The Landry-Guillain-Barré Strohl Syndrome 1859 to 1992
A Historical Perspective

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ستحاول المقالة التالية مراجعة تاريخ وتطوير متلازمة غيلان باريه (غ.ب) ولاسيما معرفة الأشكال السريرية وخصائص السائل الدماغي الشوكي التي بدأها لا ندري عام ١٨٥٩ وباريه عام ١٩١٦. ثم تحديد الخصائص النسيجية والتي نشرت أساساً في ثلاثة أوراق لـ هاي ميكر وكيرنوهان ١٩٤٩ وواكسمان وآدمز ١٩٥٥ وأسباري وارناسون وأدمز عام ١٩٦٩.

وعلى الرغم من أن متلازمة غ.ب تعتبر آفة مناعية. إلا أن الآليات الامراضية المناعية المؤدية لإزالة النخاعين لم تحدد بدقة حتى الأن. ومن المحتمل أنها تؤثر على المستويين الخلوي والهرموني.

وقد تطورت أساليب المعالجة من التدليك الى المعالجة الداعمة وتبديل البلاسما وحقن الغلوبيولينات المناعية وريدياً. وعلى العموم. فإن الإنذار مهم كما تم تأكيد ذلك مراراً. وقد تم التعرف على الدلالات السريرية والكهربائية الفيزيولوجية التي تدعو لتوقع إنذار سيء.

The history of the development of knowledge about Guillain-Barré-Syndrome (GBS) is reviewed. The clinical profile, including characteristic CSF findings, were established by Landry in 1859 and Barré in 1916. Pathologic features of GBS were defined in three landmark papers by Haymaker and Kernohan in 1949, Waksman and Adams in 1955, and Asbury, Arnason and Adams in 1969. Although GBS is considered to be an immune-mediated disorder, the exact immune mechanism(s) leading to demyelination is not yet well established but probably involves both cellular and humoral responses. Treatment modalities have progressed from massages and volatile liniments used by Landry to anticipatory and supportive care, plasma exchange, and intravenous immunoglobulin. Outcome continues to be generally favorable as originally emphasized. Clinical and electrophysiologic predictors of unfavorable outcome have been identified.

Key Words: *Guillain-Barré Syndrome, Landry's Paralysis, Historical Perspective, Ascending Paralysis, AIDP*

INTRODUCTION

Peripheral neuropathy may result from either demyelinating or axonal disorders. The demyelinating neuropathies are either acquired or genetically determined. The acquired neuropathies include the acute inflammatory demyelinating polyneuropathy (AIDP, Guillain-Barré syndrome) and the chronic inflammatory demyelinating polyneuropathy (CIDP)[1]. The purpose of this manuscript is to review the history of development of knowledge about Guillain-Barré syndrome (GBS) from the time Landry described the first such use in 1859 to the present.

CLINICAL SYNDROME

Two landmark publications have established the clinical basis of the GBS[2,3]. Although similar cases may have been described before, Octave Landry[2] is credited with the first reported case of what later came to be known as the GBS. In 1859, Landry described a neurologic condition characterized by ascending motor paralysis with poor prognosis that he referred to as "ascending paralysis". Although literature reports emphasize the ascending type of motor paralysis, Landry originally described three types of presentations in ten patients. The first part of his historic article was devoted to a description of one

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patient with classical ascending type of motor paralysis without sensory signs or symptoms. In the second part of his article, Landry discussed nine other patients with three types of clinical picture: 1) ascending paralysis without sensory signs and symptoms, 2) ascending paralysis with concomitant ascending anesthesia and analgesia, and 3) progressive generalized polyradiculoneuritis. Landry searched for antecedent and associated conditions in exploring the etiology of the new condition he reported. He noted that "the paucity of facts makes it impossible to study the etiology of this process, but the circumstances in which it developed can be noted"[2]. The circumstances he observed included convalescence from acute illness, background of menstrual difficulties, exposure to cold, and convalescence from childbirth[2]. In one case with menstrual difficulties, leeches applied to the vulva led to recovery. In another case, menstrual difficulties during a "moral crisis" were followed by acute ascending paralysis[2]. Landry's contribution to medical literature ceased shortly after his 1859 report. He left academic pursuits[4] to manage an institute of hydrotherapy for the treatment of the nervous disorders.

