Diplegia facciale post vaccino COVID-19

Caterina Francesca Bagella

UOC Neurologia, Azienda Ospedaliero-Universitaria Sassari

SARS-CoV-2 (COVID-19) Pandemic

- Coronavirus cases 2021-10-04 (www.worldometers.info/coronavirus/)

Coronavirus Cases:

236,006,818

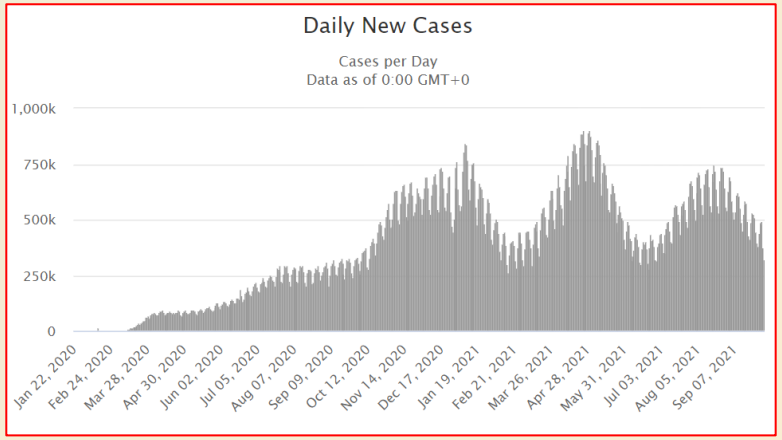
view by country

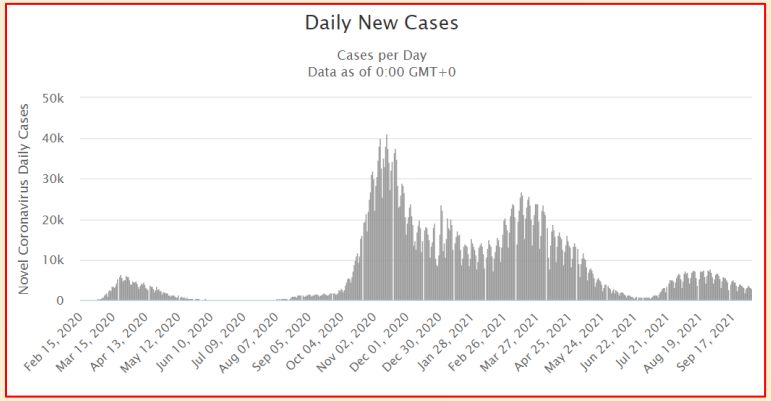
Deaths:

4,819,962

Recovered:

