の問題である。
B19 はエンベロープを有さないウイルスであるため、溶媒－界面活性剤処理には抵抗性であるが、60℃で 10 時間低温殺菌すると迅速に不活化することを示したとの報告もある。
ウイルス不活化の新たな方法や B19 陽性単位の棄却などの多くの戦略は、血液製剤の安全性を増すのに有用である。

報告企業の意見	今後の対応
アルブミン投与後にパルボウイルス B19 感染が疑われた症例の報告である。 当社血漿分画製剤は最終製品において NAT 検査を行い、パルボウイルス B19DNA 陰性であることを確認している。	今後ともパルボウイルス B19 に関する血漿分画製剤の安全性に関する情報に留意していく。

使用上の注意記載状況・その他参考事項等

慎重投与(次の患者には**慎重**に投与すること)
・溶血性・失血性貧血の患者〔ヒトパルボウイルスＢ19 の感染を起こす可能性を否定できない。感染した場合には、発熱と急激な貧血を伴う重篤な全身症状を起こすことがある。〕
・免疫不全患者・免疫抑制状態の患者〔ヒトパルボウイルスＢ19 の感染を起こす可能性を否定できない。感染した場合には、持続性の貧血を起こすことがある。〕

重要な基本的注意
(1)本剤の原材料となる‥〔スクリーニング項目、不活化･除去工程〕‥投与に際しては、次の点に十分注意すること。
1)血漿分画製剤の現在の製造工程では、ヒトパルボウイルス B19 等のウイルスを完全に不活化・除去することが困難であるため、本剤の投与によりその感染の可能性を否定できないので、投与後の経過を十分に観察すること。

妊婦、産婦、授乳婦等への投与
妊婦又は妊娠している可能性のある婦人には治療上の有益性が危険性を上回ると判断される場合にのみ投与すること。〔妊娠中の投与に関する安全性は確立していない。本剤の投与によりヒトパルボウイルス B19 の感染の可能性を否定できない。感染した場合には胎児への障害（流産、胎児水腫、胎児死亡）が起こる可能性がある。〕