Fifty seven years after Landry's article was published, Guillain, Barré and Strohl[3], in 1916, described a condition similar to that of Landry, with two distinctive features: 1) better prognosis, 2) unique cerebrospinal fluid findings of increased protein with no increase in cells. Their paper described two French soldiers whose clinical picture was similar and consisted of (1) motor difficulties, (2) areflexia, (3) preservation of cutaneous reflexes, (4) paresthesias with slight impairment of objective sensations, (5) muscle tenderness, (6) slight alteration in nerve conduction, (7) remarkable increase in CSF albumin in the absence of cellular reaction (albuminocytologic dissociation). Their paper was published in the Bulletin of the Society of Medicine of the Hospital of Paris. The motivation for performing a spinal tap in these two patients is uncertain. It is believed, however, that the authors performed a spinal tap either to rule out an infectious process, or because spinal taps were fashionable[5] having been described by Quincke 25 years earlier, in 1891. In spite of the similarity to what Landry described earlier, no mention of Landry is to be found in Guillain, Barré, and Strohl 1916 article. Guillain even resisted identifying his cases with those of Landry's claiming that "His disease" was benign whereas Landry's had a poor outcome. In an article published in 1919[6] Guillain and Barré referred to Landry's–type paralysis when they reported a fatal case of acute polyneuritis with albuminocytologic dissociation after typhoid vaccination. Subsequent publications on this syndrome did not include the name of Strohl. There are different versions of why Strohl's name was dropped from such publications, they include the fact that he was a radiologist with broad ranging medical interests[7] which made him less credible as a neurologist, his origin from Alsace[8], and his youth[9], having just graduated from medical school.

The clinical picture of what came to be known as the GBS was thus well established in the early part of the twentieth century. In 1978, and in response to demands for more definitive criteria for the diagnosis of GBS following the epidemic of this condition in association with influenza vaccination in the U.S.A, the National Institute of Neurologic Communication Disorders and Stroke (NINCDS) criteria were established[10]. Furthermore, as more cases were reported, variants of the GBS were reported. Variants are classified according to the prevailing modality of clinical picture (pure motor, pure sensory, pure dysautonomia), region affected (bulbar-appendicular), temporal course (relapsing, chronic)[11].

PATHOLOGY

Three landmark papers established the pathology and patho-physiology of GBS. In Landry's original cases[2], the spinal cord was "intact in its entirety and in all its elements. The nerve origins were well-formed. The gray and white matter were histologically normal". The focus on spinal cord and peripheral nerve

pathology characterized pathologic reports from the 1860's through 1880's, when it was established that GBS is definitely a neuropathy[12]. Further studies characterized the neuropathy as an inflammatory one. Studies out of Europe appearing in the French and German literature between 1930 and 1966 recognized the inflammatory nature of the pathology. In contrast, studies in the USA between 1936 and 1949 emphasized the edematous nature of nerve pathology[13]. In their classic paper published in 1949, Haymaker and Kernohan[14] proposed that nerve edema led to myelin sheath breakdown, that lymphocytic infiltration was a late occurrence as part of a reparative process. In 1955, Waksman and Adams[15] reported on an experimental model of GBS, experimental allergic neuritis (EAN), in which they emphasized the inflammatory nature of the pathology. They described perivascular infiltrates of mononuclear cells in nerve roots, spinal and peripheral nerves and suggested that this reaction was an autoimmune response to myelin products. Waksman and Adams[15] originally produced EAN by the injection of whole nerve extracts. Subsequently EAN has been produced by the injection of peripheral myelin, one of the myelin basic proteins (P2), peptides of P2, as well as galactocerebroside component of peripheral nerve myelin. In 1969, Asbury[16] reported that as in EAN, human nerve pathology in the GBS was characterized by perivascular (perivenular) monocular inflammatory infiltrate and adjacent segmental demyelination, and that contrary to Haymaker and Kernohan[14] observations, edema of the nerve root was not a major feature of the pathology; furthermore, they reported widespread distribution of inflammatory infiltrates including the nerve roots, sensory ganglia, cranial nerves, plexus and peripheral nerves.