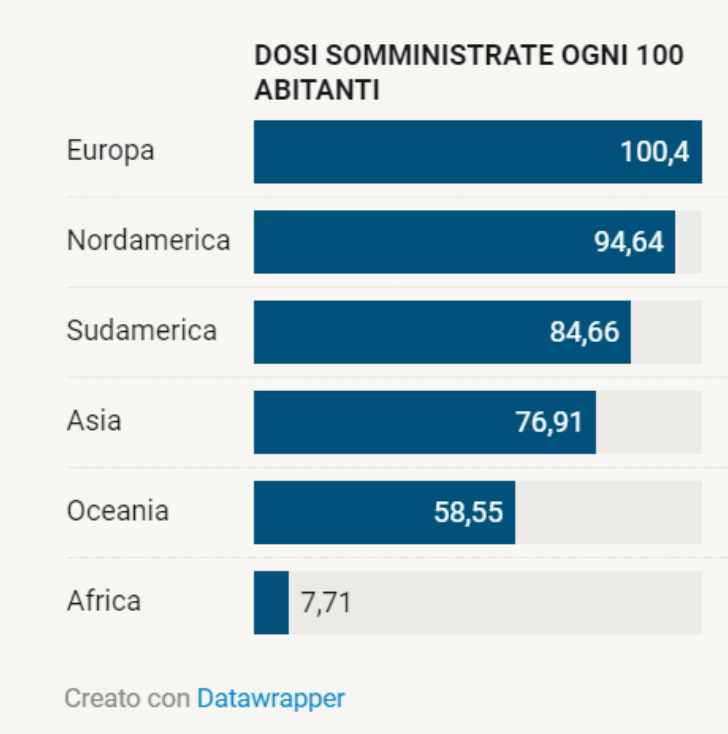
213,002,194

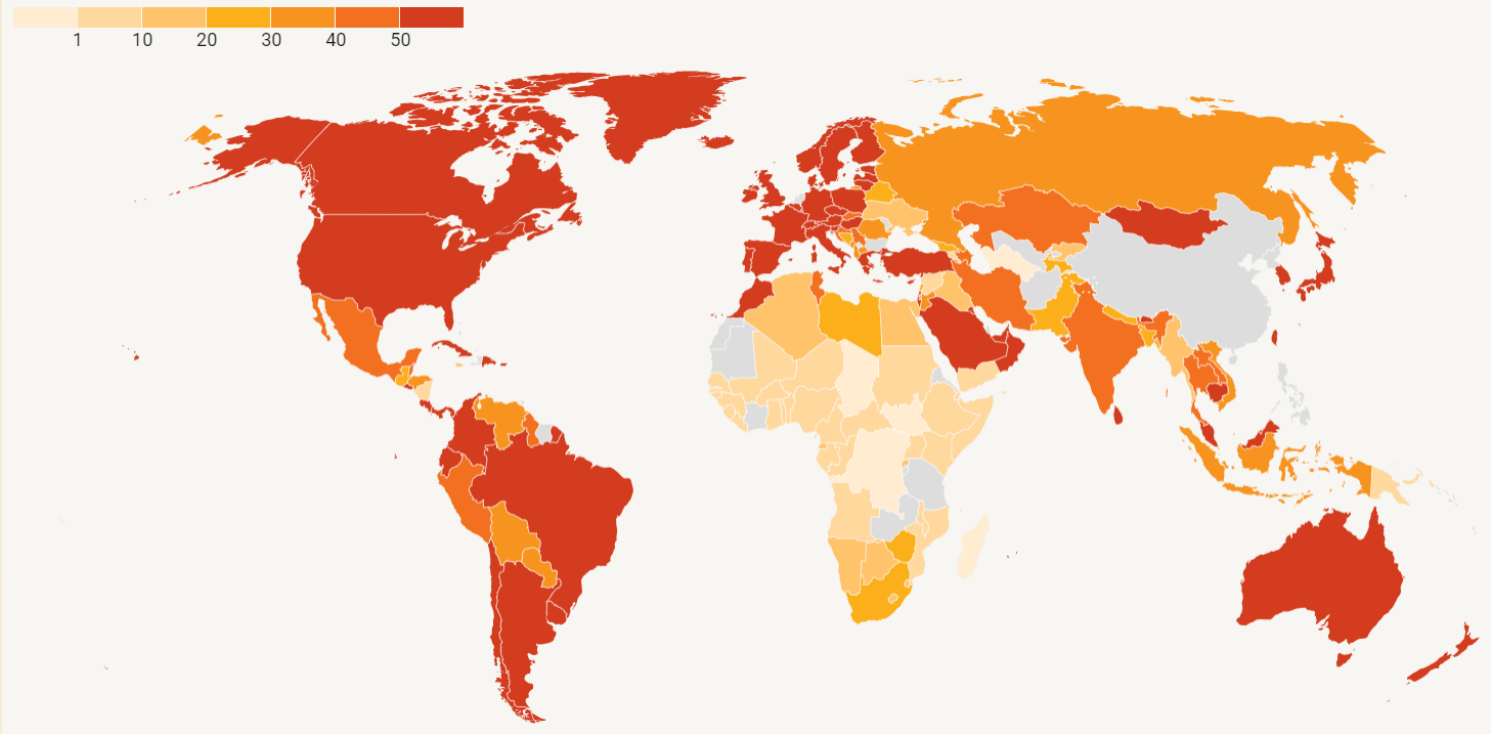




COVID-19 Vaccination (lab24.ilsole24ore.com/vaccinazioni-mondo/)

- 6.335.400.500 doses administered to date

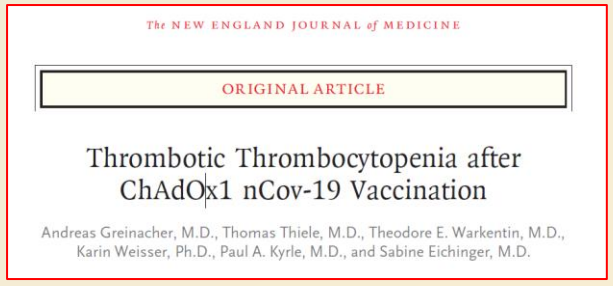




Adverse Event Following Immunization

- «Un evento avverso che segue la vaccinazione è un qualsiasi episodio sfavorevole di natura medica che si verifica dopo la somministrazione di un vaccino (relazione temporale), ma che non necessariamente è causato dalla vaccinazione (relazione causale)» (www.aifa.gov.it)

- *"It is therefore inevitable that many thousands of sporadic cases of GBS caused by other factors will appear temporally associated with COVID-19 vaccination. But, as any statistician can confirm, this cannot be considered causal"* (Lunn et. al. 2020)


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination

Andreas Greinacher, M.D., Thomas Thiele, M.D., Theodore E. Warkentin, M.D., Karin Weisser, Ph.D., Paul A. Kyrle, M.D., and Sabine Eichinger, M.D.

COVID-19 vaccine and Guillain-Barré syndrome: let's not leap to associations

Patient 1, male, 49 years

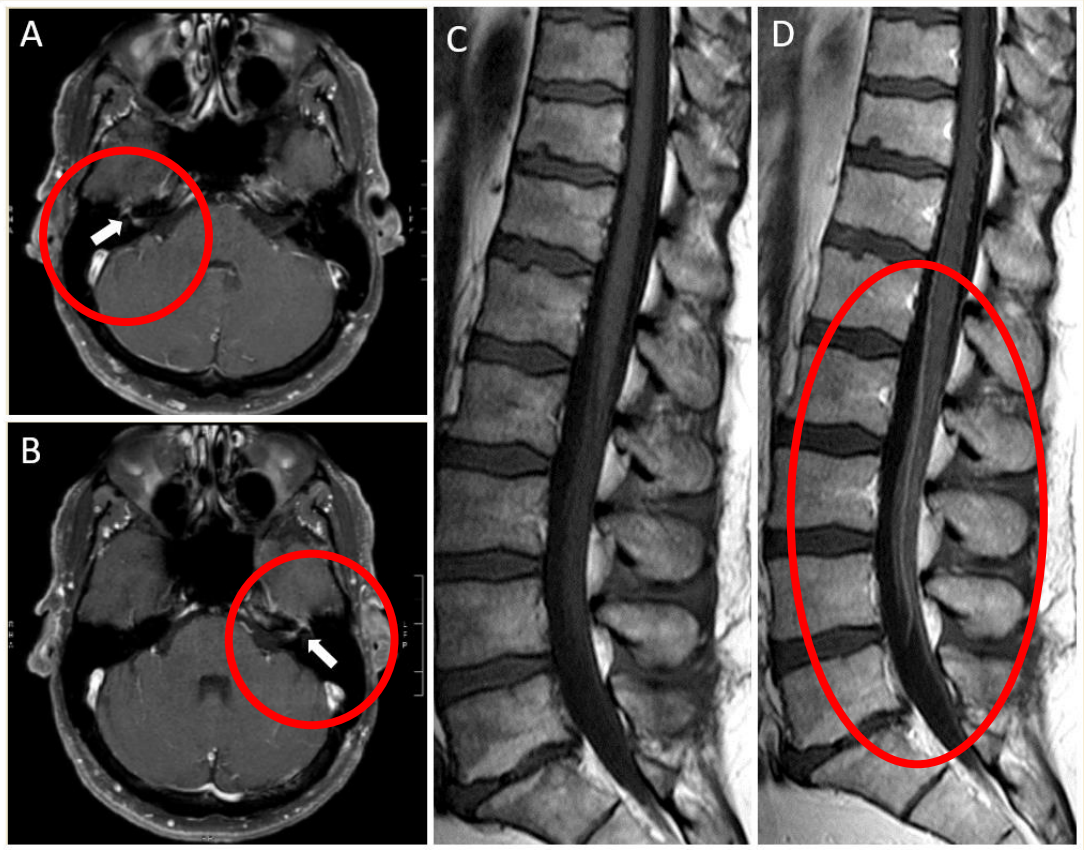
- A 49-year-old man who presented asymmetric bilateral facial weakness, and paresthesias in the tongue and face.
  - Sixteen days before symptoms onset he received the first dose of ChAdOx1 nCoV-19 vaccine. He denied infections within the prior month.
- Neurologic examination showed severe bilateral facial paresis, more prominent on the right, and lower limbs areflexia