In spite of the delineation of pathology in the GBS, the exact immune mechanism leading to demyelination is not yet well established. It is however believed that GBS is induced by both cell-mediated and antibody-mediated immune responses (cellular and humoral), and that the two responses are interdependent.

TREATMENT

Treatment of the original cases of Landry[2] consisted of massages with volatile liniments (turpentine, quinine), electric stimulation and substantial nourishment. Guillain[17] later prescribed antiseptic remedies, rubs with colloidal silver, electrotherapy, warm baths and irradiation. He felt that arsenicals were contraindicated. The mainstay of current therapy consists of supportive care(management of airway and respiratory infection, maintaining fluid and salt balance, safeguarding blood pressure and cardiovascular function, adequate nourishment, prevention and treatment of bed sores, dealing with anxiety, anger and depression, and effective rehabilitation). The importance of attending to the psychological aspects of the illness is brought out in personal accounts of GBS written by physicians[18-20] afflicted by the disorder. Until recently, the only proven method of therapy was plasmapheresis. The first report on the use of plasmapheresis came out of Hammersmith Hospital in 1978[21]. The beneficial effect of plasmapheresis was confirmed by the Guillain-Barré Study Group in the USA in 1985[22], and the French Cooperative Study in 1987[23]. Besides confirming the Guillain-Barré Study Group findings, the French Cooperative study showed no benefit of fresh plasma over albumin solution. Plasmapheresis was shown to be particularly effective when given early in the disease and in severely affected patients. Beneficial effects include shorter duration on the respirator, shorter recovery time, and greater overall improvement. In contrast to plasmapheresis, steroids in conventional doses have no place in drug therapy[24]. There are anecdotal reports of benefit with high dose intravenous steroid therapy. Possible adverse effects of the use of steroids such as increased incidence of recurrent disease have been reported[24]. Although cytotoxic drugs have been used, there are not enough controlled data on their usefulness. Reports on the use of polyunsaturated fatty acid diet are

anecdotal[25]. Such diets presumably act by inhibiting in vitro lymphocyte function. Intravenous immunoglobulins are recent additions to drug therapy. They were first used in the treatment of chronic inflammatory demyelinating polyneuropathy in 1987[26] and in GBS one year later in 1988[27]. A randomized trial[28] comparing intravenous immune globulin and plasma exchange showed that intravenous immune globulin is at least as effective as, and may be superior, to plasma exchange. The exact mechanism of intravenous immunoglobulin action in GBS has not been established with certainty. Possible mechanisms of action include a non-specific effect on natural killer cells, induction of higher activity of non-specific T-suppressor lymphocytes, inhibition of macrophages, and inhibition of antibody production[29]. The use of protein-A immunoadsorption (PAIA) has been recently reported in two patients with good results[30]. PAIA presumably allows selective removal of immunoglobulins from plasma. The use of two other modes of therapy[31,32] (cyclo-oxygenase inhibitors, and oxygen radical scavengers) has been limited to experimental animal models of GBS.

OUTCOME

The generally good prognosis emphasized by Guillain, Barré and Strohl in their original contribution has been confirmed in subsequent reports. In spite of the expected good outcome, approximately 3-6% of patients die and about 10-15% are left with permanent deficits. Of the many predictors of poor outcome reported in the literature, the following have been confirmed in several studies: fibrillation potentials on EMG early in the disease process, marked early reduction in compound muscle action potentials (CMAP), plateau period of more than ten days before the beginning of clinical improvement, and the need for ventilator support.

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