Two days after onset

Investigations

- Blood investigations
  - All normal (including vasculitis screen, HIV serology, hepatitis screen and syphilis serology all negative)
  - COVID-19 swab: negative at presentation and throughout patient's inpatient stay
  - Serum search for ganglioside autoantibodies negative, including anti-GQ1b, anti-GD1b and anti-GM1 antibodies.
- Cerebrospinal fluid: elevated proteins (110 mg/dl; normal range <45 mg/dl) without pleocytosis and absence of intrathecal IgG synthesis

MRI of the lower thoracic spinal cord



- Axial post-gadolinium T1-weighted images of the brain showing enhancement of the right (A, arrow) and left (B, arrow) facial nerves.
- Sagittal T1-weighted images before (C) and after (D) gadolinium administration showing diffuse enhancement of the cauda equina and lower thoracic nerve roots.

Neurophysiology

- Nerve conduction studies: normal
- Blink reflex test displayed bilateral involvement of the motor efferent pathway, while the remaining of the EMG study was normal

	R1 (ms)	R2 Ipsilateral (ms)	R2 Contralateral (ms)
Left stimulation	**12.0**	**32.9**	**Absent**
Right stimulation	**Absent**	**Absent**	**34.4**
Normal values	**12.1**	**38**	**40**

Treatment

- Intravenous immunoglobulins (IVIg; 0.4 g/kg/die for 5 days)
  - Initiated 3 days after symptoms onset
  - Mild improvement of the bifacial paresis, and resolution of the hypoesthesia

Guillain–Barré and Miller Fisher syndromes classification (Wakerley et al. 2014)

- Bifacial weakness with paraesthesias
  - Facial weakness and limb areflexia/hyporeflexia
  - Absence of ophthalmoplegia, ataxia and limb weakness
  - In some patients, limb paraesthesias may be absent and muscle stretch reflexes may be normal
  - Electrophysiological evidence of neuropathy
  - ~20% of GBS

Table 1 | Clinical features of GBS, MFS and their subtypes

Category	Clinical features		
	Pattern of weakness	Ataxia	Hypersomnolence
GBS			
Classic GBS	Four limbs	No or minimal	No
Pharyngeal–cervical–brachial weakness*	Bulbar, cervical and upper limbs	No	No
Acute pharyngeal weakness‡	Bulbar	No	No
Paraparetic GBS*	Lower limbs	No	No
Bifacial weakness with paraesthesias*	Facial	No	No
MFS			
Classic MFS	Ophthalmoplegia	Yes	No
Acute ophthalmoparesis§	Ophthalmoplegia	No	No
Acute ataxic neuropathy§	No weakness	Yes	No
Acute ptosis§	Ptosis	No	No
Acute mydriasis§	Paralytic mydriasis	No	No
BBE‖	Ophthalmoplegia	Yes	Yes
Acute ataxic hypersomnolence¶	No weakness	Yes	Yes

*Localized subtypes of GBS. ‡Incomplete form of pharyngeal–cervical–brachial weakness. §Incomplete forms of MFS. ‖CNS subtype of MFS. ¶Incomplete form of BBE. Abbreviations: BBE, Bickerstaff brainstem encephalitis; GBS, Guillain–Barré syndrome; MFS, Miller Fisher syndrome.

Follow up (two months after onset)

- Approximately two months after presentation his symptoms worsened with painful paresthesias and progressive weakness of the lower limbs, more prominent during right foot dorsiflexion (4-/5 MRC)

Neurophysiology

- ENG showed reduced nerve conduction velocities also in the lower limbs
  - Diagnosis of chronic inflammatory demyelinating polyneuropathy was made according to established criteria
    - Definite, typical CIDP (Van den Bergh et al. 2021)
  - He received a second cycle of IVIg with improvement of paresthesias.

Nerve	VC M(m/s)	Amplitude (mV)
Median right	31.3	3.7
Median left	31.3	6.4
Peroneal right	34.8	2.2
Peroneal left	32	4.1

Patient 2, male, 55 years

- Bifacial paresis and absent ankle reflexes, 22 days after he received the first dose of ChAdOx1 nCoV-19 vaccine
  - Blink reflex: delay of all potentials (R1i, R2i, R2c) with both stimulating sides
  - ENG: absence of demyelinating/axonal neuropathy at upper and lower extremities
  - Cerebrospinal fluid: Protein: 270 mg/dL; Cells: 22/mL;
  - Brain MRI: Enhancement of facial nerves
- Treatment with IVIg 0.4 g/kg/die for 5 days
  - Stabilized after two weeks

Available main case series

Study	N	Clinical features	Vaccine	Response to treatment
Allen et al. 2021 Ann Neurol	4	GBS with bifacial weakness with paresthesia	ChAdOx1-S/nCoV-19 (3 weeks)	Stabilized after Prednisolone or IVIg
Maramattom et al 2021 Ann Neurol	7	Severe GBS with facial diplegia or bifacial weakness	ChAdOx1-S/nCoV-19 (2 weeks)	Still hospitalized after IVIg
Bonifacio et al. 2021 JNNP	5	Severe GBS with facial diplegia and paresthesia	ChAdOx1-S/nCoV-19 (1-1.5 weeks)	Favourable prognosis after IVIg

Vaccines and Guillain-Barre´ Syndrome

- "... with rare exceptions, associations between vaccines and GBS have been only temporal. There is little evidence to support a causal association with most vaccines" (Haber et al. 2009)
- It is inevitable that many thousands of sporadic cases of GBS caused by other factors will appear temporally associated with COVID-19 vaccination (Lunn et al. 2020)
  - Guillain-Barrè syndrome is infrequent among recipients of the BNT162b2 mRNA COVID-19 vaccine
    - Incidence of 0.18/100,000 administered doses during a timeframe of 30 days (García-Grimshaw et al. 2021)
    - In a cohort of 702 patients with history of GBS, only 1 needed short medical care for relapse of previous syndrome (Shapiro Ben David et al. 2021)

Conclusions

- Bifacial weakness and paresthesias is a specific form of GBS, which has been described in rare cases in association with COVID-19 vaccination
  - ChAdOx1-S/nCoV-19 is reported in most cases
  - The phenotype suggests a pattern associated with the vaccination
- The frequency of GBS was reported to be 1.4- to 10-fold higher than that expected (Maramattom et al. 2021)
- The syndrome could result from the generation of host antibodies against peripheral myelin (Allen et. 2021)
  - Direct response to the SARS-CoV-2 spike protein?
  - Less specific immune response, to other components of the vector?

Grazie per l'attenzione…